ABSTRACT

Objectives  The hypertriglyceridaemic waist (HTGW) phenotype, an indicator to assess metabolic syndrome, could be a useful predictive marker for the risk of acute pancreatitis. This study aimed to evaluate the association between the HTGW phenotype and the risk of acute pancreatitis with a nationwide population-based cohort.

Design  A retrospective, nationwide cohort study.

Setting  Registry of health check-up result from Korean National Health Insurance Service.

Participants  A total of 3912551 adults who underwent health checkups under the National Health Insurance Service in 2009 were enrolled in this study.

Interventions  Subjects with both increased waist circumference (WC) and elevated blood triglyceride concentrations were defined as the HTGW phenotype. The participants were divided into four groups, classified as NWNT (normal WC-normal triglycerides), EWNT (elevated WC-normal triglycerides), NWET (normal WC-elevated triglycerides) and HTGW. The WC triglyceride index (WTI) is a quantitative indicator of the HTGW phenotype which is calculated by multiplying WC (cm) by triglyceride levels (mmol/L).

Primary outcome measure  The subjects were followed until 31 December 2018. The adjusted HRs of acute pancreatitis in each group were estimated.

Results  During the follow-up, there were a total of 8933 cases of acute pancreatitis that occurred. The incidence of acute pancreatitis in all subjects was 0.278 per 1000 person-years. The HTGW group had the highest incidence (0.444), followed by the NWET (0.381), and EWNT (0.316) groups. The HTGW group had a significant higher incidence of acute pancreatitis than the NWNT groups (HR 1.364 (95% CI 1.279 to 1.454)). The risk of acute pancreatitis steadily increased as the WTI increased (HR 1.847 (95% CI 1.657 to 2.058) in 10th decile).

Conclusions  The HTGW phenotype is confirmed to be an independent risk factor that increases the risk of acute pancreatitis.

STRENGTHS AND LIMITATIONS OF THIS STUDY

This study was based on large-scale nationwide cohort so that representing the entire Korean population.

Despite being a big data study, detailed clinical parameters such as anthropometric variables, medical history, lifestyle and blood chemistry results were available which can affect the occurrence of acute pancreatitis (AP).

Relatively long-term follow-up of 9 years using a relatively simple indicator can reveal risk factors for diseases with relatively low incidence.

The diagnosis of AP could have been inaccurate or omitted in some subjects which is the fundamental limitations of claims and health check-up data.

It was impossible to classify the causes of AP, as well as the severity of AP.

INTRODUCTION

Acute pancreatitis (AP) is known as one of the major causes of hospitalisation for gastrointestinal diseases, and hospitalisations for AP are gradually increasing. The main two causes of AP are gallstone disease and alcohol consumption. Other various triggers such as hypertriglyceridaemia, genetic factors and environmental toxin can also cause AP. However, there are a significant number of cases in which the provoking cause cannot be found, and various risk factors have been identified in addition to the triggering factors mentioned above. The occurrence of pancreatitis in comparison to the number of people with gallstone disease or morbid alcohol consumption is rare, and therefore, an unknown necessary condition may be the cause for pancreatitis. By identifying such conditions, the mechanism of pancreatitis...
can be further elucidated. Also, removing such factors in advance may help prevent pancreatitis.

Metabolic syndrome, including obesity, is considered as one of the major risk factors for AP.7–10 The recent surge in the obese population and the increased incidence of AP are estimated to have some level of association.7 The concept of hypertriglyceridaemic waist (HTGW) phenotype as an indicator to assess metabolic syndrome was defined by Lemieux et al11 and has recently gained increasing attention. It can be used as a simple tool to estimate the risk of cardiovascular disease,12 13 atherosclerosis14 and visceral fat.15 16 It is also significantly correlated with early diabetic nephropathy in type 2 patients with diabetes.17 In a community-based cohort study conducted in China, it was independently associated with an increased risk of chronic kidney disease (CKD) prevalence and development in the elderly, aged ≥60 years.18 The HTGW phenotype is determined by measuring two components: the waist circumference (WC) and blood triglyceride levels. Also, it is anticipated to be a predictive marker for the risk of AP. However, there is limited research investigating the association between HTGW and AP.

