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Prognostic value of resting heart rate in predicting undiagnosed diabetes in adults: Korean National Health and Nutrition Examination Survey 2008–2018

Dong-Hyuk Park [a,b], Seon Young Goo [a], Sung Hyun Hong [a], Ji-hee Min [c], Ji Yong Byeon [a], Mi-Kyung Lee [a,d], Hae Dong Lee [d,e], Byoung Wook Ahn [f], Heejin Kimm [g], Sun Ha Jee [g], Dong Hoon Lee [h], Yong-ho Lee [i], Eun Seok Kang [i], Justin Y. Jeon [a,b,d,*]

[a] *Department of Sport Industry Studies, Yonsei University, Seoul, South Korea*
[b] *Exercise Medicine Center for Diabetes and Cancer Patients, ICONS, Yonsei University, Seoul, South Korea*
[c] *Department of Convergence Medicine, Yonsei University Wonju College of Medicine, Wonju, South Korea*
[d] *Frontier Research Institute of Convergence Sports Science, FRICSS, Yonsei University, Seoul, South Korea*
[e] *Department of Physical Education, Yonsei University, Seoul, South Korea*
[f] *Leisure Marine Sports, Hanseo University, Chungcheongnam-do, South Korea*
[g] *Graduate School of Public Health, Institute for Health Promotion, Yonsei University, Seoul, South Korea*
[h] *Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA, USA*
[i] *Department of Internal Medicine, Yonsei University College of Medicine, Seoul, South Korea*

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Abstract *Background and aim:* Although resting heart rate (RHR) is associated with prevalence and incidence of diabetes, whether it is associated with undiagnosed diabetes is still unclear. We aimed to investigate whether the RHR is associated with the prevalence of undiagnosed diabetes in a large Korean national dataset.

Methods and results: The Korean National Health and Nutrition Examination Survey data from 2008 to 2018 were used. After screening, 51,637 participants were included in this study. The odds ratios and 95% confidence intervals (CIs) for undiagnosed diabetes were calculated using multivariable-adjusted logistic regression analyses.

Analyses showed that participants with a RHR of ≥90 bpm showed a 4.00- (95% CI: 2.77–5.77) and 3.21-times (95% CI: 2.01–5.14) higher prevalence of undiagnosed diabetes for men and women, respectively, than those with a RHR of <60 bpm. The linear dose-response analyses showed that each 10-bpm increment in RHR was associated with a 1.39- (95% CI: 1.32–1.48) and 1.28-times (95% CI: 1.19–1.37) higher prevalence of undiagnosed diabetes for men and women, respectively. In the stratified analyses, the positive association between RHR and the prevalence of undiagnosed diabetes was tended to be stronger among those who were younger (age: <40 years) and lean (BMI: <23 kg/m^2).

Conclusions: Elevated RHR was significantly associated with a higher prevalence of undiagnosed diabetes in Korean men and women, independent of demographic, lifestyle, and medical factors. Accordingly, the value of RHR as a clinical indicator and health marker, especially in reducing the prevalence of undiagnosed diabetes, is suggestible.

* Corresponding author. Department of Sport Industry Studies and Exercise Medicine Center for Diabetes and Cancer Patients, Yonsei University, Seoul, South Korea,

E-mail address: jjeon@yonsei.ac.kr (J.Y. Jeon).

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1. Introduction

Type 2 diabetes is a globally prevalent disease, affecting almost 500 million patients worldwide [1]. Its prevalence in Korea has been continually rising in recent years, from 9.7% in 2012 to 13.9% in 2020 [2]. Type 2 diabetes is also ranked as one of the leading causes of death among Koreans [3]. The considerable morbidity and mortality related to type 2 diabetes are attributed to its complications [4–8].

One important strategy to prevent diabetic complications is early diagnosis, leading to effective management [9,10]. However, the proportion of undiagnosed diabetes in type 2 diabetes is 37.4% in Korea [11] and 29.3% in US [12]. Undiagnosed diabetes is associated with an increased risk of diabetic complications [13]. Diabetic patients with more than two complications are reported to have a higher risk of death [14]. Since the delayed diagnosis of diabetes is a risk factor for an increased risk of diabetic complications, early detection of undiagnosed diabetes may be important to prevent complications and provide proper treatment.

Resting heart rate (RHR) has a potential to be used to indicate undiagnosed diabetes. Smoking [15], obesity [16], physical inactivity [17], low fitness level [18], and chronic stress [19] increase the risk of diabetes and these lifestyle factors also increase RHR [20–24]. A recent meta-analysis of 12 prospective cohort studies [25] reported that an increase in RHR of 10 bpm was associated with a 19% increased risk of type 2 diabetes in the fully adjusted model (hazard ratio: 1.19; 95% CI: 1.14–1.24). Kim et al. [26] reported that participants whose RHR increased by > 10 beats per minute (bpm) within 2 years had a 1.31-times higher incidence of diabetes than those whose RHR increased by < 5 bpm, even when the baseline blood glucose and hemoglobin A1c (HbA1c) levels were controlled. These studies showed a close relationship between higher RHR and increased risk of type 2 diabetes, suggesting that RHR may be used to predict undiagnosed diabetes.

Physiologically, there should be no difference in the association between RHR and the prevalence of diabetes whether diagnosed or not. However, one additional implication of RHR may apply for undiagnosed diabetes: a significant association between RHR and undiagnosed diabetes would provide evidence that RHR could be used to increase awareness of undiagnosed diabetes. To the best of our knowledge, only one study has examined the association between RHR and the prevalence of undiagnosed diabetes; however, this study included only the elderly population who lived in rural China [27]. With the lack of studies regarding RHR and the prevalence of undiagnosed diabetes, further research is needed, especially with a more generally applicable dataset. Therefore, we aimed to investigate the association between RHR and the prevalence of undiagnosed diabetes using large nationally representative data in Korea.

2. Methods

2.1. Study population

Data from the Korean National Health and Nutrition Examination Survey (KNHANES) over a span of 11 years (2008–2018) were used in this study. The KNHANES is a nationwide cross-sectional survey targeting non-institutionalized civilians conducted annually by the Korea Centers for Disease Control and Prevention. Statistics from this survey regarding the health and nutritional status of Koreans have been used as a resource for monitoring the health of the public, grasping health trends, and guiding policies. The KNHANES was first conducted in 1998 and has continued to this day: I (1998), II (2001), III (2005), Ⅳ (2007–2009), Ⅴ (2010–2012), Ⅵ (2013–2015), Ⅶ (2016–2018), and Ⅷ (2019–2021). It comprises three parts: health interviews, health examinations, and nutrition surveys. Trained medical teams perform all health examinations, and all equipment is regularly calibrated. Each year, 25 households from 192 regions are extracted as a probability sample, and approximately 10,000 household members aged ≥1 year are surveyed. Further details can be found in the KNHANES data resource profiles.

