



Relationships Between Reproductive History and Mortality From Cardiovascular Diseases Among Japanese Women: The Japan Collaborative Cohort Study for Evaluation of Cancer Risk (JACC) Study

Kanami Tanigawa¹, Satoyo Ikehara¹, Takashi Kimura², Hironori Imano¹, Isao Muraki¹, Kokoro Shirai¹, Akiko Tamakoshi², Hiroyasu Iso^{1,3}; JACC study group

¹Public Health, Department of Social Medicine, Osaka University Graduate School of Medicine, Osaka, Japan

²Faculty of Medicine, Hokkaido University, Hokkaido, Japan

³Department of Public Health Medicine, Faculty of Medicine, University of Tsukuba, Ibaraki, Japan

Received February 20, 2019; accepted October 2, 2019; released online November 16, 2019

ABSTRACT

Background: Reproductive history has been addressed as a risk factor for cardiovascular disease (CVD). We examined the relationship between reproductive history and CVD mortality in Japanese women.

Methods: We followed 53,836 women without previous CVD or cancer history from 1988–1990 to 2009 in a prospective cohort study. Hazard ratios (HRs) and 95% confidence intervals (CIs) of CVD mortality were estimated according to the number of deliveries and maternal age at first delivery.

Results: During the follow-up, 2,982 CVD-related deaths were identified. There was U-shaped association between the number of deliveries and risk of CVD mortality with reference to three deliveries, although the excess risk of CVD mortality associated with ≥ 5 deliveries was of borderline statistical significance. The corresponding multivariable HRs were 1.33 (95% CI, 1.12–1.58) and 1.11 (95% CI, 0.99–1.24). In addition, higher CVD mortality was associated with maternal age ≥ 28 years at first delivery than maternal age of 24–27 years at first delivery. The multivariable HRs were 1.22 (95% CI, 1.10–1.36) for 28–31 years at first delivery and 1.26 (95% CI, 1.04–1.52) for ≥ 32 years at first delivery. Moreover, among women with ≥ 3 deliveries, maternal age ≥ 28 years at first delivery was associated with 1.2- to 1.5-fold increased CVD mortality.

Conclusion: The number of deliveries showed a U-shaped association with risk of CVD mortality. Higher maternal age at first delivery was associated with an increased risk of CVD mortality, and excessive risk in women aged ≥ 28 years at first delivery was noted in those with ≥ 3 deliveries.

Key words: maternal age; parity; cardiovascular diseases; mortality; prospective studies

Copyright © 2019 Kanami Tanigawa et al. This is an open access article distributed under the terms of Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death and disability in the world, and 17.9 million deaths due to CVD occurred worldwide in 2016.¹ The latest guidelines on CVD prevention in women from the American Heart Association have indicated that reproductive history related to pregnancy should be taken account to identify high-risk women for CVD.² The reproductive history related to pregnancy, such as the number of deliveries and maternal age at first delivery, is related to lifetime experiences of large hormonal changes during pregnancy, which may affect metabolic profiles during and after pregnancy and subsequent risk of CVD. However, the association between reproductive history and risk of CVD remains controversial. Some prospective cohort studies have shown a U-shaped relationship between the number of deliveries and risks of CVD

incidence³ and CVD mortality.^{4–8} However, other studies have found positive association with risks of CVD incidence^{9,10} and CVD mortality,¹¹ inverse association with risk of CVD mortality,¹² and no association with risk of CVD mortality.^{13,14} In addition to the association with the number of deliveries, a number of prospective cohort studies have shown that early maternal age at first delivery was a risk factor for risk of CVD mortality,^{4,14–16} but other studies showed no inverse association between maternal age at first delivery and risk of CVD mortality.^{15–17} The higher maternal age at first delivery was associated with risk of mortality from subarachnoid hemorrhage¹⁸ and incidence of coronary heart disease (CHD).¹⁹

Between 1945 and 2017, total fertility rate (TFR) has rapidly decreased and maternal age at first delivery has increased in Japan. Now, Japan is one of the countries with the lowest TFR (1.43 in 2017) and the highest maternal age at first delivery (30.7

Address for correspondence. Hiroyasu Iso, Public Health, Department of Social Medicine, Osaka University Graduate School of Medicine, 2-2 Yamadaoka, Suita, Osaka 565-0871, Japan (e-mail: iso@pbhel.med.osaka-u.ac.jp).



Received May 10, 2019; accepted August 28, 2019; released online December 14, 2019

Diabetes and mortality from respiratory diseases: the Japan Collaborative Cohort Study

Running title: Diabetes and mortality from respiratory diseases

Mengying Wang¹, Isao Muraki², Keyang Liu², Kokoro Shirai², Akiko Tamakoshi³,
Yonghua Hu¹, Hiroyasu Iso^{2*}

¹ School of Public Health, Peking University, Beijing, China

² Public Health, Department of Social Medicine, Osaka University Graduate School of
Medicine, Osaka, Japan

³ Department of Public Health, Faculty of Medicine Hokkaido University, Sapporo,
Japan

Corresponding to:

Hiroyasu Iso, PhD, Professor, Public Health, Department of Social Medicine, Osaka
University Graduate School of Medicine, Osaka, Japan.

E-mail: iso@pbhel.med.osaka-u.ac.jp

Number of tables: 5

Abstract

Background: A little evidence was found about the association between diabetes and respiratory diseases mortality among Japanese populations. We aimed to explore the association between diabetes and the risk of respiratory diseases mortality through a nationwide prospective study in Japan.

Methods: 95,056 participants (39,925 men and 55,131 women) were followed up for median 17.1 years. The information about diabetes status, sociodemographic characteristics, and lifestyles was collected at baseline. Cox proportional hazards regression models were used to estimate hazard ratios (HRs) of mortality from respiratory diseases associated with baseline diabetes status.

Results: We identified 2,838 deaths from total respiratory diseases (1,759 respiratory infection, 432 chronic obstructive pulmonary disease, and 647 other respiratory diseases). The association between diabetes and total respiratory diseases mortality was statistically significant among women (HR=1.81, 95% CI, 1.39-2.37) but of borderline statistical significance in men (P for interaction<0.01). Besides, there were significant associations between diabetes and mortality from respiratory infection among both men and women (HR=1.39, 95% CI, 1.10-1.76; HR=2.30, 95% CI, 1.71-3.11; P for interaction<0.001). However, we failed to detect any statistically significant association between diabetes and COPD mortality. Moreover, the subgroup analysis revealed that the association between diabetes and total respiratory diseases mortality was stronger in never smokers when compared with ever smokers (P for interaction=0.02).

Conclusions: Significant association was observed between diabetes and the risk of total respiratory diseases mortality in particular from respiratory infection. Prevention and control of respiratory diseases, especially respiratory infection should be paid more attention among people with diabetes in clinical and public health practice.

