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TV viewing and incident venous thromboembolism: the Atherosclerotic Risk in Communities Study

Yasuhiko Kubota[1] · Mary Cushman[2] · Neil Zakai[2] · Wayne D. Rosamond[3] · Aaron R. Folsom[1]

Abstract
TV viewing is associated with risk of arterial vascular diseases, but has not been evaluated in relation to venous thromboembolism (VTE) risk in Western populations. In 1987–1989, the Atherosclerosis Risk in Communities Study obtained information on the frequency of TV viewing in participants aged 45–64 and followed them prospectively. In individuals free of prebaseline VTE (n = 15, 158), we used a Cox proportional hazards models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) of incident VTE according to frequency of TV viewing ("Never or seldom", "Sometimes", "Often" or "Very often"). During the 299,767 person-years of follow-up, we identified 691 VTE events. In a multivariable-adjusted model, the frequency of TV viewing showed a positive dose–response relation with VTE incidence (*P* for trend = 0.036), in which "very often" viewing TV carried 1.71 (95% CI 1.26–2.32) times the risk of VTE compared with "never or seldom" viewing TV. This association to some degree was mediated by obesity (25% mediation, 95% CI 10.7–27.5). Even among individuals who met a recommended level of physical activity, viewing TV "very often" carried 1.80 (1.04–3.09) times the risk of VTE, compared to viewing TV "never or seldom". Greater frequency of TV viewing was independently associated with increased risk of VTE, partially mediated by obesity. Achieving a recommended physical activity level did not eliminate the increased VTE risk associated with frequent TV viewing. Avoiding frequent TV viewing as well as increasing physical activity and controlling body weight might be beneficial for VTE prevention.

Keywords TV · Venous thromboembolism · Physical activity · Sedentary behavior

Introduction

TV viewing is the most common sedentary behavior in many populations around the world, and is associated with adverse health outcomes including major cardiovascular diseases, independent of other measures of physical activity [1–6]. In recent decades, an increase in the number of TV sets and hours spent viewing TV paralleled the population rise in obesity [6].

Venous thromboembolism (VTE), manifested by deep venous thrombosis (DVT) and pulmonary embolism, is a common medical problem with a substantial increase in the incidence of VTE, mostly due to an increasing incidence of pulmonary embolism [7]. Patients who develop VTE have high mortality rates [8]. Thus, prevention of VTE is important. A recent study reported a positive association between TV viewing and risk of mortality from pulmonary embolism in an Asian population [9]. To date, however, there is no prospective study investigating the association between TV viewing and VTE risk in Western populations. VTE incidence is higher in Western populations than in Asian populations [7], and thus, there may be a great deal of relevance to a study of TV viewing and VTE in Western populations.

We prospectively tested the hypothesis that the frequency of TV viewing is positively associated with VTE incidence independent of other measured VTE risk factors in the population based Atherosclerosis Risk in Communities (ARIC)

✉ Yasuhiko Kubota
kubot007@umn.edu

[1] Division of Epidemiology and Community Health, School of Public Health, University of Minnesota, 1300 South 2nd Street, Minneapolis, MN 55454, USA

[2] Departments of Medicine and Pathology and Laboratory Medicine, Larner College of Medicine at the University of Vermont, Burlington, VT, USA

[3] Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC, USA

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Study cohort. Further, we evaluated the potential mediating role of obesity in this relationship.

Materials and methods

Study design, setting, and population

ARIC is an ongoing population-based prospective study of atherosclerotic diseases within 4 U.S. communities [Washington County, Maryland; Forsyth County, North Carolina; Jackson, Mississippi (African Americans only); and suburbs of Minneapolis, Minnesota] [10]. The ARIC Study enrolled 15,792 mostly white or African American men and women aged 45 to 64 years in 1987–1989. The participants were followed-up in 1990–1992 (visit 2, 93% return), in 1993–1995 (visit 3, 86% return), 1996–1998 (visit 4, 80% return) and 2009–2011 (visit 5, 41% return). Home interviews and clinic examinations measured various demographic characteristics, cardiovascular conditions, and health behaviors.