From the original KNHANES 2008–2018 sample (n = 72,093), we excluded participants with missing data on RHR, diabetes diagnosis, fasting glucose level, HbA1c level, or implausible RHR data (<40 bpm or >200 bpm); those with myocardial infarction, angina, or thyroid cancer pregnant women; and those with a fasting time of <8 h, resulting in a total of 51,637 remaining participants. This study was conducted in accordance with the Declaration of Helsinki and written informed consent was obtained from all participants. All procedures including study participants were approved by the Institutional Review Board (IRB) of the Korea Centers for Disease Control and Prevention (IRB no. 2007-02CON-04-P, 2008-04EXP-01-C, 2009-01CON-03-2C, 2010-02CON-21-C, 2011-02CON-06-C, 2012-01EXP-01-2C, 2013-07CON-03-4C, 2013-12EXP-03-5C, 2015-01-02-6C, 2018-01-03-P-A).

2.2. Measurement variables

The measurement methods for the KNHANES data used in this study were as follows. Weight (kg) and height (cm) were measured to calculate body mass index (BMI) (weight scale: GL-6000-20, G-tech, Korea; height scale: Seca 225, Seca, Germany) [28]. Self-reported questionnaires were used to assess the demographic characteristics, including smoking (never, past, or current), educational level (elementary school, middle school, high school, or complemented university), and income (low, middle-low, middle-high, or high). Physical activity was measured using the International Physical Activity Questionnaire (IPAQ, 2008–2013) and Global Physical Activity Questionnaire (GPAQ, 2014–2018). The scores for the IPAQ

(Cohen's kappa: 0.37–0.62) [29] and GPAQ (Cohen's kappa: 0.60–067) [30] translated into Korean were calculated and summed in minutes per week for each domain [28]. Blood was collected by experts using two SST tubes (8 mL) and two EDTA tubes (2 mL and 5 mL). We assessed fasting glucose, HbA1c, cholesterol, triglyceride, high density lipoprotein (HDL)- cholesterol, glutamic oxaloacetic transaminase (GOT), and glutamic pyruvic transaminase (GPT) levels through blood collection.

2.3. RHR measurements

After a 5-min rest in a seated position, experts measured the subjects' heart rate on their wrist for 15 s and multiplied by 4 to express it in heart rate per minute. The heart rate was measured again for an entire minute when the subjects showed an irregular, slow (<15 bpm), or rapid (>26 bpm) pulse.

2.4. Definition of diabetes

All subjects with a fasting blood glucose level of ≥126 mg/dL (n = 4931) or an HbA1c level of ≥6.5% (n = 5826), those previously diagnosed, and those who had received treatment or taken medications for diabetes were considered to have diabetes. Meanwhile, those with a fasting blood glucose level of ≥126 mg/dL (n = 1456) or an HbA1c level of ≥6.5% (n = 1497) but who had not been diagnosed yet were considered to have undiagnosed diabetes.

2.5. Statistical analyses

Initially, the characteristics of the study subjects were classified by sex (Tables 1 and 2). The subjects were sorted according to their RHR: <60, 60–69, 70–79, 80–89, and ≥90 bpm. To evaluate the demographic characteristics of the different RHR groups, we used descriptive analysis, frequency analysis, crossover analysis, chi-square test, and analysis of covariance (ANCOVA). The odds ratio (OR) for the prevalence of undiagnosed diabetes according to RHR groups was calculated using logistic regression. The logistic regression analysis was divided into four models. The first model was adjusted for age. The second model was adjusted for the same variable as in the first model, but additionally adjusted for educational level, income, drinking, smoking, total physical activity, BMI, menopause, and family history of diabetes. The third model was adjusted for the same variables as the second model but also for total cholesterol, triglyceride, HDL-cholesterol, GOT, and GPT levels. The fourth model was adjusted for the same variables as the third model but also for hypertension. Since hypertension may affect RHR and the prevalence of undiagnosed diabetes, a sensitivity analysis was conducted after excluding participants with hypertension. Stratified analyses between RHR and undiagnosed diabetes prevalence by potential effect modifiers were done as well. All analyses were performed using SPSS version 25 (IBM Corp.), and a *p*-value of <0.05 was considered statistically significant.

Supplementary analyses were performed to further understand the association between RHR and the prevalence of undiagnosed diabetes. In these analyses, participants were categorized according to quintiles of RHR rather than every 10-bpm increase. The results of these supplementary analyses are presented in Supplementary Tables 1–4. To assess the robustness of our findings, we also conducted a sensitivity analysis restricting to diagnosed diabetes cases and stratified analysis of non-diabetes, undiagnosed diabetes, and diagnosed diabetes (results shown in supplementary materials 5–8).

3. Results

The primary analyses included 51,637 participants, of whom 22,752 were men and 28,885 were women. Among them, we identified 2021 participants with undiagnosed diabetes (Men: 1,102, Women: 919). In our supplementary analysis, we identified 4454 participants with diabetes (Men: 2,257, Women: 2197; Fig. 1, Supplementary Table 6) among 56,091 participants (Men 25,009, Women: 31,082). Tables 1 and 2 show the characteristics of the five RHR groups (<60, 60–69, 70–79, 80–89, and ≥90 bpm). The trends observed between the RHR and some characteristics were as follows: The RHR was positively associated with the prevalence of undiagnosed diabetes, hypertension, smoking, physical activity, fasting blood glucose, blood pressure, HbA1c, total cholesterol, and triglyceride level but inversely associated with education and income level. The proportion of the participants with the lowest BMI (<23.0 kg/m^2) increased in the higher RHR groups.

Our analyses showed that the participants with RHR of ≥90 bpm had a 4.00- (95% CI: 2.77–5.77) and 3.21-times (95% CI: 2.01–5.14) higher prevalence of undiagnosed diabetes for men and women, respectively, than those with RHR of <60 bpm after adjusting for age, educational level, income, drinking, smoking, total physical activity, BMI, menopause, family history of diabetes, and hypertension. The linear dose-response analyses showed that with each 10-bpm increment in RHR, men and women were 1.39- (95% CI: 1.32–1.48) and 1.28-times (95% CI: 1.19–1.37) more likely to have undiagnosed diabetes, respectively (Table 3). Our supplementary analyses also showed a similar association between RHR and diagnosed diabetes (vs. undiagnosed diabetes). Participants with a RHR of ≥90 bpm had a 3.99- (95% CI: 3.04–5.23) and 3.13-times (95% CI: 2.28–4.31) higher prevalence of diagnosed diabetes for men and women, respectively, than those with RHR of <60 bpm (Supplementary Table 7).

