Effect of the addition of thiazolidinedione to sodium-glucose cotransporter 2 inhibitor therapy on lipid levels in type 2 diabetes mellitus: a retrospective study using Korean National Health Insurance Service data

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Background: Dyslipidemia is common in patients with type 2 diabetes mellitus (T2D) and contributes to an increased risk of cardiovascular disease. Previous studies have shown that treatment with thiazolidinediones (TZDs) and sodium-glucose cotransporter-2 inhibitors (SGLT2-i) may help to improve dyslipidemia in T2D patients. In this study, we investigated whether patients treated with TZD and SGLT2-i showed greater improvement in high-density lipoprotein cholesterol (HDL-C) levels than those treated with only SGLT2-i.

Methods: From the National Health Insurance Service database of Korea, we extracted all patients who first received SGLT2-i from 2014 to 2016. Propensity score matching was performed to balance the two groups: group A (SGLT2-i and TZD, regardless of other antidiabetic medications) and group B (SGLT2-i only without TZD, regardless of other antidiabetic medications). Posttreatment HDL-C levels were compared by the Student t-test.

Results: In total, 1,400 T2D patients (700 in each group) were matched by propensity score matching. There was a significant posttreatment increase in HDL-C in group A (49.54±20.03 to 51.6±12.92 mg/dL, P=0.007), but not in group B (49.14±13.52 to 49.1±2.15 mg/dL, P=0.937). Group A also showed significantly higher posttreatment HDL-C levels than group B (51.6±12.92 vs. 49.1±12.15 mg/dL, P<0.001). Regarding the secondary endpoints, posttreatment triglyceride levels were lower (P<0.001), but total cholesterol (P=0.131) and low-density lipoprotein cholesterol levels (P=0.054) were not different after treatment.

Conclusions: The combination of SGLT2-i and TZD may be more effective in ameliorating dyslipidemia in T2D patients than SGLT2-i alone. However, further studies are needed to confirm this finding.

Keywords: Type 2 diabetes mellitus; Dyslipidemias; Sodium-glucose transporter 2 inhibitors; Thiazolidinedione; Drug combination
INTRODUCTION

Type 2 diabetes (T2D) is a significant risk factor for cardiovascular disease (CVD). Coronary artery disease and stroke are the main causes of death in T2D patients [1–4]. Dyslipidemia is a major modifiable factor for CVD prevention [3,4]. Therefore, the management of dyslipidemia is necessary to reduce mortality due to CVD in patients with T2D [5,6].

Low levels of high-density lipoprotein cholesterol (HDL-C) are a key feature of diabetic dyslipidemia [6–9], as well as a major independent risk factor for CVD [10]. While statins are the mainstay of dyslipidemia management, they have limited effects on HDL-C [11]. A previous study found that HDL-C levels increased when sodium-glucose cotransporter-2 inhibitors (SGLT2-i) and thiazolidinediones (TZDs) were administered alone or in combination [4,7,12–19]. Therefore, it was expected that a combination of TZD and SGLT2-i would increase HDL-C levels more than treatment with only SGLT2-i.

Some clinical trials have added SGLT2-i to background TZD treatment [7,17,18,20], but to our knowledge, there have been no clinical trials in which TZD was added to SGLT2-i treatment. In this study, using national health insurance data, we aimed to investigate whether treatment with a combination of TZD and SGLT2-i resulted in a greater improvement in HDL-C levels than treatment with SGLT2-i alone.

METHODS

Ethical statement
This study was approved by the Institutional Review Board of Sungkyunkwan University (No. 2021-05-017). Participants who underwent national health checkup examinations provided written informed consent for the use of their data for research purposes. All personal information was deleted, and only de-identified data were included in the analysis.

Study setting and data source
Korea has a mandatory social health insurance system, called the National Health Insurance Service (NHIS), which is run by the government (i.e., the Ministry of Health and Welfare). The entire Korean population is covered by the NHIS, except for the lowest-income segment of the population (approximately 3%), who are covered by medical aid. In Korea, all medical providers are compulsorily designated by the NHIS, and the providers must register all disease diagnoses, medical procedures, and drug prescription information for reimbursement from the NHIS. All administrative procedures for NHIS subscribers and the medical aid population are performed by the NHIS, which is a public corporation.

The Korean government also operates the National Health Screening Program (NHSP). All insured adults are eligible for a regular health checkup every 2 years. In 2014, the target population’s participation rate in the program’s general health examination was 74.8% [21]. Currently, Korea’s NHSP is the world’s most extensive health screening program.

This retrospective study used the NHIS database. The NHIS maintains five databases: the qualification database, the national health checkup database, the medical use database, the long-term care insurance database (since 2014), and the healthcare provider database [22]. The NHIS operates the National Health Information Sharing Service to support policies and academic research by providing information (Wonju, NHIS; https://nhiss.nhis.or.kr). The NHIS databases have been extensively used for medical and health policy research.

For this research, we used a custom NHIS database, which was designed according to the researchers’ needs [22]. Data extraction was performed by medical record technicians at the NHIS Center, who had no conflicts of interest related to this study.

Study population
We extracted 129,666 T2D patients (International Classification of Diseases 10th revision [ICD-10] codes, E10–E14) who were first prescribed SGLT2-i from the NHIS database from October 1, 2014 to December 31, 2016. Of these, 127,066 adults aged 30 years or older were selected.