Korea has a national health insurance system and provides a health check-up programme for all citizens. The health check-up includes anthropometric data such as height, weight and WC, and various blood tests including blood triglyceride levels. Therefore, in this nationwide population-based study, we aimed to evaluate the association between the HTGW phenotype and the risk of AP.

MATERIALS AND METHODS

Data source
The National Health Insurance Service (NHIS) is the single national insurer responsible for compulsory and comprehensive medical care that covers 97% of the total Korean population, and also offers medical benefits for the remaining 3% composed of low-income earners.19 The NHIS database includes information regarding subscribers’ demographic data (age, sex, income level, etc), use of medical facilities (all claims of both inpatient and outpatient medical expenses), and diagnosis codes according to the International Classification of Diseases 10th Revision (ICD-10). The NHIS also offers general health checkups for all subscribers 20 years and older, or all employers regardless of age. This health check-up includes anthropometric data, a self-administered questionnaire on medical history or health-related behaviours (smoking, alcohol consumption, physical activity), and blood and urine biochemical tests. This database is considered as representative of the Korean population and can be used for research through anonymisation and deidentification).20

Study population
This study included patients who underwent a national health check-up in 2009. The total number of examinees in 2009 was about 10 million, and based on such figures, we performed a cohort study by receiving data that sampled about 40% of the examinees through a standardisation process in accordance with the data provision regulation of the NHIS. Eligible criteria included examinees aged 20 years or older. We established a wash-out period as long as possible by excluding subjects with a diagnosis code of AP from 2002 to the time of the health check-up. We also set a lag period of 1 year, and thus subjects diagnosed with AP within a year of the health check-up were also excluded. Further exclusion criteria included subjects with missing variables. During the follow-up period, the diagnosis of pancreatitis was established as a case in which hospitalisation was confirmed along with the ICD-10 code of AP (K85.x) as principal diagnosis. The follow-up of all subjects continued until 31 December 2018. The flowchart regarding the selection process of study subjects is presented in online supplemental figure 1.

Clinical parameters
Anthropometric measurements of the subjects during health examinations were performed by medical professionals. The parameters measured were height, weight, WC, and systolic and diastolic blood pressures. Detailed information of the subjects’ lifestyles was obtained through standardised self-reported questionnaires. Subjects were classified as non-smokers, former smokers or current smokers according to their smoking status. Subjects consuming more than 30 g of alcohol per day were classified as heavy drinkers.21 Regular physical activity was defined as performing a moderate physical activity for more than 30 min at least five times a week or vigorous physical activity for more than 20 min at least three times a week.22 Comorbidities of subjects (hypertension, diabetes, dyslipidaemia, coronary artery disease and cerebrovascular disease) were identified by combining data from past medical history questionnaires, ICD-10 codes and prescription database. Blood sampling was performed after overnight fasting, and serum glucose, total cholesterol, triglyceride, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, aspartate aminotransferase (AST) alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT) and creatinine concentrations were measured. Estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease Study equation. CKD was defined as eGFR less than 60 mL/min/1.73 m2.23

Definition of the HTGW phenotype and WC triglyceride index
In this study, hypertriglyceridaemia was defined as 150 mg/dL (1.7 mmol/L) or higher in reference to the existing guidelines,24–26 and abdominal obesity was defined as WC ≥90 cm in males and ≥85 cm in females based on the study using Korean Health and Nutritional Examination Survey which is a cross-sectional health survey of a nationally representative sample of Koreans.27 Those with both elevated WC and elevated blood triglyceride concentrations were defined as the HTGW phenotype.11 The subjects were divided into four groups, classified as NWNT (normal WC-normal cholesterol, normal triglyceride, normal weight, normal obesity) and other groups.
triglycerides), EWNT (elevated WC-normal triglycerides), NWET (normal WC-elevated triglycerides) and HTGW (elevated WC-elevated triglycerides).\(^1\) The WC triglyceride index (WTI) is a quantitative indicator of the HTGW phenotype. WTI was calculated as follows: \(WTI (cm \times mmol/L) = WC (cm) \times TG (mmol/L)\).\(^1\)