The stratified analyses by potential effect modifiers, including age, BMI, smoking, physical activity, and hypertension, were performed for men and women separately. Men aged <40 years showed notably higher ORs as RHR increased. A similar tendency was observed for the age

Table 1 Characteristics of participants according to resting heart rate (Men).

Participants	Men	<60 bpm	60–69 bpm	70–79 bpm	80–89 bpm	≥90 bpm	*p*-trend
	n = 22,752	n = 2160	n = 11,498	n = 5434	n = 3117	n = 543	
Resting heart rate, bpm	74.1 ± 0.0	54.0 ± 0.1	64.1 ± 0.0	73.5 ± 0.0	82.7 ± 0.1	96.6 ± 0.1	<0.001
Undiagnosed diabetes, n (%)	1102 (4.8)	75 (3.5)	450 (3.9)	310 (5.7)	206 (6.6)	61 (11.2)	<0.001
Hypertension, n (%)	7492 (32.9)	722 (33.4)	3647 (31.7)	1772 (32.6)	1126 (36.1)	225 (41.4)	<0.001
Age, mean ± SD, n (%)	47.7 ± 16.0	52.0 ± 15.6	48.1 ± 15.7	46.4 ± 16.0	45.7 ± 16.3	46.9 ± 17.4	<0.001
<40 years	7377 (32.4)	483 (22.4)	3541 (30.8)	1942 (35.7)	1204 (38.6)	207 (38.1)	<0.001
40–59 years	10,956 (48.2)	1085 (50.2)	5729 (49.8)	2539 (46.7)	1381 (44.3)	222 (40.9)	
≥60 years	4419 (19.4)	592 (27.4)	2228 (19.4)	953 (17.5)	532 (17.1)	114 (21.0)	
BMI, kg/m^2, mean ± SE, n (%)	23.20 ± 0.03	24.00 ± 0.07	24.20 ± 0.03	24.20 ± 0.04	24.10 ± 0.06	23.60 ± 0.14	<0.001
<23	8344 (36.7)	809 (37.5)	4071 (35.4)	2005 (36.9)	1207 (38.7)	252 (46.4)	<0.001
23–24.9	5906 (26.0)	605 (28.0)	3131 (27.2)	1321 (24.3)	724 (23.2)	125 (23.0)	
≥25	8433 (37.1)	744 (34.4)	4260 (37.0)	2091 (38.5)	1173 (37.6)	165 (30.4)	
Missing	69 (0.3)	2 (0.1)	36 (0.3)	17 (0.3)	13 (0.4)	1 (0.2)	
Smoking, n (%)							<0.001
Never	4891 (21.5)	438 (20.3)	2505 (21.8)	1150 (21.2)	685 (22.0)	113 (20.8)	
Past	6533 (28.7)	753 (34.9)	3483 (30.3)	1483 (27.3)	703 (22.6)	111 (20.4)	
Current	10,763 (47.3)	916 (42.4)	5239 (45.6)	2659 (48.9)	1641 (52.6)	308 (56.7)	
Missing	565 (2.5)	53 (2.5)	271 (2.4)	142 (2.6)	88 (2.8)	11 (2.0)	
Educational level, n (%)							<0.001
Elementary school	3037 (13.3)	365 (16.9)	1470 (12.8)	681 (12.5)	411 (13.2)	110 (20.3)	
Middle school	2165 (9.5)	257 (11.9)	1108 (9.6)	485 (8.9)	264 (8.5)	51 (9.4)	
High school	8086 (35.5)	677 (31.3)	4068 (35.4)	1981 (36.5)	1160 (37.2)	200 (36.8)	
Complemented University	8428 (37.0)	758 (35.1)	4360 (37.9)	2020 (37.2)	1132 (36.3)	158 (29.1)	
Missing	1036 (4.6)	103 (4.8)	492 (4.3)	267 (4.9)	150 (4.8)	24 (4.4)	
Income, n (%)							<0.001
Low	5341 (23.5)	481 (22.3)	2519 (21.9)	1314 (24.2)	834 (26.8)	193 (35.5)	
Middle low	5682 (25.0)	524 (24.3)	2901 (25.2)	1342 (24.7)	773 (24.8)	142 (26.2)	
Middle high	5780 (25.4)	541 (25.0)	3009 (26.2)	1395 (25.7)	730 (23.4)	105 (19.3)	
High	5725 (25.2)	592 (27.4)	2970 (25.8)	1313 (24.2)	750 (24.1)	100 (18.4)	
Missing	224 (1.0)	22 (1.0)	99 (0.9)	70 (1.3)	30 (1.0)	3 (0.6)	
Physical activity, n (%)							<0.001
<150 min/week	12,240 (53.8)	1069 (49.5)	6090 (53.0)	2958 (54.4)	1781 (57.1)	342 (63.0)	
≥150 min/week	9496 (41.7)	993 (46.0)	4919 (42.8)	2218 (40.8)	1188 (38.1)	178 (32.8)	
Missing	1016 (4.5)	98 (4.5)	489 (4.3)	258 (4.7)	148 (4.7)	23 (4.2)	
SBP, mmHg, mean ± SE	121.5 ± 0.2	119.6 ± 0.4	120.2 ± 0.2	120.9 ± 0.2	121.6 ± 0.3	125.1 ± 0.7	<0.001
DBP, mmHg, mean ± SE	78.9 ± 0.1	75.3 ± 0.3	78.2 ± 0.1	79.5 ± 0.2	80.1 ± 0.2	81.2 ± 0.5	<0.001
Blood parameters							
Glucose level, mg/dL, mean ± SE	101.1 ± 0.2	95.6 ± 0.5	97.8 ± 0.2	100.3 ± 0.3	101.5 ± 0.4	110.5 ± 1.0	<0.001
HbA1c level, %, mean ± SE	5.68 ± 0.01	5.57 ± 0.02	5.59 ± 0.01	5.67 ± 0.01	5.69 ± 0.01	5.85 ± 0.03	<0.001
HbA1c level, mmol/mol, mean ± SE	38.51 ± 0.09	37.39 ± 0.18	37.63 ± 0.07	38.44 ± 0.11	38.62 ± 0.15	40.45 ± 0.35	<0.001
TC level, mg/dL, mean ± SE	192.3 ± 0.5	188.5 ± 0.9	191.0 ± 0.4	194.0 ± 0.6	193.9 ± 0.8	194.3 ± 1.8	<0.001
<200	14,172 (62.3)	1412 (65.4)	7264 (63.2)	3267 (60.1)	1897 (60.9)	332 (61.1)	<0.001
≥200	8579 (37.7)	748 (34.6)	4233 (36.8)	2167 (39.9)	1220 (39.1)	211 (38.9)	
Missing	10 (0.0)	0 (0.0)	10 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
TG level, mg/dL, mean ± SE	166.2 ± 1.7	136.2 ± 3.4	150.7 ± 1.4	169.7 ± 2.1	180.7 ± 2.9	193.7 ± 6.8	<0.001
<150	14,226 (62.5)	1510 (69.9)	7407 (64.4)	3221 (59.3)	1783 (57.2)	305 (56.2)	<0.001
≥150	8525 (37.5)	650 (30.1)	4090 (35.6)	2213 (40.7)	1334 (42.8)	238 (43.8)	
Missing	10 (0.0)	0 (0.0)	10 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
HDL-C level, mg/dL, mean ± SE	47.7 ± 0.1	48.3 ± 0.3	47.8 ± 0.1	47.3 ± 0.2	47.1 ± 0.2	48.1 ± 0.6	0.004
<40	16,583 (72.9)	1568 (72.6)	8484 (73.8)	3954 (72.8)	2196 (70.5)	381 (70.2)	0.003
≥40	6166 (27.1)	592 (27.4)	3013 (26.2)	1479 (27.2)	920 (29.5)	162 (29.8)	
Missing	30 (0.0)	0 (0.0)	10 (0.0)	10 (0.0)	10 (0.0)	0 (0.0)	
GOT level, IU/L, mean ± SE	25.6 ± 0.2	23.6 ± 0.4	24.3 ± 0.2	25.0 ± 0.2	26.3 ± 0.3	28.7 ± 0.8	<0.001
GPT level, IU/L, mean ± SE	27.6 ± 0.3	24.4 ± 0.6	25.8 ± 0.2	27.7 ± 0.4	29.4 ± 0.5	30.6 ± 1.1	<0.001
GOT/GPT ratio	1.10 ± 0.01	1.10 ± 0.02	1.10 ± 0.01	1.10 ± 0.01	1.10 ± 0.02	1.10 ± 0.05	0.259
<1	10,102 (44.4)	748 (34.6)	5018 (43.6)	2581 (47.5)	1518 (48.7)	237 (43.6)	<0.001
1–1.9	11,959 (52.6)	1335 (61.8)	6161 (53.6)	2696 (49.6)	1490 (47.8)	277 (51.0)	
≥2	690 (3.0)	77 (3.6)	318 (2.8)	157 (2.9)	109 (3.5)	29 (5.3)	
Missing	10 (0.0)	0 (0.0)	10 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	