Key words: Diabetes; Mortality; Respiratory diseases; Cohort studies



Received November 13, 2019; accepted December 2, 2019; released online December 27, 2019

Alcohol consumption and risk of gastric cancer: The Japan Collaborative

Cohort study

Yuting LI¹, Ehab S. Eshak^{1,2}, Shirai Kokoro¹, Keyang Liu¹, Dong JY¹, Hiroyasu Iso¹,
Akiko Tamakoshi³ and JACC Study Group

¹Public Health, Department of Social Medicine, Osaka University Graduate School of
Medicine, Osaka, Japan

²Department of Public Health and Community Medicine Department, Faculty of
Medicine, Minia University, Minia, Egypt

³Department of Public Health, Hokkaido University Graduate School of Medicine,
Sapporo

Running title: Alcohol consumption and risk of gastric cancer

Number of figures and tables: 3 tables and 2 supplement tables

Word count: 233 words (abstract), 3,260 words (text)

Number of Reference: 51

Correspondence: Hiroyasu Iso, MD, Ph.D, MPH, Professor of Public Health,
Department of Social Medicine, Osaka University Graduate School of Medicine,
Suita-shi, Osaka 565-0871, Japan.

Phone: +81-6-6879-3911; Fax: +81-6-6879-3919; E-mail: iso@pbhel.med.osaka-
u.ac.jp

1 **ABSTRACT**

2 **Background:** Alcohol consumption is a potential risk factor for gastric cancer.

3 However, findings from cohort studies that examined the relationship between alcohol
4 consumption and gastric cancer risk among Japanese population are not conclusive.

5 **Methods:** A total of 54,682 Japanese men and women participating in the Japan
6 Collaborative Cohort study completed a questionnaire including alcohol consumption
7 information. The Cox proportional hazard model was used to calculate the hazard
8 ratios (HRs) and 95% confidence intervals (CIs).

9 **Results:** After a median 13.4-year follow-up, we documented 801 men and 466
10 women incident cases of gastric cancer. Alcohol consumption was associated with
11 increased risk of gastric cancer among men (HRs in ex-drinkers and current alcohol
12 consumption of <23g, 23-<46g, 46-<69g and \geq 69g/d categories versus never drinkers
13 were 1.82; 95% CI, 1.38-2.42, 1.41; 95% CI, 1.10-1.80, 1.47; 95% CI, 1.17-1.85,
14 1.88; 95% CI, 1.48-2.38 and 1.85; 95% CI, 1.35-2.53, respectively, and that for 10g
15 increment of alcohol consumption after excluding ex-drinkers was 1.07; 95% CI,
16 1.04-1.10). The association in men were observed for cardia and non-cardia gastric
17 cancer (HRs in the highest alcohol consumption category versus never drinkers were
18 9.96; 95% CI, 2.22-44.67 for cardia cancer, and 2.40; 95% CI, 1.64-3.52 for non-
19 cardia cancer). However, no such trend was observed in women.

20 **Conclusions:** Alcohol consumption is associated with increased risk of gastric cancer
21 among Japanese men, regardless of anatomical subsite of the cancer.



The association of conventionally medicated systolic and diastolic blood pressure level and mortality from cardiovascular disease: is the lower the better in high stroke population?

Ryoto Sakaniwa^{1,2} · Jasper Tromp^{2,3,4} · Kokoro Shirai¹ · Kazumasa Yamagishi⁵ · Akiko Tamakoshi⁶ · Hiroyasu Iso^{1,5}

Received: 10 September 2019 / Accepted: 2 December 2019
© Springer-Verlag GmbH Germany, part of Springer Nature 2020

Keywords Hypertension · Conventional blood pressure · Cardiovascular disease · Coronary heart disease · Stroke

Sirs:

Hypertension has become majority morbidity and a leading factors for the cardiovascular disease mortalities in the current society [1, 2]. While hypertensive managements has improved since the twentieth century [3], the optimal blood pressure (BP) among hypertensive patients remains in question. The new American Heart Association/American College of Cardiology (AHA/ACC) guidelines suggest health benefit for systolic blood pressure (SBP) below 130 mmHg and diastolic blood pressure (DBP) below 80 mmHg [4]. It remains unclear whether this is also favorable for Asian and East-European population where, in contrast to Western countries, mortality from stroke has been higher than that from coronary heart disease (CHD) [2]. We recently

examined an association of the combined category of SBP/DBP with mortality from cardiovascular disease (CVD); the results showed J-curved CVD mortality association among the participants with ongoing antihypertensive treatment but not normotensive participants [5]. However, the individual impact of SBP and DBP on CVD mortality among treated patients for hypertension has not been examined.

We performed an analysis of 10,061 individuals from the Japan Collaborative Cohort (JACC) Study, from 1988 to 1990 at baseline [6], who were on current antihypertensive medication and without history of CVD or cancer, from 45 communities across Japan where recorded mortality from stroke has been higher than from CHD. Informed consent was obtained from participants or community leaders. The ethics committees of the Nagoya University and Osaka University approved the protocol of this investigation. Our primary aim of study was to investigate the conventionally medicated BPs on CVD outcomes. Then, the medicated BP level was assessed by self-report questionnaire. SBP and DBP were categorized into five groups: for SBP (< 130, 130–139, 140–149, 150–159, and \geq 160 mmHg) and DBP (< 70, 70–79, 80–89, 90–99, and \geq 100 mmHg). Mortality data were centralized at the Ministry of Health and Welfare, and the underlying causes of death were coded according to the International Statistical Classification of Diseases-10th edition. Participants who died after removal from their original communities were treated as censored cases until the end of 2009. The mortality was categorized as total CVD (I01–I99), stroke (I60–I69), and CHD (I20–I25). The validity of self-BP report was examined with assessed BP at health check-up in 2678/10,061 participants. Baseline characteristics were examined for each of SBP and DBP groups. Normal distribution is displayed as mean or percentage and skewed data as median. The differences between the groups were calculated using one-way analysis of covariance,

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s00392-019-01587-8>) contains supplementary material, which is available to authorized users.