**Statistical analysis**
Continuous variables were expressed as means±SD or median and IQR for variables that did not follow normal distribution. Categorical variables were presented as numbers and percentages. The incidence rate of AP was calculated by dividing the number of incident cases in each group by the total follow-up period of per 1000 person-years. The Cox proportional hazards model evaluated HRs and 95% CI values for AP. A multivariable-adjusted proportional hazards model was applied: (1) model 1 was adjusted for age, sex, smoking, alcohol consumption, regular physical activity and income, (2) model 2 was further adjusted for diabetes, hypertension, CKD and chronic pancreatitis and (3) model 3 was further adjusted for coronary artery disease and cerebrovascular disease. To assess the potential multicollinearity between the variables, variance inflation factor (VIF) was calculated and the results are presented in online supplemental table 1. No variable exhibited a VIF greater than 2. The cox.zph procedure was employed to assess the proportional hazards assumption through a test of Schoenfeld residuals (online supplemental table 2). When analysing the risk of AP according to WC, the reference group was 85–90 cm for males and 80–85 cm for females used the normal WC cut-off for Koreans. The remaining participants were divided into groups based on 5 cm intervals. Regarding triglyceride levels, a reference group was established as less than 100 mg/dL, and the remaining participants were divided into groups based on 50 mg/dL intervals. When analysing the risk of AP in the HTGW phenotype, the HR was calculated using the NWNT group as the reference group among the four groups. When analysing the risk of AP based on WTI, all patients were divided into 10 deciles according to WTI, and the HR was estimated using the first decile as the reference group. Statistical analyses were performed using Statistical Analysis System (SAS) V.9.4 (SAS Institute), and a p value less than 0.05 was considered statistically significant.

**Patient and public involvement**
No patient involved.

**RESULTS**

**Baseline characteristics of study population**
The baseline characteristics of the study population categorised by blood triglyceride levels and WC are described in table 1. Regarding the group with elevated triglyceride (NWET and HTGW), the proportion of males tended to be higher, and the proportion of current smokers and heavy drinkers was also higher. The group with increased WC (EWNT and HTGW) had a higher mean age and a higher prevalence of diabetes and hypertension. In addition, the prevalence of cardiovascular disease, cerebrovascular disease and CKD also tended to be higher in this group. In terms of body measurement, mean body mass index, WC and systolic blood pressure were higher in the group with increased WC (EWNT and HTGW). Also, blood test results showed fasting glucose, total cholesterol, triglyceride, AST, ALT and GGT levels to gradually increase in the order of NWNT, EWNT, NWET and HTGW.

**Risk of AP in the HTGW phenotype**
During the follow-up, a total of 8933 APs occurred and the incidence of AP in all subjects were 0.278 per 1000 person-year. The incidence rate of AP showed a tendency to increase from 0.213 to 0.439 as the WC increased, and also rose from 0.195 to 0.470 with elevated blood triglyceride levels (table 2). Regarding to the four categories, HTGW had the highest incidence (0.444, HR 1.364 (95% CI 1.279 to 1.454)), followed by the NWET (0.381, HR 1.358 (95% CI 1.29 to 1.429)) and EWNT (0.316, HR 1.08 (95% CI 1.007 to 1.158)) groups. The NWNT group had the lowest incidence rate (0.211, reference) (table 2 and figure 1). The HRs of AP which were adjusted for age, sex, smoking, alcohol consumption, regular exercise and income (model 1), further adjusted for diabetes, hypertension, CKD and chronic pancreatitis (model 2) and further adjusted for coronary artery disease, and cerebrovascular disease (model 3) gradually increased according to elevated WCs and triglyceride levels. It also showed incremental increase in the order of NWNT, EWNT, NWET and HTGW.

**Risk of AP according to WTI**
The mean WTI for each group was NWNT 75.69±28.87, EWNT 106.51±45.12, NWET 216.81±130.37 and HTGW 266.47±130.23. When divided by deciles, NWNT corresponds to the 4th decile, EWNT corresponds to the 6th decile, NWET corresponds to the 9th decile and HTGW corresponds to the 10th decile. As the WTI increased, the incidence rate of AP increased from 0.138 to 0.533. The HR of AP in each decile also increased along with increased WTI. The HR in the fifth decile is significantly higher than that in the first decile (reference). And in the eighth decile, the HR surged along with the increase of WTI, even after adjusting for age, sex, smoking, alcohol consumption, regular exercise and income (model 1), further adjusting for diabetes, hypertension, CKD and chronic pancreatitis (model 2), and further adjusted for coronary artery disease, and cerebrovascular disease (table 3 and figure 2).