Data are presented as means±SDs or SEs or n (%). All variables were tested using ANCOVA. ANCOVA was performed with age as the covariate. SD = standard deviation, SE = standard error, SBP = systolic blood pressure, DBP = diastolic blood pressure, TC = total cholesterol, TG = triglyceride, HDL-C = high density lipoprotein cholesterol, GOT = glutamic oxaloacetic transaminase, GPT = glutamic pyruvic transaminase.

Table 2 Characteristics of participants according to resting heart rate (Women).

Participants	Women	<60 bpm	60–69 bpm	70–79 bpm	80–89 bpm	≥90 bpm	*p*-trend
	n = 28,885	n = 1516	n = 13,792	n = 7885	n = 4825	n = 867	
Resting heart rate, bpm	74.10 ± 0.03	54.20 ± 0.08	64.40 ± 0.03	73.50 ± 0.03	82.70 ± 0.04	95.50 ± 0.10	<0.001
Undiagnosed diabetes, n (%)	919 (3.2)	36 (2.4)	402 (2.9)	243 (3.1)	193 (4.0)	45 (5.2)	<0.001
Hypertension, n (%)	7068 (24.5)	491 (32.4)	3483 (25.3)	1772 (22.5)	1097 (22.7)	225 (26.0)	<0.001
Age, mean ± SD, n (%)	48.0 ± 16.1	54.5 ± 14.3	49.4 ± 15.3	46.8 ± 16.2	44.4 ± 17.0	43.3 ± 17.8	<0.001
<40 years	9283 (32.1)	222 (14.6)	3679 (26.7)	2790 (35.4)	2156 (44.7)	436 (50.3)	<0.001
40–59 years	13,896 (48.1)	862 (56.9)	7330 (53.1)	3619 (45.9)	1810 (37.5)	275 (31.7)	
≥60 years	5706 (19.8)	432 (28.5)	2783 (20.2)	1476 (18.7)	859 (17.8)	156 (18.0)	
BMI, kg/m^2, mean ± SE, n (%)	23.20 ± 0.03	23.30 ± 0.09	23.20 ± 0.03	23.20 ± 0.04	23.20 ± 0.05	23.00 ± 0.12	0.430
<23	14,966 (51.8)	683 (45.1)	6940 (50.3)	4155 (52.7)	2674 (55.4)	514 (59.3)	<0.001
23–24.9	6074 (21.0)	376 (24.8)	3072 (22.3)	1596 (20.2)	896 (18.6)	134 (15.5)	
≥25	7782 (26.9)	451 (29.7)	3751 (27.2)	2117 (26.8)	1247 (25.8)	216 (24.9)	
Missing	63 (0.2)	6 (0.4)	29 (0.2)	17 (0.2)	8 (0.2)	3 (0.3)	
Smoking, n (%)							0.020
Never	25,130 (87.0)	1340 (88.4)	12,098 (87.7)	6808 (86.3)	4152 (86.1)	732 (84.4)	
Past	1233 (4.3)	54 (3.6)	576 (4.2)	341 (4.3)	216 (4.5)	46 (5.3)	
Current	1946 (6.7)	98 (6.5)	857 (6.2)	571 (7.2)	352 (7.3)	68 (7.8)	
Missing	576 (2.0)	24 (1.6)	261 (1.9)	165 (2.1)	105 (2.2)	21 (2.4)	
Educational level, n (%)							<0.001
Elementary school	6854 (23.7)	506 (33.4)	3403 (24.7)	1741 (22.1)	1027 (21.3)	177 (20.4)	
Middle school	2642 (9.1)	187 (12.3)	1423 (10.3)	669 (8.5)	307 (6.4)	56 (6.5)	
High school	9526 (33.0)	483 (31.9)	4475 (32.4)	2626 (33.3)	1628 (33.7)	314 (36.2)	
Complemented University	8824 (30.5)	296 (19.5)	4008 (29.1)	2550 (32.3)	1683 (34.9)	287 (33.1)	
Missing	1039 (3.6)	44 (2.9)	483 (3.5)	299 (3.8)	180 (3.7)	33 (3.8)	
Income, n (%)							<0.001
Low	6944 (24.0)	362 (23.9)	3071 (22.3)	1932 (24.5)	1317 (27.3)	262 (30.2)	
Middle low	7160 (24.8)	367 (24.2)	3409 (24.7)	1954 (24.8)	1217 (25.2)	213 (24.6)	
Middle high	7259 (25.1)	379 (25.0)	3515 (25.5)	2019 (25.6)	1140 (23.6)	206 (23.8)	
High	7242 (25.1)	393 (25.9)	3658 (26.5)	1904 (24.1)	1104 (22.9)	183 (21.1)	
Missing	280 (1.0)	15 (1.0)	139 (1.0)	76 (1.0)	47 (1.0)	3 (0.3)	