✉ Hiroyasu Iso
iso@pbhel.med.osaka-u.ac.jp

¹ Public Health, Department of Social Medicine, Osaka University Graduate School of Medicine, 2-2 Yamadaoka, Suita, Osaka 565-0871, Japan

² Department of Cardiology, University Medical Centre Groningen, University of Groningen, Groningen, The Netherlands

³ National Heart Centre Singapore, Singapore, Singapore

⁴ Duke-NUS Medical School, Singapore, Singapore

⁵ Department of Public Health Medicine, Faculty of Medicine, and Health Services Research and Development Center, University of Tsukuba, Tsukuba, Japan

⁶ Department of Public Health, Hokkaido University Graduate School of Medicine, Sapporo, Japan

Preventive Effect of Oral Self-Care on Pneumonia Death among the Elderly with Tooth Loss: The Ohsaki Cohort 2006 Study

Kaoru Manabe,^{1,*} Fumiya Tanji,^{1,*} Yasutake Tomata,¹ Shu Zhang¹ and Ichiro Tsuji¹

¹Division of Epidemiology, Department of Health Informatics and Public Health, Tohoku University School of Public Health, Graduate School of Medicine, Sendai, Miyagi, Japan

Tooth loss is a risk factor for pneumonia mortality, but it is unclear whether oral care negates excess mortality due to pneumonia among community-dwelling elderly with tooth loss. The purpose of this study was to examine the influence of oral care on the association between the number of remaining teeth and the risk of pneumonia death. We analyzed for 18,098 individuals (aged ≥ 65 years) participating in a prospective cohort study. In a 2006 baseline survey, the following data were collected: the number of remaining teeth, oral care, history of disease, smoking, alcohol drinking, education level and so forth. We also obtained data on dates and causes of death between 2006 and 2014. The primary outcome was mortality due to pneumonia. Compared with those having ≥ 20 teeth, the risk of pneumonia mortality was increased among participants having 10-19 or 0-9 teeth; the multivariate hazard ratios (HRs) (95% confidence intervals [CI]) were 1.45 (1.03-2.04) and 1.38 (1.01-1.87), respectively. Among those having 0-9 teeth, a significantly increased risk of mortality due to pneumonia was disappeared for those who brushed their teeth ≥ 2 times per day, for those with visiting a dentist, and for those with use of denture, whereas the risk persisted among those who brushed their teeth ≤ 2 times per day, for those without visiting a dentist, and for those without use of denture. Tooth-brushing, visiting a dentist or use of denture may negate the increased risk of pneumonia death among the elderly with tooth loss.

Keywords: cohort study; mortality; oral care; pneumonia; tooth loss

Tohoku J. Exp. Med., 2019 April, 247 (4), 251-257. © 2019 Tohoku University Medical Press

Introduction

With the aging of the Japanese population, the rate of mortality due to pneumonia has been increasing rapidly. Since 2011, pneumonia has ranked third highest among causes of death in Japan. In 2016, about 119,000 people died of pneumonia, accounting for 9.1% of all deaths. In addition, over 95% of deaths due to pneumonia were in individuals over 65 years old (Ministry of Health, Labour and Welfare in Japan 2017).

Accordingly, various measures to prevent pneumonia are being considered. Recently, in this context, interest in the importance of oral health has been growing. The “Stop Pneumonia Campaign” launched by the Japanese Respiratory Society has emphasized oral care offered by health care workers as a preventive measure against pneumonia (The Japanese Respirator Society 2014). The World Health Organization has indicated that oral health is particularly important in disadvantaged older people and that avoiding tooth loss is crucial for healthy ageing (World

Health Organization 2015).

Tooth loss is known to be a risk factor for not only mortality (Abnet et al. 2005; Holm-Pedersen et al. 2008) but also incident functional disability (Bando et al. 2017) and dementia (Takeuchi et al. 2017) among community-dwelling elderly. In addition, it has been reported that tooth loss is a risk factor for morbidity (Azarpazhooh and Leake 2006) and mortality due to pneumonia (Aida et al. 2011; Suma et al. 2018). Suma et al. (2018) have reported that the multivariate-adjusted hazard ratio was 2.07 (95% CI, 1.09-3.95) for edentulous individuals and 1.60 (95% CI, 0.83-3.10) for loss of 15-27 teeth relative to loss of 0-14 teeth (P trend = 0.026).

A randomized controlled trial by Yoneyama et al. (1999) has proved that oral care lowers the risk of pneumonia among institutionalized elderly: the relative risk of developing pneumonia in individuals with no active oral care was 1.67 (95% CI, 1.01-2.75 P = 0.04) in comparison with oral care such as tooth cleaning and visiting a dentist.

However, it is still unclear whether oral care negates

Received February 20, 2019; revised and accepted April 2, 2019. Published online April 17, 2019; doi: 10.1620/tjem.247.251.

*These two authors contributed equally to this work.

Correspondence: Ichiro Tsuji, Division of Epidemiology, Department of Health Informatics and Public Health, Tohoku University School of Public Health, Graduate School of Medicine, 2-1 Seiryomachi, Aoba-ku, Sendai, Miyagi 980-8575, Japan.

e-mail: tsuji1@med.tohoku.ac.jp



Contents lists available at ScienceDirect

Journal of Psychiatric Research

journal homepage: www.elsevier.com/locate/jpsychires

The association between emotional and instrumental social support and risk of suicide death: A population-based cohort study



Tatsui Otsuka^{a,b}, Yasutake Tomata^{a,*}, Shu Zhang^a, Fumiya Tanji^a, Yumi Sugawara^a, Ichiro Tsuji^a

^a Division of Epidemiology, Department of Health Informatics and Public Health, Tohoku University School of Public Health, Graduate School of Medicine, Sendai, Japan

^b Child and Adolescent Psychiatry, Miyagi Psychiatric Center, Natori, Japan

ARTICLE INFO

Keywords:

Suicide
Social support
Emotional
Instrumental
Cohort study

ABSTRACT

Suicide is an important public health issue and previous studies have suggested that social support can one preventive factor. However, the association between emotional and instrumental social support and suicide death has not been investigated in detail. The purpose of this study was to investigate the association between each type of social support and suicide death based on a population-based cohort study. We analyzed follow-up data for 47,223 subjects (aged ≥ 40 y) participating in a community-based, prospective cohort study. At the baseline, the subjects were asked five questions about social support. The end point of the study was suicide mortality, based on data from the National Vital Statistics. The Cox model was used to estimate the multivariate-adjusted hazard ratios of suicide death. In addition, stratified analysis was conducted to test the interaction of each type of social support with gender (male/female) and age ($< 65/\geq 65$ y) separately. Among 320,880 person-years of follow-up, 90 cases of suicide death were documented. There were significant association between instrumental social support and lower risk of suicide death, and the hazard ratio was 0.60 (95% CI: 0.38–0.94). Emotional social support was also associated with a lower risk of suicide death, but not to a significant degree, and the hazard ratio was 0.70 (95% CI: 0.42–1.17). It is suggested that instrumental social support was significantly associated with a lower risk of suicide death, and emotional social support tended to be associated with a lower risk of suicide death.

1. Introduction

Suicide is an important public health issue. In 2015, there were an estimated 788,000 suicide deaths worldwide and an annual global age-standardized suicide rate of 10.7 per 100,000 population. As suicide deaths are preventable, there is an urgent need for preventive interventions that are effective. According to a report from the WHO (WHO, 2014), risk factors for suicide encompass areas that cover a wide range of systemic, societal, community, relationship (social connectedness to immediate family and friends) and individual factors. Among relationship risk factors, lack of social support has been highlighted as a key target for development of strategies aimed at suicide prevention.