**DISCUSSION**
This nationwide cohort study displayed solid results indicating that AP occurs more frequently in subjects with increased WC and elevated triglyceride levels. Moreover,
the combination of central obesity and hypertriglyceridemia which is the HTGW phenotype distinguished higher-risk group. The risk of AP is gradually enhanced with increases in the WTI. Triglyceride levels and WC varied in accordance to sex, age, smoking and drinking habits, and comorbidities such as diabetes, hypertension, cardiovascular disease, cerebrovascular disease and CKD.

### Table 1  Baseline characteristics of the study population

<table>
<thead>
<tr>
<th></th>
<th>NWNT</th>
<th>EWNT</th>
<th>NWET</th>
<th>HTGW</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>2345642</td>
<td>401486</td>
<td>796995</td>
<td>368373</td>
<td></td>
</tr>
<tr>
<td>Age (mean±SD)</td>
<td>45.2±13.95</td>
<td>53.12±14.18</td>
<td>48.15±13.02</td>
<td>50.98±13.75</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>1116480 (47.6)</td>
<td>205577 (51.2)</td>
<td>560086 (70.27)</td>
<td>251103 (68.17)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Smoking status</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-smoker</td>
<td>1532807 (65.35)</td>
<td>258187 (64.31)</td>
<td>366255 (45.95)</td>
<td>176216 (47.84)</td>
<td></td>
</tr>
<tr>
<td>Former smoker</td>
<td>293202 (12.5)</td>
<td>64457 (16.05)</td>
<td>135045 (16.94)</td>
<td>67695 (18.38)</td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>519633 (22.15)</td>
<td>78842 (19.64)</td>
<td>295695 (37.1)</td>
<td>124462 (33.79)</td>
<td></td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1262856 (53.84)</td>
<td>234483 (58.4)</td>
<td>352433 (44.22)</td>
<td>172342 (46.78)</td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>945352 (40.3)</td>
<td>137351 (34.21)</td>
<td>351136 (44.06)</td>
<td>147135 (39.94)</td>
<td></td>
</tr>
<tr>
<td>Heavy</td>
<td>137434 (5.86)</td>
<td>29652 (7.39)</td>
<td>93426 (11.72)</td>
<td>48896 (13.27)</td>
<td></td>
</tr>
<tr>
<td>Regular physical activity</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low household income</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>120435 (5.13)</td>
<td>57882 (14.42)</td>
<td>91278 (11.45)</td>
<td>72225 (19.61)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>444252 (18.94)</td>
<td>184038 (45.84)</td>
<td>247043 (31)</td>
<td>183232 (49.74)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Chronic pancreatitis</td>
<td>2712 (0.12)</td>
<td>532 (0.13)</td>
<td>878 (0.11)</td>
<td>471 (0.13)</td>
<td>0.0015</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>138140 (5.89)</td>
<td>36044 (8.98)</td>
<td>60566 (7.6)</td>
<td>35201 (9.56)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>76943 (3.28)</td>
<td>33366 (8.31)</td>
<td>33806 (4.24)</td>
<td>26959 (7.32)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>65830 (2.81)</td>
<td>26115 (6.5)</td>
<td>29474 (3.7)</td>
<td>21639 (5.87)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Body measurements</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²) (mean±SD)</td>
<td>22.41±3</td>
<td>27.28±2.84</td>
<td>23.85±2.36</td>
<td>27.73±2.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Waist circumference (cm) (mean±SD)</td>
<td>75.94±7.07</td>
<td>92.14±7.9</td>
<td>80.72±5.68</td>
<td>93.45±7.54</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Systolic BP (mm Hg) (mean±SD)</td>
<td>119.43±14.39</td>
<td>127.62±15.03</td>
<td>125.25±14.55</td>
<td>130±15.04</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg) (mean±SD)</td>
<td>74.44±9.67</td>
<td>78.95±10.06</td>
<td>78.32±9.77</td>
<td>81.05±10.18</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Laboratory findings</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting glucose (mg/dL) (mean±SD)</td>
<td>93.77±18.91</td>
<td>101.04±24.56</td>
<td>101.18±28.84</td>
<td>107.26±33.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total cholesterol (mg/dL) (mean±SD)</td>
<td>188.14±38.47</td>
<td>196.38±41.35</td>
<td>207.89±43.23</td>
<td>212.37±45.56</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HDL-C (mg/dL) (mean±SD)</td>
<td>59.08±26.96</td>
<td>55.09±29.42</td>
<td>52.6±45</td>
<td>49.56±36.46</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LDL-C (mg/dL) (mean±SD)</td>
<td>121.77±250.39</td>
<td>125.38±125.8</td>
<td>118.28±159.07</td>
<td>119.45±139.84</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Triglyceride (mg/dL)*</td>
<td>85 (63–111)</td>
<td>104 (81–126)</td>
<td>201 (171–260)</td>
<td>214 (177–282)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>AST (IU/L)*</td>
<td>21 (18–26)</td>
<td>24 (20–30)</td>
<td>24 (20–30)</td>
<td>26 (21–34)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ALT (IU/L)*</td>
<td>18 (13–24)</td>
<td>23 (17–34)</td>
<td>24 (18–35)</td>
<td>30 (21–45)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>r-GTP (IU/L)*</td>
<td>19 (14–29)</td>
<td>27 (18–43)</td>
<td>33 (21–57)</td>
<td>42 (26–72)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*Median (IQR).
·ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; BP, blood pressure; EWNT, elevated waist circumference-normal triglycerides; HDL-C, high-density lipoprotein cholesterol; HTGW, elevated waist circumference-elevated triglycerides; LDL-C, low-density lipoprotein cholesterol; NWET, normal waist circumference-elevated triglycerides; NWNT, normal waist circumference-normal triglycerides.
However, the aforementioned tendency was maintained after adjusting for such factors.