Physical activity, n (%)							<0.001
<150 min/week	18,217 (63.1)	927 (61.1)	8509 (61.7)	5070 (64.3)	3119 (64.6)	592 (68.3)	
≥150 min/week	9652 (33.4)	547 (36.1)	4810 (34.9)	2528 (32.1)	1523 (31.6)	244 (28.1)	
Missing	1016 (3.5)	42 (2.8)	473 (3.4)	287 (3.6)	183 (3.8)	31 (3.6)	
SBP, mmHg, mean ± SE	116.2 ± 0.2	115.7 ± 0.5	115.3 ± 0.1	115.4 ± 0.2	116.2 ± 0.3	118.2 ± 0.6	<0.001
DBP, mmHg, mean ± SE	73.6 ± 0.1	70.7 ± 0.3	73.4 ± 0.1	74.0 ± 0.1	74.6 ± 0.2	75.4 ± 0.4	<0.001
Blood parameters							
Glucose level, mg/dL, mean ± SE	95.7 ± 0.2	91.3 ± 0.5	93.7 ± 0.2	95.0 ± 0.2	97.3 ± 0.3	101.2 ± 0.7	<0.001
HbA1c level, % mean ± SE	5.60 ± 0.01	5.55 ± 0.02	5.57 ± 0.01	5.59 ± 0.01	5.63 ± 0.01	5.67 ± 0.02	<0.001
HbA1c level, mmol/mol, mean ± SE	37.69 ± 0.07	37.12 ± 0.19	37.35 ± 0.06	37.53 ± 0.08	38.03 ± 0.10	38.43 ± 0.25	<0.001
TC level, mg/dL, mean ± SE	193.2 ± 0.4	191.1 ± 1.1	193.1 ± 0.3	194.5 ± 0.5	194.2 ± 0.6	193.4 ± 1.5	0.022
<200	17,836 (61.7)	885 (58.4)	8370 (60.7)	4887 (62.0)	3126 (64.8)	568 (65.5)	<0.001
≥200	11,044 (38.2)	631 (41.6)	5418 (39.3)	2998 (38.0)	1699 (35.2)	298 (34.4)	
Missing	50 (0.0)	0 (0.0)	40 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	
TG level, mg/dL, mean ± SE	113.4 ± 0.9	101.3 ± 2.6	108.5 ± 0.8	114.4 ± 1.0	119.9 ± 1.4	123.1 ± 3.4	<0.001
<150	23,211 (80.4)	1231 (81.2)	11,176 (81.0)	6335 (80.3)	3780 (78.3)	689 (79.5)	0.001
≥150	5669 (19.6)	285 (18.8)	2612 (18.9)	1550 (19.7)	1045 (21.7)	177 (20.4)	
Missing	50 (0.0)	0 (0.0)	40 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)	
HDL-C level, mg/dL, mean ± SE	54.1 ± 0.1	55.0 ± 0.4	54.7 ± 0.1	54.5 ± 0.2	53.7 ± 0.2	52.6 ± 0.5	<0.001
<50	16,635 (57.6)	853 (56.3)	8043 (58.3)	4553 (57.7)	2705 (56.1)	481 (55.5)	0.034
≥50	12,240 (42.4)	663 (43.7)	5743 (41.6)	3330 (42.2)	2119 (43.9)	385 (44.4)	
Missing	10 (0.0)	0 (0.0)	60 (0.0)	20 (0.0)	10 (0.0)	1 (0.1)	
GOT level, IU/L, mean ± SE	20.7 ± 0.1	20.5 ± 0.3	20.5 ± 0.1	20.4 ± 0.1	21.0 ± 0.2	21.0 ± 0.4	0.016
GPT level, IU/L, mean ± SE	17.4 ± 0.2	16.9 ± 0.4	17.4 ± 0.1	17.2 ± 0.2	18.1 ± 0.2	17.5 ± 0.6	0.016
GOT/GPT ratio	1.30 ± 0.00	1.40 ± 0.01	1.30 ± 0.00	1.30 ± 0.01	1.30 ± 0.01	1.40 ± 0.02	0.072
<1	4928 (17.1)	244 (16.1)	2307 (16.7)	1365 (17.3)	873 (18.1)	139 (16.0)	0.139
1–1.9	22,190 (76.8)	1182 (78.0)	10,666 (77.3)	6033 (76.5)	3651 (75.7)	658 (75.9)	
≥2	1759 (6.1)	90 (5.9)	814 (5.9)	486 (6.2)	300 (6.2)	69 (8.0)	
Missing	80 (0.0)	0 (0.0)	50 (0.0)	10 (0.0)	10 (0.0)	1 (0.1)	

Data are presented as means±SDs or SEs or n (%). All variables were tested using ANCOVA. ANCOVA was performed with age as the covariate. SD = standard deviation, SE = standard error, SBP = systolic blood pressure, DBP = diastolic blood pressure, TC = total cholesterol, TG = triglyceride, HDL-C = high density lipoprotein cholesterol, GOT = glutamic oxaloacetic transaminase, GPT = glutamic pyruvic transaminase.