Among the 15,792 participants, we excluded participants who reported pre-baseline VTE or baseline anticoagulant use (n = 349), those missing exposure (n = 32); non-white/black participants in Forsyth County or non-white participants in Washington County or Minneapolis (n = 103) in order to allow adjustment for race and study site [11]; and participants with missing covariates (n = 150). Finally, 15,158 participants were included in the present analyses.

The study protocol was approved by the institutional review boards of the collaborating universities, and ARIC obtained written informed consent from all participants.

Main exposure: frequency of television viewing

Using the Baecke physical activity questionnaire [12], ARIC asked participants to select their frequency of TV viewing during leisure time from the following, "Never", "Seldom, "Sometimes", "Often" or "Very often" at baseline. ARIC also asked about TV viewing at visit 3 (1993–1995) and visit 5 (2009–2011). The percent exact agreement on the four categories of TV viewing for visit 1 versus visit 3 was 54% (kappa = 0.40). The kappa was 0.26 for visit 1 versus visit 5 and this was 0.30 for visit 3 versus visit 5. The percentages of participants reported viewing TV "very often" were 6.8, 7.5, and 14.7% across the respective visits. We used the frequency of TV viewing as a time-varying exposure.

Potential confounding and mediating factors

The following potential confounding factors were assessed; age, sex, race (white or African American), smoking status (current, former, or never), physical activity levels, estimated glomerular filtration rate (eGFR, ml/min/1.73 m^2), and prevalent cardiovascular disease (coronary heart disease, heart failure and stroke). Using the Baecke physical activity questionnaire, participants were also asked about the usual frequency and number of hours they walked and participation in up to four sports during the previous year [12]. Each sport activity was converted into metabolic equivalents of task (METs) via the Compendium of Physical Activities [13, 14]. The reliability and validity of the Baecke questionnaire has been evaluated in several populations and reported elsewhere [15–18]. Moderate activities were defined as those involving a workload of 3–6 METs and vigorous activities were those involving a workload of > 6 METs. Physical activity levels were categorized into three levels based on American Heart Association (AHA) recommendations as "recommended" (≥ 75 min/week of vigorous intensity or ≥ 150 min/week of any combination of moderate + vigorous intensity), "intermediate" (1–74 min/week of vigorous intensity or 1–149 min/week of any combination of moderate + vigorous intensity), or "poor" (0 min/week of moderate or vigorous intensity) [19].

We considered body mass index (BMI, kg/m^2) as a factor that might mediate the association between TV viewing and VTE.

Confirmation of venous thromboembolism

ARIC contacted participants annually or semi-annually by phone to ask about all hospitalizations in the previous year. Using standard criteria, two physicians validated possible VTEs through 2011 using hospital records [20]. "Provoked VTE" was defined as VTEs associated with cancer, major trauma, surgery or marked immobility, while all others were classified as "unprovoked VTE". Pulmonary embolism and deep venous thrombosis were distinguished using imaging tests [20].

Statistical analysis

SAS version 9.4 software (SAS Institute Inc., Cary, NC) was used for statistical analyses. All statistical tests were two-tailed and P values < 0.05 were regarded as significant.

Because very few participants reported "Never" viewing TV (n = 293), we categorized participants' TV viewing frequency into the following four groups: "never or seldom", "sometimes", "often" or "very often". We computed mean levels or percentages of VTE risk factors at baseline according to the frequency of TV viewing. Person-years of follow-up were calculated from the baseline to the first endpoint: VTE, death, loss to follow-up, or administrative censoring at December 31, 2011. Hazard ratios (HRs) of VTE occurrence and their 95% confidence intervals (CIs) in relation to a time-varying TV viewing variable were calculated after adjustment

for potential confounding factors using Cox proportional hazards model. The proportional hazards assumption in Cox regression was tested using risk factor-by-time interactions and was not violated. Since we found no statistical interactions between sex or race and TV viewing in relation to VTE risk (P for interaction > 0.05), we pooled the analysis across sex and race. Model 1 adjusted for age, sex, and race/ARIC field center; and Model 2 (main model) additionally for smoking status, physical activity, eGFR, and prevalent cardiovascular disease.