The two main causes of AP are known to be gallstone disease (39%–44%) and alcohol consumption (17%–25%). In addition, hypertriglyceridaemia, genetic factors, drugs, infection and duct damage/obstruction are also causes of AP, accounting for less than 5% each. There are also many reports of idiopathic pancreatitis, which cause is unknown (15%–22%). Although such factors often precede the development of pancreatitis, they do not seem to be sufficient causes of pancreatitis. In fact, AP develops in only a small percentage of patients who have such conditions. It is known that AP occurs in only 3%–7% of patients with cholelithiasis and less than 10% of alcoholics. In addition, exposure to tobacco, or other environmental toxins, or diseases such as obesity and diabetes that often accompany AP may contribute to the development of pancreatitis. Therefore, we need to know more about the underlying causes and mechanisms of pancreatitis rather than the apparent causes of pancreatitis, such as cholelithiasis or alcoholism.

There have been previous studies suggesting that metabolic syndrome such as diabetes and obesity may be related to the occurrence of pancreatitis. In some aspects, our study agrees with previous studies by showing that abdominal obesity and dyslipidaemia, two representative
Figure 1  The incidence ratio and HR of acute pancreatitis according to hypertriglyceridaemic waist phenotype. NWNT (normal waist-normal triglycerides), EWNT (elevated waist-normal triglycerides), NWET (normal waist-elevated triglycerides) and HTGW (elevated waist-elevated triglycerides). Bar plot represents crude incidence ratio. Model 1 (solid line) was adjusted for age, sex, smoking, alcohol consumption, regular exercise and income and model 2 (dashed line) was further adjusted for diabetes, hypertension, chronic kidney disease and chronic pancreatitis.