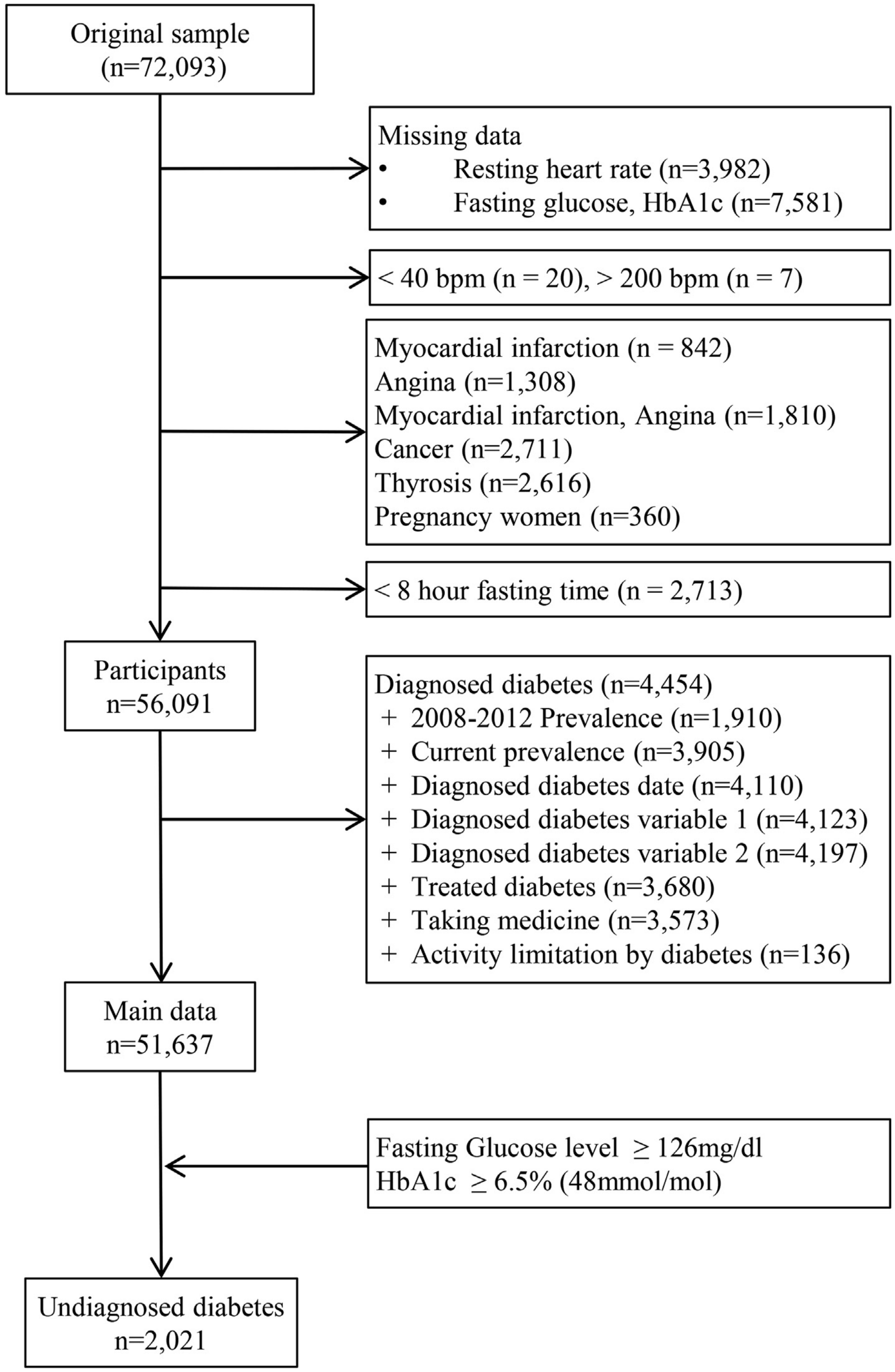

Figure 1 Flowchart of the study sample

groups in women but was less dramatic than that in men. Nevertheless, a positive association between RHR and the prevalence of undiagnosed diabetes was observed in all age groups. Men with BMI of <23 kg/m^2 showed the greatest increase in the OR per 10-bpm RHR increment. All BMI groups for both sexes showed a positive association between the RHR and the prevalence of undiagnosed diabetes. The association appeared stronger among those without hypertension: Those with RHR of ≥90 bpm showed a 5.93- (95% CI: 3.40–10.33) and 3.59-times (95% CI: 1.65–7.82) higher prevalence of undiagnosed diabetes than those with RHR of <60 bpm for men and women, respectively (Table 4).

4. Discussion

Based on a nationally representative sample of 51,637 individuals from the KNHANES, a positive association

Table 3 Association between resting heart rate and the prevalence of undiagnosed diabetes.

RHR (bpm)	Number of cases (%)	Unadjusted OR (95% CI)	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)	Model 4 OR (95% CI)
Men (n = 22,752)						
<60 bpm	75/2160 (3.5)	1	1	1	1	1
60–69 bpm	450/11,498 (3.9)	1.13 (0.88–1.45)	1.29 (1.01–1.66)	1.25 (0.97–1.61)	1.19 (0.92–1.54)	1.19 (0.92–1.53)
70–79 bpm	310/5434 (5.7)	1.68 (1.30–2.18)	2.03 (1.57–2.63)	1.96 (1.51–2.55)	1.81 (1.39–2.35)	1.78 (1.37–2.32)
80–89 bpm	206/3117 (6.6)	1.97 (1.50–2.58)	2.43 (1.85–3.19)	2.48 (1.88–3.27)	2.25 (1.70–2.97)	2.19 (1.65–2.89)
≥90 bpm	61/543 (11.2)	3.52 (2.47–5.00)	4.16 (2.91–5.95)	4.51 (3.13–6.49)	4.18 (2.90–6.04)	4.00 (2.77–5.77)
p for linear trend		<0.001	<0.001	<0.001	<0.001	<0.001
Per 10-bpm increment in the RHR		1.35 (1.27–1.44)	1.41 (1.33–1.50)	1.44 (1.35–1.53)	1.41 (1.32–1.50)	1.39 (1.31–1.48)
Women (n = 28,885)						
<60 bpm	36/1516 (2.4)	1	1	1	1	1
60–69 bpm	402/13,792 (2.9)	1.23 (0.87–1.74)	1.50 (1.06–2.12)	1.50 (1.06–2.14)	1.39 (0.98–1.98)	1.40 (0.98–1.99)
70–79 bpm	243/7885 (3.1)	1.31 (0.92–1.86)	1.72 (1.21–2.46)	1.73 (1.21–2.49)	1.58 (1.10–2.28)	1.60 (1.11–2.30)
80–89 bpm	193/4825 (4.0)	1.71 (1.19–2.46)	2.44 (1.70–3.51)	2.50 (1.72–3.62)	2.20 (1.52–3.19)	2.19 (1.51–3.19)
≥90 bpm	45/867 (5.2)	2.25 (1.44–3.52)	3.28 (2.09–5.16)	3.56 (2.24–5.68)	3.29 (2.06–5.26)	3.21 (2.01–5.14)
p for linear trend		<0.001	<0.001	<0.001	<0.001	<0.001
Per 10-bpm increment in the RHR		1.19 (1.11–1.27)	1.29 (1.21–1.38)	1.31 (1.22–1.41)	1.28 (1.19–1.38)	1.28 (1.19–1.37)