Social support is thought to be a protective factor for mental health. In addition to the direct effect of support, the buffering hypothesis (Cohen and Wills, 1985) has proposed that mobilization of social support to help a person to cope with a stressor can reduce its negative effects on health. A previous study has suggested that the perception of support by recipients is more closely linked to their health and well-being than the objective

behavior involved in such interaction (Wethington and Kessler, 1986). Studies employing a cross-sectional design have examined the association between social support and various forms of suicidal behavior such as attempted suicide (Batterham and Christensen, 2012; Hirsch and Barton, 2011; Miller et al., 2015; Rojas et al., 2017) and suicidal ideation (Awata et al., 2005; Batterham and Christensen, 2012; Beutel et al., 2017; Hirsch and Barton, 2011; Miller et al., 2015; Noguchi et al., 2014; Park et al., 2010), and some employing a longitudinal design have also examined the same issues (Kleiman and Liu, 2013; Mackin et al., 2017; Teismann et al., 2016). Their findings have suggested that social support may be one of the most important factors for suicide prevention. However, the relationship of social support to actual suicide death has not been well studied; to our knowledge only one such study employing a longitudinal design has been reported (Poudel-Tandukar et al., 2011), and the results suggested that social support aimed at boosting self-esteem and confidence could be effective for suicide prevention, particularly in women.

Social support represents the functional content of relationships that can be categorized into four broad types of supportive behavior or

* Corresponding author. Division of Epidemiology, Department of Health Informatics and Public Health, Tohoku University School of Public Health, Graduate School of Medicine, 2-1, Seiryomachi, Aoba-ku, Sendai, Miyagi, 980-8595, Japan.

E-mail address: y-tomata@med.tohoku.ac.jp (Y. Tomata).

<https://doi.org/10.1016/j.jpsychires.2019.04.012>

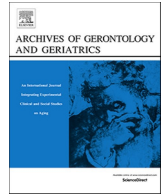
Received 17 November 2018; Received in revised form 21 March 2019; Accepted 16 April 2019

0022-3956/ © 2019 Elsevier Ltd. All rights reserved.



Contents lists available at ScienceDirect

Archives of Gerontology and Geriatrics

journal homepage: www.elsevier.com/locate/archger

Emotional support (giving or receiving) and risk of incident dementia: The Ohsaki Cohort 2006 Study

Yingxu Liu, Shu Zhang*, Yasutake Tomata, Tatsui Otsuka, Dieta Nurriika, Yumi Sugawara, Ichiro Tsuji

Division of Epidemiology, Department of Health Informatics and Public Health, Tohoku University School of Public Health, Graduate School of Medicine

ARTICLE INFO

Keywords:

Emotional support
Dementia
Prospective cohort study

ABSTRACT

Previous studies have suggested that emotional support may promote cognition; however, the effects of giving or receiving emotional support on incident dementia remain unclear. Therefore, we sought to investigate the relationship between emotional support (giving or receiving) and incident dementia. In December 2006, we conducted a prospective cohort study of 31,694 Japanese individuals aged ≥ 65 years who lived in Ohsaki City, Miyagi Prefecture, Japan. A self-reported questionnaire including items on emotional support and lifestyle factors was distributed. After excluding those who did not provide consent or responses to all items, 13,636 eligible responses were analyzed for this study. According to responses of “yes” or “no” for emotional support, we made two categories for both giving (gave or did not give) and receiving (received or did not receive) emotional support. Furthermore, we combined giving and receiving emotional support into four categories (“giving = no & receiving = no”, “giving = no & receiving = yes”, “giving = yes & receiving = no”, “giving = yes & receiving = yes”). Data on incident dementia were retrieved from the Long-term Care Insurance Database in which participants were followed up for 5.7 years. Using multivariate Cox proportional hazards models, we found that compared with participants who did not give emotional support to others, those who did give had a lower risk of dementia (multivariate-adjusted hazard ratio [HR]: 0.61 [95% confidence interval [CI]: 0.52, 0.71]). However, a nonsignificant relationship was observed for receiving emotional support. Additionally, compared to “giving = no & receiving = no” for emotional support, “giving = no & receiving = yes” showed a higher risk of dementia (multivariate-adjusted HR: 1.51 [95% CI: 1.07, 2.14]).

1. Introduction

Dementia imposes a significant health burden on older people worldwide (Prince et al., 2013). In the absence of curative treatment, strategies for the prevention of dementia are important. Researchers have reported that low/no social contact in social activities may contribute to higher risk of dementia (Fratiglioni, Paillard-Borg, & Winblad, 2004; Kuiper et al., 2015). However, evaluating the efficacy of an individual's social contact is complex. Based on previous research, we know the number of social ties, frequency of contact, satisfaction with relationships, and receiving social support are beneficial in preventing dementia (Crooks, Lubben, Petitti, Little, & Chiu, 2008; Fratiglioni, Wang, Ericsson, Maytan, & Winblad, 2000; Helmer et al., 1999). Conversely, one study found that negative experiences with social support increase the risk of dementia (Khondoker, Rafnsson, Morris, Orrell, & Steptoe, 2017). As far as gerontologists are concerned, social support typically refers to instrumental, informational and

emotional support (Thoits, 2011). As people grow older they tend to place a greater need on emotional support (Herron & Skinner, 2013). Studies have shown that emotional support provides benefits to the aging, such as changes in cardiovascular, neuroendocrine, and immune function (Uchino, 2006). Further, previous studies found that emotional support is more beneficial than instrumental support in preventing cognitive decline (Ellwardt, Aartsen, Deeg, & Steverink, 2013; Glymour, Weuve, Fay, Glass, & Berkman, 2008).

To date, previous studies on emotional support in the aging have mainly focused on cognitive function. Older people who receive more emotional support have been shown to have better cognitive performance as measured by the mini-mental state examination (MMSE) (Ellwardt et al., 2013; Seeman, Lusignolo, Albert, & Berkman, 2001). Additionally, receiving emotional support has also been associated with higher cognitive ability as measured by the Short Portable Mental Status Questionnaire (Chen & Chang, 2016). If emotional support is seen as an exchange process (i.e. people serve not only as receivers but

* Corresponding author at: 2-1 Seiryomachi, Aoba-ku, Sendai, 980-8575, Japan.
E-mail address: zhangshu@med.tohoku.ac.jp (S. Zhang).

<https://doi.org/10.1016/j.archger.2019.103964>

Received 29 May 2019; Received in revised form 26 September 2019; Accepted 11 October 2019

Available online 19 October 2019

0167-4943/ © 2019 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).