We also evaluated potential mediation by obesity in Model 3 including BMI, using bootstrapping (1000 replicate samples) [21]. The percentage attenuation in the HR was calculated as ([HR without BMI] − [HR ratio with BMI])/(HR without BMI − 1) × 100%. The 95% CI of the change in the TV viewing HR for VTE was calculated from the 2.5th and 97.5th percentiles of the replicate sample distribution for TV viewing HR.

For sensitivity analysis, we reran models by excluding those with early VTE events (5 years from baseline) to assess the possibility of reverse causation.

Results

Baseline characteristics according to frequency of TV viewing

The prevalences of participants who viewed TV "never or seldom", "sometimes", "often" and "very often" were 18.6, 46.8, 26.5 and 8.1%, respectively (Table 1). Individuals who viewed TV more frequently were more likely to be African American, be current smokers, and have a history of cardiovascular disease. They were less likely to meet the AHA recommended level of physical activity. They had higher levels of body mass index.

Association of frequency of TV viewing with incidence of venous thromboembolism

There were 691 incident VTE events during the 299,767 person-years of follow-up for the 15,158 ARIC participants (Table 2). The age-, sex-, and race-adjusted model (Model 1) showed a positive dose–response relation between the frequency of TV viewing and VTE incidence (p for trend = 0.007). Further adjustment for potential confounding

Table 1 Baseline characteristics according to frequency of television viewing (n = 15,158), ARIC, 1987–1989

	Never or seldom	Sometimes	Often	Very often
Participants, n	2815	7094	4023	1226
Age, years	53.6 ± 5.7	54.0 ± 5.7	54.6 ± 5.8	54.5 ± 5.9
Female, %	58.9	57.3	47.9	54.0
African American, %	15.7	25.1	27.0	54.4
Current smoker, %	20.1	24.1	28.9	38.2
Recommended physical activity, %	46.1	38.7	33.4	25.3
eGFR, ml/min/1.73 m^2	102.1 ± 14.0	102.6 ± 15.2	102.1 ± 16.4	104.2 ± 20.2
Prevalent cardiovascular disease, %	6.7	8.3	11.1	15.9
Potential mediator				
Body mass index, kg/m^2	26.8 ± 4.9	27.6 ± 5.3	28.0 ± 5.3	28.7 ± 6.1

Table 2 Hazard ratios and 95% CIs for incident venous thromboembolism (VTE) according to frequency of television viewing (n = 15,158), ARIC, 1987–2011

	Never or seldom	Sometimes	Often	Very often	P for trend
Participants, n	2815	7094	4023	1226	
Person-years	57,657	142,653	77,635	21,823	
Total VTE, cases	116	307	186	82	
Model 1	1	1.17 (0.93–1.48)	1.31 (1.02–1.68)	1.88 (1.39–2.55)	0.007
Model 2	1	1.16 (0.91–1.46)	1.26 (0.98–1.62)	1.71 (1.26–2.32)	0.036
Mediator analysis					
Model 3	1	1.13 (0.90–1.44)	1.20 (0.94–1.54)	1.53 (1.13–2.08)	0.153

Model 1: Adjusted for age, sex, and race/ARIC field center

Model 2: Adjusted for Model 1 + smoking status, leisure-time physical activity, eGFR and prevalent cardiovascular disease

Model 3: Adjusted for Model 2 + body mass index

factors (Model 2) attenuated but did not substantially change the association; individuals who viewed TV "very often" had 1.71 (95% CI 1.26–2.32) times the risk of VTE compared with those who "never or seldom" viewed TV. Regardless of VTE subtypes [unprovoked versus provoked VTE and pulmonary embolism (with or without deep venous thromboembolism) vs. deep vein thrombosis alone], the frequency of TV viewing was positively associated with VTE risk (Table 3).