Data are presented as n (%) or ORs (95% CIs). Model 1 = adjusted for age; Model 2 = adjusted for model 1 variables plus educational level, income, drinking, smoking, total physical activity, BMI, menopause, and family history of diabetes; Model 3 = adjusted for model 2 variables plus cholesterol level, triglyceride level, high density lipoprotein cholesterol level and GOT/GPT ratio; Model 4 = adjusted for model 3 variables plus hypertension. RHR = resting heart rate, OR = odds ratio, GOT = glutamic oxaloacetic transaminase, GPT = glutamic pyruvic transaminase.

between RHR and the prevalence of undiagnosed diabetes was observed. Participants with RHR of ≥90 bpm had a 4.00- and 3.21-times higher prevalence of undiagnosed diabetes for men and women, respectively, than those with RHR of <60 bpm. The association between RHR and the prevalence of undiagnosed diabetes remained significant after adjusting for age, educational level, income, drinking, smoking, total physical activity, BMI, menopause, family history of diabetes, cholesterol, triglyceride, HDL-cholesterol, GOT/GPT ratio and hypertension. When stratified by potential effect modifiers, we consistently found a positive association between RHR and the prevalence of undiagnosed diabetes regardless of age, BMI, smoking, physical activity and hypertension. Although there were no significant interactions, the positive association tended to be stronger in younger or leaner individuals.

The main findings of this study are consistent with those of previous studies reporting the association between RHR and the prevalence of diabetes. Aune et al. [31] conducted a dose-response meta-analysis of 10 cohort studies on RHR and the incidence of type 2 diabetes. In these 10 cohort studies, 5628 cases and 119,915 participants were included. In the dose-response analysis, the relative risk of type 2 diabetes was 1.20 (95% CI: 1.07–1.34, I^2 = 93%) per 10-bpm increment in RHR. Except for the incidence of type 2 diabetes, our study showed similar results. The OR for the prevalence of undiagnosed diabetes per 10-bpm RHR increment was 1.39 (95% CI: 1.31–1.48) and 1.28 (95% CI: 1.19–1.37) for men and women, respectively. Therefore, higher RHR could be considered a valuable measurement to predict undiagnosed diabetes.

The stratified analyses showed that the association between RHR and the prevalence of undiagnosed diabetes held true in all subgroups. Lee et al. [25] analyzed the incidence of type 2 diabetes associated with the RHR stratified by risk factors in US men. Even considering different diagnostic BMI criteria in Korea and US, the relationship between RHR and the risk of diabetes was stronger in the lowest BMI group of these countries. In addition, there was a stronger positive relationship found between RHR and the risk of diabetes in non-hypertensive cases than in hypertensive cases.

Although there was no statistically significant interaction between age groups, we tended to observe a stronger association between RHR and undiagnosed diabetes in those aged <40 years, with 1.66 times and 1.57 times higher odds of having undiagnosed diabetes for every 10-bpm increment of RHR men and women, respectively. Furthermore, The proportion of participants unaware of their diabetes was also highest among the youngest age group (<40 years); 64.7% of men and 47.7% of women of those with diabetes are unaware they have diabetes. According to our data, diabetes unawareness is 2–3 times greater among participants younger than 40 years compared to participants older than 40 years, implicating that RHR could be a good indicator for undiagnosed diabetes, especially among the young population (Supplementary Table 5). Given that we had relatively small number of cases in younger group, study with larger sample size are needed to examine the role of age in the association between RHR and undiagnosed diabetes.

As our study is cross-sectional, we can only speculate that the increase in RHR would precede the onset of

Table 4 Stratified analyses on the association between resting heart rate and the prevalence of undiagnosed diabetes by potential effect modifiers.