Smoking cessation and incident dementia in elderly Japanese: the Ohsaki Cohort 2006 Study

Yukai Lu¹ · Yumi Sugawara¹ · Shu Zhang¹ · Yasutake Tomata¹ · Ichiro Tsuji¹

Received: 14 June 2019 / Accepted: 3 February 2020
© The Author(s) 2020

Abstract

To investigate the association of smoking status and years since smoking cessation with the risk of incident dementia among elderly Japanese. We conducted a longitudinal analysis of smoking status and smoking cessation with dementia in prospective cohort study of 12,489 Japanese individuals aged ≥ 65 years who were followed up for 5.7 years. Information on smoking status and other lifestyle factors was collected via a questionnaire in 2006. Data on incident dementia were retrieved from the public Long-term Care Insurance Database. The Cox proportional hazards model was used to estimate the multivariable-adjusted hazard ratios (HRs) and 95% confidence intervals (95% CIs) for incident dementia. During 61,613 person-years of follow-up, 1110 cases (8.9%) of incident dementia were documented. Compared with individuals who had never smoked, current smokers showed a higher risk of dementia (HR 1.46, 95% CI 1.17, 1.80). Among ex-smokers, the risk for those who had stopped smoking for ≤ 2 years was still high (HR 1.39, 95% CI 0.96, 2.01), however, quitting smoking for 3 years or longer mitigated the increased risk incurred by smokers; the multivariable HRs (95% CIs) were 1.03 (0.70, 1.53) for those who had stopped smoking for 3–5 years, 1.04 (0.74, 1.45) for 6–10 years, 1.19 (0.84, 1.69) for 11–15 years, and 0.92 (0.73, 1.15) for > 15 years. Our study suggests that the risk of incident dementia among ex-smokers becomes the same level as that of never smokers if they maintain abstinence from smoking for at least 3 years.

Keywords Smoking · Smoking cessation · Incident dementia · Cohort study · Elderly population

Introduction

Dementia is a major cause of disability and dependency among the elderly, having a significant impact on individuals as well as families, communities and societies. In 2015, dementia affected about 47 million people worldwide, and it is estimated that globally nearly 9.9 million people develop dementia each year [1]. Thus, it is critical to identify more modifiable factors to reduce the incidence of dementia.

The association between smoking status and dementia has been examined extensively [2–12], and a recent meta-analysis

indicated that current smokers have a significantly higher risk of dementia [13]. However, it has been suggested that smoking cessation would attenuate the excess risk of dementia [13], in addition to other diseases such as cardiovascular diseases (CVDs) [14–17], cancers [18], and chronic obstructive pulmonary disease (COPD) [19]. Previous studies have indicated the risk of CVDs among smokers starts to decline within 2–4 years after smoking cessation [14–16]. On the other hand, it appears that over 10 years of smoking cessation would be necessary until the risk of cancer began to decline [18]. However, it is still uncertain how long a period of smoking cessation would begin to reduce the risk of dementia. One study has compared the risk of all-cause dementia, Alzheimer's disease (AD), and vascular dementia (VaD) between current smokers and ex-smokers, and found that the risk decreased in those who had quit for 4 years or longer [20].

The present cohort study examined the association of smoking status and smoking cessation with incident dementia, focusing particularly on how long a period of abstinence would be necessary in order for the risk of dementia among ex-smokers to reach the same level as that in never smokers.

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s10654-020-00612-9>) contains supplementary material, which is available to authorized users.

✉ Yumi Sugawara
yumi1717@med.tohoku.ac.jp

¹ Division of Epidemiology, Department of Health Informatics and Public Health, Tohoku University School of Public Health, Graduate School of Medicine, 2-1 Seiryomachi, Aoba-ku, Sendai, Miyagi 980-8575, Japan

Journal of the American Heart Association. 2019;8:e012121.

Age - Related Trends in Home Blood Pressure, Home Pulse Rate, and Day - to - Day Blood Pressure and Pulse Rate Variability Based on Longitudinal Cohort Data: The Ohasama Study

Michihiro Satoh, Hirohito Metoki, Kei Asayama, Takahisa Murakami, Ryusuke Inoue, Megumi Tsubota-Utsugi, Ayako Matsuda, Takuo Hirose, Azusa Hara, Taku Obara, Masahiro Kikuya, Kyoko Nomura, Atsushi Hozawa, Yutaka Imai, Takayoshi Ohkubo.

Abstract

Background

Home blood pressure is a more accurate prognosticator than office blood pressure and allows the observation of day - to - day blood pressure variability. Information on blood pressure change during the life course links the prediction of blood pressure elevation with age. We prospectively assessed age - related trends in home blood pressure, home pulse rate, and their day - to - day variability evaluated as a coefficient of variation.

Methods and Results

We examined 1665 participants (men, 36.0%; mean age, 56.2 years) from the general population of Ohasama, Japan. A repeated - measures mixed linear model was used to estimate the age - related trends. In a mean of 15.9 years, we observed 5438 points of measurements including those at baseline. The home systolic blood pressure linearly increased with age and was higher in men than in women aged <70 years. There was an inverse - U - shaped age - related trend in home diastolic blood pressure. The day - to - day home systolic blood pressure linearly increased with age in individuals aged >40 years. However, an U - shaped age - related trend in day - to - day diastolic blood pressure variability with the nadir point at 65 to 69 years of age was observed. No significant sex differences in the day - to - day blood pressure variability were observed ($P \geq 0.22$). The average and day - to - day variability of home pulse rate decreased with age but were lower and higher, respectively, in men than in women.

Conclusions

The current descriptive data are needed to predict future home blood pressure and pulse rate. The data also provide information on the mechanism of day - to - day blood pressure and pulse rate variability.

Journal of Hypertens. 2019;37:1437-1447.

Moderate morning rise in blood pressure has lowest risk of stroke but only in women.

Geoffrey Head, Yusuke Sata, Yukata Imai, Masahiro Kikuya, Takayoshi Ohkubo, Christopher Reid, Barry McGrath, Elena Lukoshkova.

Abstract

BACKGROUND:

The morning period which is recognized as the highest risk for cardiovascular events is associated with a surge in blood pressure (BP). However, it is unclear what aspect of this rise is important.

AIM:

To determine whether the rate of rise (RoR), the magnitude (day night difference) or the product [BP power (BPPower)] is associated with increased cardiovascular risk.

METHODS:

We developed a logistic equation method to fit individual 24-h patterns of BP to determine RoR, amplitude and BPPower using the ambulatory recordings from the Ohasama study including 564 men and 971 women (16.6 years follow-up).