We also assessed the extent to which the observed association between the frequency of TV viewing and VTE risk might be mediated by obesity at baseline by adjusting for BMI and then seeing how much the association was attenuated (Model 3 in Table 2). Adjustment for BMI accounted for 25.3% (95% CI 10.7–27.5) of the association of TV viewing with VTE risk.

Joint associations of frequency of TV viewing and physical activity or obesity with risk of venous thromboembolism

There was a similar association of TV viewing with risk of VTE regardless of level of physical activity, as illustrated in Fig. 1 (p for multiplicative interaction of TV viewing and physical activity level = 0.41). For example, even individuals who met the AHA recommended level of physical activity

Table 3 Hazard ratios and 95% CIs for incident venous thromboembolism (VTE) according to frequency of television viewing, stratified by VTE subtypes (n = 15,158), ARIC, 1987–2011

	Never or seldom	Sometimes	Often	Very often	P for trend
Participants, n	2815	7094	4023	1226	
Person-years	57,657	142,653	77,635	21,823	
Unprovoked VTE, cases	43	117	73	32	
Model 2	1	1.07 (0.73–1.56)	1.17 (0.78–1.73)	1.79 (1.12–2.87)	0.175
Provoked VTE, cases	73	190	113	50	
Model 2	1	1.22 (0.90–1.64)	1.33 (0.97–1.83)	1.66 (1.11–2.48)	0.102
Pulmonary embolism, cases	60	154	82	38	
Model 2	1	1.00 (0.73–1.38)	0.97 (0.68–1.36)	1.67 (1.10–2.53)	0.207
Deep venous thrombosis only, cases	56	153	104	44	
Model 2	1	1.36 (0.95–1.93)	1.65 (1.15–2.37)	1.80 (1.14–2.82)	0.084

Model 2: Adjusted for Model 1 + smoking status, leisure-time physical activity, eGFR and prevalent cardiovascular disease