Undiagnosed diabetes	Number of cases (%)	<60 bpm Ref	60–69 bpm OR (95% CI)	70–79 bpm OR (95% CI)	80–89 bpm OR (95% CI)	≥90 bpm OR (95% CI)	10-bpm increment OR (95% CI)	*p* for interaction
Men (n = 22,752)								
Age								0.430
<40 years	101/7377 (1.4)	1	4.16 (0.56–30.86)	5.52 (0.74–41.13)	9.54 (1.28–71.31)	19.66 (2.43 –159.37)	1.66 (1.34–2.04)	
40–59 years	681/10,956 (6.2)	1	1.22 (0.87–1.72)	2.00 (1.41–2.85)	2.34 (1.62–3.40)	4.12 (2.49–6.82)	1.42 (1.31–1.54)	
≥60 years	320/4419 (7.2)	1	1.03 (0.70–1.54)	1.45 (0.95–2.22)	1.81 (1.14–2.86)	3.38 (1.81–6.30)	1.33 (1.18–1.49)	
BMI								0.610
<23 kg/m^2	250/8344 (3.0)	1	1.17 (0.70–1.96)	1.59 (0.93–2.74)	1.94 (1.10–3.42)	6.28 (3.31–11.90)	1.47 (1.29–1.66)	
23–24.9 kg/m^2	261/5906 (4.4)	1	1.18 (0.74–1.89)	1.42 (0.86–2.35)	1.93 (1.13–3.30)	3.06 (1.40–6.67)	1.28 (1.12–1.46)	
≥25 kg/m^2	586/8433 (6.9)	1	1.21 (0.83–1.76)	2.09 (1.42–3.08)	2.47 (1.65–3.72)	2.78 (1.54–5.01)	1.40 (1.27–1.53)	
Smoking								0.670
Never	174/4891 (3.6)	1	1.95 (0.88–4.34)	3.01 (1.32–6.89)	4.75 (2.05–11.03)	9.25 (3.28–26.06)	1.63 (1.38–1.92)	
Previous	391/6533 (6.0)	1	1.15 (0.78–1.70)	1.67 (1.11–2.52)	2.22 (1.43–3.44)	3.54 (1.81–6.92)	1.37 (1.23–1.53)	
Current	492/10,763 (4.6)	1	1.01 (0.68–1.48)	1.52 (1.02–2.26)	1.70 (1.12–2.58)	3.01 (1.79–5.09)	1.32 (1.21–1.45)	
Physical activity								0.541
<150 min/week	620/12,240 (5.1)	1	1.11 (0.79–1.57)	1.66 (1.16–2.38)	2.21 (1.52–3.19)	3.66 (2.27–5.91)	1.41 (1.29–1.53)	
≥150 min/week	399/9496 (4.2)	1	1.41 (0.93–2.14)	2.09 (1.35–3.24)	2.41 (1.50–3.86)	4.64 (2.42–8.92)	1.39 (1.24–1.55)	
Hypertension								0.158
No	492/15,260 (3.2)	1	1.34 (0.90–1.99)	2.08 (1.39–3.13)	2.72 (1.77–4.17)	5.93 (3.40–10.33)	1.49 (1.35, 1.64)	
Yes	610/7492 (8.1)	1	1.07 (0.77–1.50)	1.57 (1.11–2.22)	1.77 (1.23–2.56)	2.97 (1.83–4.84)	1.31 (1.20, 1.42)	
Women (n = 28,885)								
Age								0.956
<40 years	73/9283 (0.8)	1	0.49 (0.06–4.11)	1.27 (0.16–10.08)	1.86 (0.24–14.67)	1.64 (0.18–15.10)	1.57 (1.20–2.04)	
40–59 yearas	489/13,896 (3.5)	1	1.65 (0.99–2.74)	1.87 (1.10–3.16)	2.92 (1.70–5.01)	4.18 (2.05–8.49)	1.34 (1.21–1.49)	
≥60 years	357/5706 (6.3)	1	1.29 (0.78–2.14)	1.41 (0.84–2.39)	1.76 (1.02–3.02)	3.38 (1.72–6.66)	1.24 (1.11–1.39)	
BMI								0.959
<23 kg/m^2	161/14,966 (1.1)	1	1.53 (0.65–3.58)	1.33 (0.55–3.24)	2.77 (1.14–6.68)	6.25 (2.35–16.57)	1.45 (1.24–1.70)	
23–24.9 kg/m^2	191/6074 (3.1)	1	1.37 (0.68–2.76)	1.31 (0.63–2.75)	2.20 (1.04–4.64)	1.12 (0.29–4.29)	1.18 (1.00–1.38)	
≥25 kg/m^2	567/7782 (7.3)	1	1.38 (0.87–2.21)	1.81 (1.13–2.92)	2.08 (1.27–3.41)	2.93 (1.57–5.46)	1.26 (1.15–1.39)	
Smoking								0.554
Never	805/25,130 (3.2)	1	1.34 (0.92–1.93)	1.52 (1.04–2.23)	2.06 (1.39–3.05)	3.23 (1.97–5.30)	1.27 (1.18–1.37)	
Previous	27/1233 (2.2)	1	1.97 (0.23–17.15)	1.39 (0.15–12.82)	2.92 (0.30–28.10)	7.05 (0.53–94.30)	1.36 (0.87–2.12)	
Current	54/1946 (2.8)	1	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	1.44 (1.05–1.97)	
Physical activity								0.304
<150 min/week	610/18,217 (3.3)	1	1.36 (0.90–2.05)	1.41 (0.92–2.17)	1.83 (1.18–2.84)	3.09 (1.77–5.38)	1.21 (1.11–1.33)	
≥150 min/week	261/9652 (2.7)	1	1.68 (0.77–3.68)	2.30 (1.03–5.11)	3.74 (1.67–8.39)	4.60 (1.74–12.16)	1.46 (1.28–1.68)	
Hypertension								0.408
No	423/21,817 (1.9)	1	1.57 (0.86–2.86)	2.11 (1.15–3.87)	2.85 (1.53–5.30)	3.59 (1.65–7.82)	1.35 (1.21–1.51)	
Yes	496/7068 (7.0)	1	1.31 (0.84–2.03)	1.29 (0.81–2.05)	1.84 (1.15–2.95)	3.17 (1.75–5.72)	1.23 (1.12–1.36)	

Data are presented as n (%). Adjusted for age, educational, income, drinking, smoking, total physical activity, BMI, menopause, family history of diabetes, cholesterol level, triglyceride level, high density lipoprotein cholesterol level, and GOT/GPT ratio, and hypertension. OR = odds ratio, GOT = glutamic oxaloacetic transaminase, GPT = glutamic pyruvic transaminase diabetes. It is well known that insulin resistance, characterized by hyperinsulinemia, precedes onset of diabetes. Hyperinsulinemia would increase sympathetic tone [32] which results in increase in blood pressure as well as heart rate [33]. Further, sympathetic overactivity reduces skeletal muscle blood flow by vasoconstricting skeletal muscle [33], impairing glucose uptake in skeletal muscle [34]. Since insulin resistance and hyperinsulinemia can also increase heart rate, higher RHR may precede the onset of diabetes as well.

Aerobic exercise is one of the most effective ways to reduce insulin resistance, prevent and manage diabetes. Interestingly, aerobic exercise also reduces resting heart rate since aerobic exercise training increase in cardiac muscle contractility, ejection fraction and cardiac output. Therefore, RHR could also reflect cardiopulmonary fitness and could be one of the reasons for strong association between RHR and prevalence of diabetes [22].

This study had several limitations. First, measuring RHR could have the possibility of error. Factors, such as white-coat hypertension, may have influenced the values measured. However, regarding human error, RHR was measured by a trained medical team and was measured again when the participants showed signs of an unusual heart rate. Second, since we used cross-sectional data, we were not able to observe causality of undiagnosed diabetes. The strength of this study is the characteristics of the data used (i.e., 11-year KNHANES data). The KNHANES data are nationally representative data used for the development of Korean standards regarding health and nutrition and international comparison studies and are being used in a growing number of research studies. Another strength of our study is the relatively large data sample, which allowed us to derive meaningful results from the analyses, including the stratified analysis according to potential effect modifiers.

5. Conclusion

We demonstrated that RHR and the prevalence of undiagnosed diabetes are closely related in both men and women. Their correlation was independent of age, educational level, income, drinking, smoking, total physical activity, BMI, menopause, total cholesterol, triglyceride, HDL-cholesterol, GOT, GPT levels, and hypertension. Considering the need for an indicator of diabetes for undiagnosed patients, poor blood glucose control rate, and ease of measuring and evaluating RHR, it is worth noting the potential of RHR as a non-invasive clinical tool. We believe that further studies are needed among patients with undiagnosed diabetes, considering their proportion of the total population with diabetes.

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Author contributions

“SHH, JHM, JYB, DHL, BWA, HDL, HJK researched data. DHP, SYG, DHL, YHL, ESK, JYJ wrote the manuscript and researched data. YHL, ESK, HDL, HJK, SHJ, BWA, MKL reviewed/edited the manuscript.

Declaration of competing interest

The authors declare that they have no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.numecd.2022.09.012.

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