RESULTS:

Men had a higher risk of cardiovascular events than women (24, 16%, $P < 0.001$). Age and night BP were strong linear risk predictors. In men sorting risk by quintiles of BPPower (adjusted for age, night BP, smoking status) revealed no clear linear or nonlinear pattern. However, in women BPPower had a U-shaped relationship with the lowest risk being the 2-3rd quintile for all cardiovascular events ($P_{\text{quadratic}} = 0.01$) including cardiovascular death ($P_{\text{quadratic}} = 0.03$) and nonfatal stroke ($P_{\text{quadratic}} = 0.02$). A similar but less clear trend was observed with the RoR but only stroke (infarct) reached significance ($P_{\text{quadratic}} = 0.03$) while sorting by range showed a U shaped pattern for combined cardiovascular events ($P_{\text{quadratic}} = 0.04$).

CONCLUSION:

These findings suggest that the morning BPPower is an important independent risk factor for predicting cardiovascular events and stroke but only in women with median levels having the lowest risk.

Age-Related Trends in Home Blood Pressure, Home Pulse Rate, and Day-to-Day Blood Pressure and Pulse Rate Variability Based on Longitudinal Cohort Data: The Ohasama Study

Michihiro Satoh, PhD; Hirohito Metoki, MD, PhD; Kei Asayama, MD, PhD; Takahisa Murakami, DDS, PhD; Ryusuke Inoue, MD, PhD; Megumi Tsubota-Utsugi, MPH, PhD; Ayako Matsuda, PhD; Takuo Hirose, PhD; Azusa Hara, PhD; Taku Obara, PhD; Masahiro Kikuya, MD, PhD; Kyoko Nomura, MD, PhD; Atsushi Hozawa, MD, PhD; Yutaka Imai, MD, PhD; Takayoshi Ohkubo, MD, PhD

Background—Home blood pressure is a more accurate prognosticator than office blood pressure and allows the observation of day-to-day blood pressure variability. Information on blood pressure change during the life course links the prediction of blood pressure elevation with age. We prospectively assessed age-related trends in home blood pressure, home pulse rate, and their day-to-day variability evaluated as a coefficient of variation.

Methods and Results—We examined 1665 participants (men, 36.0%; mean age, 56.2 years) from the general population of Ohasama, Japan. A repeated-measures mixed linear model was used to estimate the age-related trends. In a mean of 15.9 years, we observed 5438 points of measurements including those at baseline. The home systolic blood pressure linearly increased with age and was higher in men than in women aged <70 years. There was an inverse-U-shaped age-related trend in home diastolic blood pressure. The day-to-day home systolic blood pressure linearly increased with age in individuals aged >40 years. However, an U-shaped age-related trend in day-to-day diastolic blood pressure variability with the nadir point at 65 to 69 years of age was observed. No significant sex differences in the day-to-day blood pressure variability were observed ($P \geq 0.22$). The average and day-to-day variability of home pulse rate decreased with age but were lower and higher, respectively, in men than in women.

Conclusions—The current descriptive data are needed to predict future home blood pressure and pulse rate. The data also provide information on the mechanism of day-to-day blood pressure and pulse rate variability. (*J Am Heart Assoc.* 2019;8:e012121. DOI: 10.1161/JAHA.119.012121.)

Key Words: blood pressure • blood pressure measurement/monitoring • epidemiology • heart rate/heart rate variability • home blood pressure

High blood pressure (BP) is still strongly related to health deterioration worldwide,¹ but is a preventable and modifiable risk factor. Information on the change in BP during the life course is essential from both clinical and public health

standpoints because it is associated with the prediction and prevention of BP elevation with age. Previous prospective studies based on the general population indicate the age-related trends in office BPs.^{2–6} However, recent guidelines

From the Divisions of Public Health, Hygiene and Epidemiology (M.S., H.M., T.M.) and Nephrology and Endocrinology (T.H.), Faculty of Medicine, Tohoku Medical and Pharmaceutical University, Sendai, Japan; Departments of Community Medical Supports (H.M.) and Preventive Medicine and Epidemiology (T. Obara, M.K., A. Hozawa), Tohoku Medical Megabank Organization, Tohoku University, Sendai, Japan; Tohoku Institute for Management of Blood Pressure, Sendai, Japan (H.M., K.A., Y.I., T. Ohkubo); Department of Hygiene and Public Health, Teikyo University School of Medicine, Tokyo, Japan (K.A., A.M., M.K., T. Ohkubo); Division of Aging and Geriatric Dentistry, Department of Oral Function and Morphology, Tohoku University Graduate School of Dentistry, Sendai, Japan (T.M.); Departments of Medical Information Technology Center (R.I.) and Pharmaceutical Sciences (T. Obara), Tohoku University Hospital, Sendai, Japan; Department of Hygiene and Preventive Medicine, Iwate Medical University School of Medicine, Iwate, Japan (M.T.-U.); Division of Drug Development and Regulatory Science, Faculty of Pharmacy, Keio University, Tokyo, Japan (A. Hara); Department of Public Health, Akita University Graduate School of Medicine, Akita, Japan (K.N.).

Accompanying Tables S1 through S4 and Figures S1 through S11 are available at <https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.012121>

Correspondence to: Michihiro Satoh, PhD, Division of Public Health, Hygiene and Epidemiology, Faculty of Medicine, Tohoku Medical and Pharmaceutical University, 1-15-1 Fukumuro, Miyagino-ku, Sendai, Miyagi 983-8536, Japan. E-mail: satoh.mchr@gmail.com

Received March 26, 2019; accepted July 1, 2019.

© 2019 The Authors. Published on behalf of the American Heart Association, Inc., by Wiley. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

High-Density Lipoprotein Cholesterol and Risk of Stroke Subtypes: Jichi Medical School Cohort Study.

Watanabe J, Takehi E, Kotani K, Kayaba K, Nakamura Y, Ishikawa S.

Asia Pacific Journal of Public Health (in press)

ABSTRACT

We aimed to investigate the relationship between high-density lipoprotein cholesterol (HDL-C) concentration and the incident stroke subtypes. We enrolled 11,027 participants between the ages of 18 and 90 years without a history of stroke in 12 Japanese communities. Cox's regression models were used for stroke subtypes, adjusted for traditional risk factors, according to the categories based on HDL-C concentrations: 1.04–1.55 mmol/L, ≥ 1.56 mmol/L, and < 1.03 mmol/L (as the reference). During a mean follow-up of 10.7 years, 412 stroke events had occurred. However, HDL-C was not significantly associated with the incidence of cerebral infarction and subarachnoid hemorrhage. High HDL-C concentration was associated with a decreased incidence of ICH in women [hazard ratio (HR), 0.23; 95% and confidence interval (CI) 0.06–0.89], but not in men (HR, 0.73; 95% and CI, 0.27–1.97). Therefore, high HDL-C concentration might have a protective effect on the incidence of ICH, particularly in women.