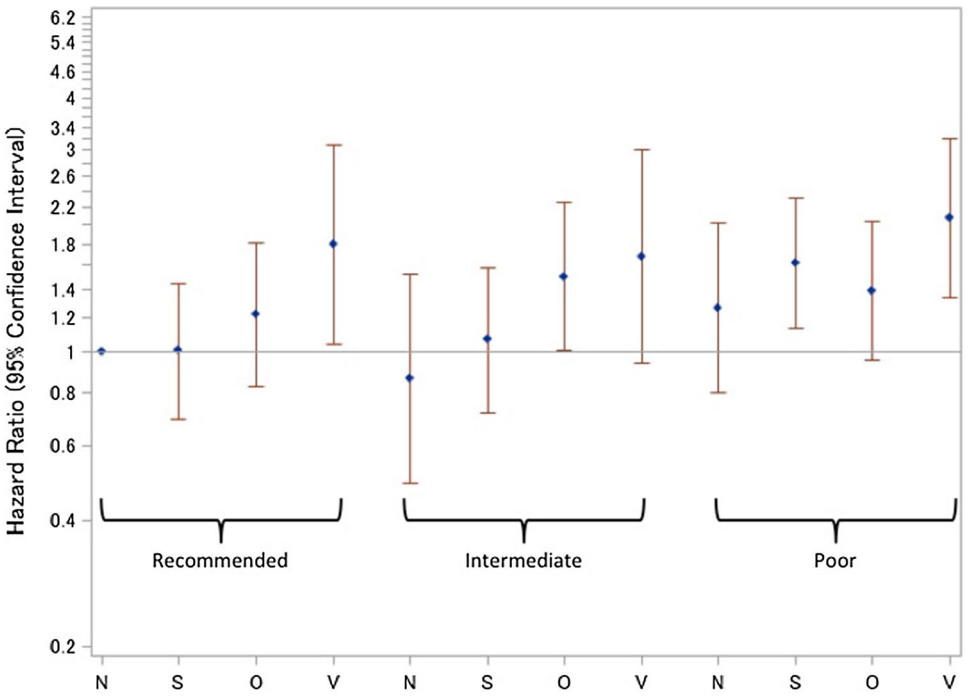

Fig. 1 Joint association of TV viewing and physical activity category with risk of venous thromboembolism. Adjusted for sex, race/ARIC field center, smoking status, leisure-time physical activity, eGFR and prevalent cardiovascular disease. N, "Never or seldom"; S, "Sometimes"; O, "Often"; and V, "Very often"

but viewed TV "very often" had a HR of VTE of 1.80 (95% CI 1.04–3.09), and those whose physical activity level was poor and who viewed TV "very often" had a similar HR of 2.07 (1.34–3.20).

As shown in Fig. 2, compared with normal weight individuals, obese participants had significantly increased risks of VTE and TV viewing appeared to add to the risk associated with obesity. Obese individuals who "very often" viewed TV had the highest HR of VTE at 3.70 (2.31–5.91), relative to normal weight individuals who "never or seldom" viewed TV. Nevertheless, the multiplicative interaction test between TV viewing and obesity categories in relation to VTE risk was not significant (p = 0.31).

Sensitivity analysis

Excluding individuals with early VTE events (within 5 years from baseline) provided similar results (data not shown).

Discussion

In the prospective population-based ARIC cohort, a higher frequency of TV viewing, especially viewing very often, was associated with increased risk of VTE, with no difference by VTE subtype. Higher BMI attenuated the association by approximately 25%, but did not explain the entire association. Even participants who met the AHA recommended level of physical activity had a higher risk of VTE when they often viewed TV than when they never or seldom viewed TV. To the best of our knowledge, this is the first prospective study investigating the association between TV viewing and incident VTE in a Western population.

TV viewing is the most common sedentary behavior around the world [1]. Of several sedentary behaviors, TV viewing may particularly allow people to be sedentary for a long time [22]. Prolonged TV viewing may promote venous stasis through inhibiting venous blood return from the lower extremities during prolonged sitting, and may also lead to increased thrombotic tendency by affecting levels of circulating hemostatic and inflammatory factors such as D-dimer, factor VIII and C-reactive protein [23–25].

It is well recognized the immobilization is a strong risk factor for VTE [7, 26]. We are aware of only a few other studies of sedentary behaviors and risk of VTE [27–29]. A previous Japanese cohort study reported that prolonged TV viewing was associated with increased risk of mortality from pulmonary embolism [9], but the study did not distinguish unprovoked and provoked VTE. Medical conditions such as cancer and trauma might have led people to have both prolonged TV viewing and increased risk of provoked VTE.

Sedentary behaviors and physical activity are independently associated with arterial vascular diseases [4, 5]. Similarly, here we observed a positive association between TV viewing and VTE risk independent of physical activity. These results suggest that sedentary behavior is not just the opposite issue from physical activity. Individuals whose physical activity level was poor had a higher risk of VTE than those who achieved the AHA recommended level of physical activity, independent of TV viewing frequency.