Table 3  Incidence and risk of AP according to the WTI in 10 deciles

<table>
<thead>
<tr>
<th>WTI group</th>
<th>WTI</th>
<th>n</th>
<th>AP</th>
<th>Duration*</th>
<th>Incidence rate†</th>
<th>HR (95% CI) Model 1‡</th>
<th>HR (95% CI) Model 2§</th>
<th>HR (95% CI) Model 3¶</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st decile</td>
<td>&lt;45.35</td>
<td>391392</td>
<td>446</td>
<td>3 236 844.08</td>
<td>0.13779</td>
<td>1 (Ref.)</td>
<td>1 (Ref.)</td>
<td>1 (Ref.)</td>
</tr>
<tr>
<td>2nd decile</td>
<td>45.35–58.35</td>
<td>391681</td>
<td>556</td>
<td>3 227 703.58</td>
<td>0.17226</td>
<td>1.022 (0.903 to 1.159)</td>
<td>1.022 (0.902 to 1.158)</td>
<td>1.022 (0.904 to 1.155)</td>
</tr>
<tr>
<td>3rd decile</td>
<td>58.35–70.78</td>
<td>390615</td>
<td>655</td>
<td>3 211 816.01</td>
<td>0.20393</td>
<td>1.08 (0.956 to 1.218)</td>
<td>1.072 (0.95 to 1.21)</td>
<td>1.072 (0.952 to 1.207)</td>
</tr>
<tr>
<td>4th decile</td>
<td>70.79–84.08</td>
<td>390761</td>
<td>711</td>
<td>3 207 685.7</td>
<td>0.22166</td>
<td>1.083 (0.961 to 1.221)</td>
<td>1.067 (0.946 to 1.202)</td>
<td>1.067 (0.948 to 1.201)</td>
</tr>
<tr>
<td>5th decile</td>
<td>84.09–98.98</td>
<td>391806</td>
<td>828</td>
<td>3 212 190.79</td>
<td>0.25777</td>
<td>1.183 (1.053 to 1.33)</td>
<td>1.156 (1.029 to 1.299)</td>
<td>1.156 (1.031 to 1.296)</td>
</tr>
<tr>
<td>6th decile</td>
<td>98.99–116.73</td>
<td>391526</td>
<td>899</td>
<td>3 208 037.34</td>
<td>0.28023</td>
<td>1.223 (1.09 to 1.373)</td>
<td>1.181 (1.053 to 1.326)</td>
<td>1.182 (1.056 to 1.323)</td>
</tr>
<tr>
<td>7th decile</td>
<td>116.74–139.61</td>
<td>390624</td>
<td>929</td>
<td>3 199 807.96</td>
<td>0.29033</td>
<td>1.225 (1.092 to 1.374)</td>
<td>1.17 (1.042 to 1.312)</td>
<td>1.171 (1.045 to 1.312)</td>
</tr>
<tr>
<td>8th decile</td>
<td>139.62–172.61</td>
<td>391652</td>
<td>1009</td>
<td>3 207 023.4</td>
<td>0.31462</td>
<td>1.291 (1.152 to 1.446)</td>
<td>1.216 (1.085 to 1.363)</td>
<td>1.217 (1.088 to 1.361)</td>
</tr>
<tr>
<td>9th decile</td>
<td>172.62–232.52</td>
<td>391394</td>
<td>1194</td>
<td>3 205 725.11</td>
<td>0.37246</td>
<td>1.491 (1.334 to 1.666)</td>
<td>1.383 (1.237 to 1.547)</td>
<td>1.382 (1.239 to 1.542)</td>
</tr>
<tr>
<td>10th decile</td>
<td>≥232.53</td>
<td>391045</td>
<td>1706</td>
<td>3 199 882.98</td>
<td>0.53314</td>
<td>2.058 (1.848 to 2.291)</td>
<td>1.847 (1.657 to 2.058)</td>
<td>1.841 (1.656 to 2.048)</td>
</tr>
</tbody>
</table>

*Duration (person-years).
†Incidence rate (per 1000 person-years).
‡Model 1: adjusted for age, sex, smoking, alcohol consumption, regular exercise and income.
§Model 2: further adjusted for diabetes, hypertension, chronic kidney disease and chronic pancreatitis.
¶Model 3: further adjusted for coronary artery disease and cerebrovascular disease.
AP, acute pancreatitis; WTI, waist circumference triglyceride index.
components of the metabolic syndrome, are associated with a high risk of AP. Hypertriglyceridaemia is known as the third most common cause of AP which accounts for approximately 5% of all cases. Generally, the risk is approximately 5% when triglyceride levels >1000 mg/dL and increases to 10%–20% when levels >2000 mg/dL. On the other hand, our study showed that the risk of pancreatitis grew even with a modest increase in triglyceride levels, and the risk gradually enhanced as the triglyceride levels increased (<100 to >200 mg/dL). This is contrary to previous studies, and the risk increased even more when the WC was elevated.