Keyword: high-density lipoprotein cholesterol; stroke; morbidity; cohort studies; Japanese.

Metabolic syndrome is a risk factor for cancer mortality in the general Japanese population: the Jichi Medical School Cohort Study.

Watanabe J, Kakehi E, Kotani K, Kayaba K, Nakamura Y, Ishikawa S.

Diabetol Metab Syndr. 2019 Jan 9;11:3. doi: 10.1186/s13098-018-0398-2. eCollection 2019.

Abstract

Background: Metabolic syndrome (MetS) and cancer are major public health problems worldwide. The relationship between MetS and cancer death is of great interest. We examined the predictive value of MetS for cancer mortality in Japan.

Methods: Study participants included 4495 men and 7028 women aged 18-90 years who were registered between 1992 and 1995 as part of the Jichi Medical School Cohort Study. We used a definition of MetS modified for the Japanese population. The primary outcome was cancer mortality. Additionally, the relationship between MetS and cancer-type specific mortality was examined. Analyses were conducted with Cox's regression models adjusted for age, smoking status, alcohol drinking status, marital status, educational attainment, physical activity, occupational category, and menopausal status (only in women).

Results: During a mean follow-up of 18.5 years, 473 men and 297 women died from cancer. MetS was positively associated with cancer mortality in women (hazard ratio [HR], 1.69; 95% confidence interval [CI] 1.21-2.36), but not in men (HR, 1.21; 95% CI 0.90-1.62). Additionally, MetS was associated with a high risk of colorectal (HR, 3.48; 95% CI 1.68-7.22) and breast (HR, 11.90; 95% CI 2.25-62.84) cancer deaths in women.

Conclusion: MetS was a significant predictor of cancer mortality in women.

Keyword: Cohort studies; Japanese; Metabolic syndrome; Mortality; Neoplasm

Combined Effect of Small Dense Low-Density Lipoprotein Cholesterol (sdLDL-C) and Remnant-Like Particle Cholesterol (RLP-C) on Low-Grade Inflammation.

Izumida T, Nakamura Y, Hino Y, Ishikawa S.

J Atheroscler Thromb. 2019 Aug 29. doi: 10.5551/jat.49528. [Epub ahead of print]

Abstract

Aims: Small dense low-density lipoprotein cholesterol (sdLDL-C) and remnant-like particle cholesterol (RLP-C) are the novel atherosclerotic risk factors and might be strongly associated with inflammation. The basic evidence supports that sdLDL and RLP have some different mechanisms inducing an inflammatory response. Many studies have focused on the mechanism of inflammation of sdLDL-C or RLP-C per se, with limited data on the association between sdLDL-C and RLP-C in the real-world, population-based setting. Thus, the aim of this study was to investigate the association between sdLDL-C and RLP-C with inflammation.

Methods: We examined the baseline cross-sectional data of participants from the Jichi Medical School-II Cohort Study. In total, 5,305 participants (2,439 men and 2,866 women) were included in this study.

Results: Of all quartiles of sdLDL-C, the fourth had the highest high-sensitivity C-reactive protein (hs-CRP) level. Once adjusted for age, sex, smoking status, homeostasis model assessment of insulin resistance, antidiabetic and antihyperglycemic medication use, and RLP-C, sdLDL-C was significantly and positively associated with hs-CRP (geometric mean, 95% confidence interval (CI), 0.36 mg/L (0.34-0.38 mg/L), 0.37 mg/L (0.35-0.39 mg/L), 0.40 mg/L (0.37-0.42 mg/L) versus 0.44 mg/L (0.42-0.47 mg/L), $P < 0.001$ for trend). After stratifying the participants into four sdLDL-C×four RLP-C categories, the group in the fourth sdLDL-C quartile and the fourth RLP-C quartile had the highest hs-CRP level (geometric mean, 95% CI, 0.52 mg/L, 0.48-0.57 mg/L, interaction $P=0.75$).

Conclusions: SdLDL-C and RLP-C had different associations with inflammation. Our results support sdLDL-C as the potential novel factor of cardiovascular disease, independently of RLP-C.

Keywords: High-sensitivity C-reactive protein; Low-grade inflammation; Remnant-like particle cholesterol; Small dense low-density lipoprotein cholesterol

The ratio of fasting plasma glucose to hemoglobin A1c as a predictor of all-cause mortality in individuals with normal glucose levels: The Jichi Medical School cohort study.

Takehi E, Kotani K, Gotoh T, Kayaba K, Ishikawa S.

SAGE Open Med. 2019 Jun 26;7:2050312119860398. doi: 10.1177/2050312119860398. eCollection 2019.

Abstract

Objectives: The fasting plasma glucose/hemoglobin A1c ratio is considered a marker associated with glucose metabolism disorders, including fasting hyperglycemia. However, it remains unclear whether this ratio can be used for the prevention of deaths in individuals with normal fasting plasma glucose levels. This study aimed to see the predictive value of the fasting plasma glucose/hemoglobin A1c ratio for all-cause mortality in a general population with normal fasting plasma glucose levels.

Methods: The study investigated prospectively a cohort of 1087 multi-regional, community-dwelling Japanese participants (women, 69.2%) for a follow-up period of 11.3 years. We included individuals with fasting plasma glucose levels <6.11 mmol/L and excluded those meeting the diabetes criteria. All-cause mortality was the primary outcome and hazard ratios were calculated using the Cox proportional hazard model after dividing the fasting plasma glucose/hemoglobin A1c ratios into tertiles.

Results: There were 54 deaths (25 women) during the follow-up period. The high tertile group had a significantly higher hazard ratio for all-cause mortality than the low tertile group in women (multivariate-adjusted hazard ratio = 4.45; 95% confidence interval = 1.26-15.72), but not clearly in men.

Conclusion: The data of the population-based cohort study suggest that a high fasting plasma glucose/hemoglobin A1c ratio can predict all-cause mortality in women with normal fasting plasma glucose levels.