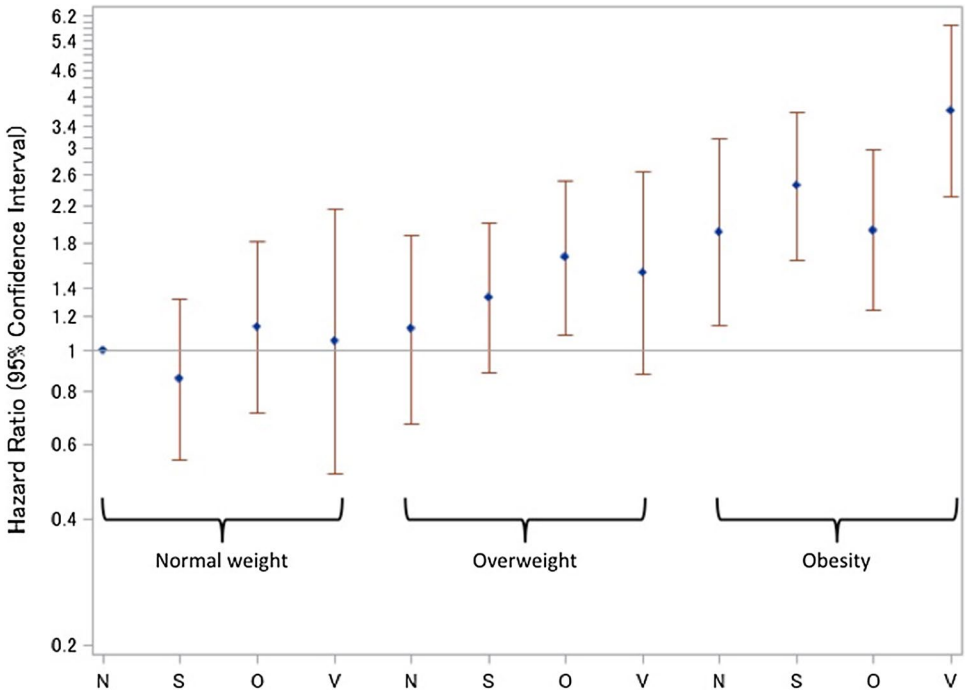

Fig. 2 Joint association of TV viewing and obesity category with risk of venous thromboembolism. Adjusted for sex, race/ARIC field center, smoking status, leisure-time physical activity, eGFR and prevalent cardiovascular disease. N, "Never or seldom"; S, "Sometimes"; O, "Often"; and V, "Very often"

However, even individuals who met the AHA recommended level of physical activity, when they viewed TV very often, had an increased risk of VTE compared with those who met the recommended level and seldom viewed TV. These results suggest that even individuals who regularly engage in physical activity should not ignore the potential harms of prolonged sedentary behaviors such as TV viewing.

Obesity is an established risk factor for VTE, including in the ARIC cohort [30–32]. TV viewing seems to increase risk of obesity [6]. In our study, not only was obesity a VTE risk factor, but obese participants who viewed TV very often had a very high risk of VTE. In addition, higher BMI also appeared to partially mediate the association between TV viewing and VTE. Thus, avoiding frequent TV viewing might reduce the risk of VTE in obese persons, and prevent weight gain.

Although we suggested venous stasis and obesity as potential mechanisms for the association between TV viewing and VTE risk, there may be the other mechanisms. Finding them might be helpful for prevention of VTE associated with TV viewing.

There are some limitations to this study. Firstly, our exposure was the qualitative frequency of TV viewing as reported by participants, but not the precise time spent viewing TV. The frequency should be correlated with time spent viewing TV, but our results therefore require careful interpretation. Secondly, the possibility of residual confounding of the observed associations by unmeasured VTE risk factors associated with TV viewing cannot be negated, as is often the case in observational studies. Strengths of the study include assessment of the exposure of TV viewing three times, which allowed analysis as a time-varying exposure. The study was also large with a large number of VTE events and high cohort retention, and the prospective design reduced the possibility of reverse causality as a reason for the findings.

Conclusions

In the ARIC cohort, a greater frequency of TV viewing was associated with increased risk of VTE, independent of physical activity and obesity. Moreover, a recommended level of physical activity did not eliminate the increased risk of VTE with frequent TV viewing. Avoiding frequent TV viewing as well as increasing physical activity and controlling body weight might be beneficial for VTE prevention.

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Compliance with ethical standards

Conflict of interest Authors declare no conflict of interest.

Ethical approval The study protocol was approved by the institutional review boards of the collaborating universities.

Informed consent ARIC obtained written informed consent from all participants.

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