A recent study has reported that patients with both hypertriglyceridaemia and abdominal obesity have an increased severity of AP and a higher incidence of local complications. Another study also reported that the HTGW phenotype was associated with systemic inflammatory response syndrome, organ failure and severity of AP. In addition, there is research showing that the HTGW phenotype is closely related to fatty pancreas, suggesting that visceral obesity and fatty pancreas may be related to AP in some way. There are several hypotheses that can explain the correlation between the HTGW phenotype, and the incidence of AP. Visceral obesity is also a risk factor for gallstones which may have caused pancreatitis. However, in other studies, obesity has been shown to increase the risk of not only gallstone pancreatitis but also non-gallstone related pancreatitis, so the direct effect of obesity in addition to gallstones should be considered. Several indirect evidences suggest that the release of lipolytic unsaturated fatty acids can exacerbate pancreatitis. Also, obesity-associated pancreatic steatosis and peripancreatic fat necrosis, which are common in obese patients, are suggested as major factors for the exacerbation of pancreatitis. Therefore, visceral fat can be a direct cause of pancreatitis itself as well as through the occurrence of cholelithiasis. The reason hypertriglyceridaemia increases the incidence of pancreatitis can also be explained in a similar context. The lipolysis of circulating triglycerides by pancreatic lipase releases unsaturated fatty acids, which may lead to acinar cell necrosis and AP. On the other hand, there is a theory that microthrombosis occurs in the pancreatic vasculature due to hypertriglyceridaemia, causing ischaemia and pancreatic infarction that leads to AP. Both WC and triglyceride levels proved to be significant indicators for predicting AP in our study. While it may be challenging to determine whether the HTGW phenotype is superior to these indicators, it is meaningful because it leads to a clearer distinction among different risk groups with integrating these two independent indicators.

The limitations of this study include the fundamental limitations of claims and health check-up data: the diagnosis of AP could have been inaccurate or omitted in some subjects. However, we compensated for these limitations as much as possible by combining the ICD-10 code and hospitalisation data. Another limitation of this study was that a large number of subjects were excluded due to missing data. However, compared with the total number of subjects, it was only 5.8%, and the exclusion of subjects due to missing data was thought to have occurred randomly, so it does not seem to have affected the study results. Lastly, it was impossible to classify the causes of AP, as well as the severity of AP.

However, this study is significant in that it was based on a large-scale cohort representing the entire Korean population. Detailed clinical parameters such as anthropometric variables, medical history, lifestyle and blood chemistry results were available. Based on such parameters, analysis was conducted with a consideration of various variables.

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Figure 2 The incidence ratio and HR of acute pancreatitis according to waist circumference triglyceride index in 10 deciles. WTI is calculated as follows: WTI (cm×mmol/L)=WC (cm)×TG (mmol/L). Bar plot represents crude incidence ratio. Model 1 (solid line) was adjusted for age, sex, smoking, alcohol consumption, regular exercise and income and model 2 (dashed line) was further adjusted for diabetes, hypertension, chronic kidney disease and chronic pancreatitis. WC, waist circumference; WTI, WC triglyceride index.
that may affect the occurrence of AP. In addition, this study confirmed the correlation between AP (a disease with a relatively low incidence) and the HTGW phenotype (a relatively simple indicator) through a long-term follow-up of 9 years after exposure to causative variables.

In conclusion, our large-scale cohort study confirmed that the HTGW phenotype is an independent risk factor that increases the risk of AP. It was also confirmed that the risk of AP increased proportionally as the WTI increased. Further research is needed to elucidate the mechanism in which triglyceride levels and WC affect pancreatitis occurrence. Also, additional research is necessary regarding the prevention and treatment of AP based on the results of this study.

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Patient consent for publication Not applicable.

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