Keywords:

Fasting plasma glucose; all-cause mortality; fasting plasma glucose/hemoglobin A1c ratio; hemoglobin A1c

Risk and population attributable fraction of metabolic syndrome and impaired fasting glucose for the incidence of type 2 diabetes mellitus among middle-aged Japanese individuals: Aichi Worker's Cohort Study

Kayo Kaneko¹ , Hiroshi Yatsuya^{1,2*}, Yuanying Li², Mayu Uemura¹, Chifa Chiang¹, Yoshihisa Hirakawa¹, Atsuhiko Ota² , Koji Tamakoshi³, Atsuko Aoyama^{1,4}

¹Department of Public Health and Health Systems, Nagoya University Graduate School of Medicine, Nagoya, Japan, ²Department of Public Health, Fujita Health University School of Medicine, Toyoake, Japan, ³Department of Nursing, Nagoya University School of Health Sciences, Nagoya, Japan, ⁴Nagoya University of Arts and Sciences, Nissin, Japan

Keywords

Impaired fasting glucose, Metabolic syndrome, Population attributable fraction and type 2 diabetes mellitus

*Correspondence

Hiroshi Yatsuya
 Tel.: +81-562-93-2452
 Fax: +81-562-93-3079
 E-mail address:
 yatsuya@gmail.com;
 yatsuya@fujita-hu.ac.jp

J Diabetes Investig 2020

doi:10.1111/jdi.13230

ABSTRACT

Aims/Introduction: The Japanese government started a nationwide screening program for metabolic syndrome (MetS) to prevent cardiovascular diseases and diabetes in 2008. Although impaired fasting glucose (IFG) is a strong predictor for type 2 diabetes mellitus, the program does not follow up IFG in non-MetS individuals. This study aimed to examine the risk and the population attributable fraction (PAF) of MetS and IFG for incidence of type 2 diabetes mellitus.

Materials and Methods: Japanese workers (3,417 men and 714 women) aged 40–64 years without a history of diabetes were prospectively followed. MetS was defined as either abdominal obesity plus two or more metabolic risk factors, or being overweight in the case of normal waist circumference plus three or more metabolic risk factors. IFG was defined as fasting blood glucose 100–125 mg/dL.

Results: During a mean 6.3 years, 240 type 2 diabetes mellitus cases were identified. Compared with those without MetS and IFG, the multivariable-adjusted hazard ratios (95% confidence interval) of non-MetS individuals with IFG, MetS individuals without IFG and MetS individuals with IFG for type 2 diabetes mellitus were 4.9 (3.4–7.1), 2.4 (1.6–3.5) and 8.3 (5.9–11.5), respectively. The corresponding PAFs for type 2 diabetes mellitus incidence were 15.6, 9.1 and 29.7%, respectively.

Conclusions: IFG represented a higher risk and PAF than MetS for type 2 diabetes mellitus incidence in middle-aged Japanese individuals. The coexistence of MetS and IFG showed the highest risk and PAF for type 2 diabetes mellitus incidence. The current Japanese MetS screening program should be reconsidered to follow up non-MetS individuals with IFG.

INTRODUCTION

The increasing trend of type 2 diabetes mellitus is one of the most significant public health threats in Japan and the world^{1–3}. Modifying lifestyles to prevent metabolic syndrome (MetS), a likely precursor of type 2 diabetes mellitus, could be an effective

approach^{4–6}. The Japanese government started an annual screening program for MetS among people aged ≥40 years in 2008^{7,8}. All public health insurers are obliged to carry out the MetS screening and provide the identified MetS individuals with health education support. In this program, MetS is defined as either abdominal obesity plus two or more metabolic risk factors, or being overweight in the case of normal waist circumference plus three or more metabolic risk factors (Table 1)⁷. This program

Received 11 September 2019; revised 13 January 2020; accepted 3 February 2020

Color: ■	
CE: Saranya R	PE: Kaviarasi N
Dispatch: 21.2.20	No. of pages: 7
WILEY	
13230	Manuscript No.
JDI	Journal Code

Smoking results in accumulation of ectopic fat in the liver

This article was published in the following Dove Press journal:
Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy

Ayako Kato¹
Yuanying Li¹
Atsuhiko Ota¹
Hisao Naito¹
Hiroya Yamada²
Takashi Nihashi³
Yo Hotta⁴
Chifa Chiang⁵
Yoshihisa Hirakawa⁵
Atsuko Aoyama^{5,6}
Koji Tamakoshi⁷
Hiroshi Yatsuya^{1,5}

¹Department of Public Health, Fujita Health University School of Medicine, Toyoake, Aichi, Japan; ²Department of Hygiene, Fujita Health University School of Medicine, Toyoake, Aichi, Japan; ³Department of Radiology, Komaki City Hospital, Komaki, Aichi, Japan; ⁴Toyoda Gosei Co., Ltd, Medical and Hygiene Designing Department, Inazawa, Aichi, Japan; ⁵Department of Public Health and Health Systems, Nagoya University Graduate School of Medicine, Nagoya, Aichi, Japan; ⁶Nagoya University of Arts and Sciences, Nissin, Aichi, Japan; ⁷Department of Nursing, Nagoya University School of Health Sciences, Nagoya, Aichi, Japan

Correspondence: Hiroshi Yatsuya
Department of Public Health, Fujita Health University School of Medicine, Toyoake, Aichi 470-1192, Japan
Tel +81 56 293 2452
Fax +81 56 293 3079
Email yatsuya@gmail.com

Objective: An association between smoking and nonalcoholic fatty liver disease has been reported. However, objective quantification of intrahepatic fat via magnetic resonance spectroscopy (MRS) in relation to smoking has rarely been performed in previous studies. Moreover, the possible pathways via which smoking could induce ectopic fat accumulation have not yet been addressed. The current study aimed to examine the association between smoking status and intrahepatic fat quantity and explore the possible mediating effects of triglycerides (TG) and adiponectin.

Subjects and methods: Magnetic resonance imager (MRI) spectra were analyzed to quantify intrahepatic fat in 45 men who were on average 62.3 years of age. Smoking status and alcohol intake were self-reported. Accelerometers were used to record daily total physical activity. Fasting blood TG and adiponectin levels were measured enzymatically. Differences in mean intrahepatic fat values according to smoking status were assessed using analysis of covariance.

Results: A stepwise increase in mean intrahepatic fat was observed between never, former, and current smokers, respectively, independent of age, physical activity, alcohol intake, and body mass index (BMI) ($P=0.005$). Adjustment for TG and adiponectin significantly attenuated this association ($P=0.074$).

Conclusion: Current smoking was significantly associated with increased intrahepatic fat, which may be a result of adipocyte dysfunction, manifested as high circulating TG concentrations and low adiponectin levels.

Keywords: intrahepatic fat, cigarette smoking, adiponectin, triglycerides, cross-sectional study

Introduction

Cigarette smoking is associated with increased risk of diabetes¹ and dyslipidemia.² Intrahepatic fat accumulation, a phenomenon in which fat is ectopically deposited in the liver, is also frequently associated with insulin resistance and dyslipidemia.³ Smoking, which is typically associated with reduced deposition of subcutaneous fat relative to non-smoking,⁴ has emerged as a potential risk factor for the progressive accumulation of intrahepatic fat. According to a few observational studies, smoking is associated with increased risk of nonalcoholic fatty liver disease (NAFLD) detected by ultrasonography.⁵ However, there is a paucity of data regarding whether smoking is actually related to increased ectopic fat,⁶ as one previous study conducted in German found that smoking was not associated with increased liver fat content quantified by magnetic resonance imaging (MRI).⁷ Moreover, the possible mediators through which