The index date was the first prescription date for T2D patients who first received SGLT2-i between 2014 and 2016. As of the index date, T2D patients who had not received a medical examination during the previous 2 years and within 2 years thereafter were excluded. We also excluded patients with type 1 diabetes mellitus (ICD-10, E10) and gestational diabetes mellitus (ICD-10, O244 and O249) from January 1, 2002 to the index date.
The group with TZD prescriptions was defined as patients who were also prescribed TZD at the time of the first prescription of SGTL2-i, and it excluded patients who received only SGTL2-i. Subsequently, we performed propensity score matching (PSM), which is known to reduce confounding in observational studies [23]. All possible covariates, including demographic and medical information (Table 1) were included in PSM, and logistic regression analysis was performed to calculate the propensity scores in a logistic model. We set the caliper for nearest-neighbor matching.

Table 1. PSM in patients treated with SGLT2-i with or without TZDs

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before PSM</th>
<th>After PSM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group A (n=702)</td>
<td>Group B (n=45,850)</td>
</tr>
<tr>
<td>Index year</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td>108 (15.38)</td>
<td>5,164 (11.26)</td>
</tr>
<tr>
<td>2015</td>
<td>331 (47.15)</td>
<td>19,434 (42.39)</td>
</tr>
<tr>
<td>2016</td>
<td>263 (37.46)</td>
<td>21,252 (46.35)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>455 (64.81)</td>
<td>29,175 (63.63)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>514 (73.22)</td>
<td>32,360 (70.58)</td>
</tr>
<tr>
<td>Income (lowest 20%)</td>
<td>122 (17.38)</td>
<td>8,811 (19.22)</td>
</tr>
<tr>
<td>Smoke</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonsmoker</td>
<td>343 (48.86)</td>
<td>25,627 (55.89)</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>190 (27.07)</td>
<td>9,794 (21.36)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>169 (240.7)</td>
<td>10,429 (22.75)</td>
</tr>
<tr>
<td>Alcohol drinking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>393 (55.98)</td>
<td>27,052 (59.00)</td>
</tr>
<tr>
<td>Mild</td>
<td>247 (35.19)</td>
<td>15,114 (32.96)</td>
</tr>
<tr>
<td>Heavy</td>
<td>62 (8.83)</td>
<td>3,684 (8.03)</td>
</tr>
<tr>
<td>Regular exercise</td>
<td>153 (21.79)</td>
<td>9,693 (21.14)</td>
</tr>
<tr>
<td>Medication when first prescribed SGTL2-i</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td>52 (7.41)</td>
<td>3,283 (7.16)</td>
</tr>
<tr>
<td>GLP-1</td>
<td>2 (0.28)</td>
<td>6 (0.01)</td>
</tr>
<tr>
<td>≥3 Oral agents</td>
<td>614 (87.46)</td>
<td>15,798 (34.46)</td>
</tr>
<tr>
<td>Medication during 1 yr prior to the first SGTL2-i prescription</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td>114 (16.24)</td>
<td>6,396 (13.95)</td>
</tr>
<tr>
<td>Sulfonylurea</td>
<td>451 (64.25)</td>
<td>25,342 (55.27)</td>
</tr>
<tr>
<td>Metformin</td>
<td>627 (89.32)</td>
<td>40,632 (88.62)</td>
</tr>
<tr>
<td>Meglitinides</td>
<td>10 (1.42)</td>
<td>368 (0.80)</td>
</tr>
<tr>
<td>TZD</td>
<td>604 (86.04)</td>
<td>7,259 (15.83)</td>
</tr>
<tr>
<td>DPP4-i</td>
<td>556 (79.20)</td>
<td>28,523 (62.21)</td>
</tr>
<tr>
<td>AGI</td>
<td>58 (8.26)</td>
<td>1,530 (3.36)</td>
</tr>
<tr>
<td>GLP-1</td>
<td>2 (0.28)</td>
<td>153 (0.33)</td>
</tr>
<tr>
<td>Male sex</td>
<td>464 (66.10)</td>
<td>25,195 (54.95)</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>56.34±9.97</td>
<td>55.62±10.13</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>165.02±9.26</td>
<td>163.63±9.17</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>72.83±14.82</td>
<td>73.30±14.04</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>26.61±4.02</td>
<td>27.26±4.00</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>126.95±14.27</td>
<td>127.62±14.39</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>77.89±9.81</td>
<td>78.59±9.74</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>166.19±58.77</td>
<td>157.49±54.34</td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>175.97±44.05</td>
<td>182.61±48.75</td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
<td>49.51±20.01</td>
<td>48.86±13.21</td>
</tr>
</tbody>
</table>

(Continued to the next page)
within the first 4 to 8 digits, allowing PSM at a 1:1 ratio. Finally, 700 patients were obtained for each group: group A (SGTL2i and TZD, regardless of other antidiabetic medications) and group B (SGTL2i only without TZD, regardless of other antidiabetic medications) (Fig. 1).

### Study endpoint

The primary endpoint was the posttreatment HDL-C level. The secondary endpoints were posttreatment triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), and total cholesterol (TC) levels.

### Statistical analysis

The absolute value of the standardized mean difference (ASD) was used to determine the balance before and after PSM, and an ASD <0.1 was used to determine whether all covariates were sufficiently balanced through PSM. Since PSM was performed and baseline characteristics of groups A and B were comparable, differences in the study endpoints between groups A and B were compared with the Student t-test without consideration of the baseline characteristics. In addition, the paired t-test was used to analyze differences between the pre- and posttreatment values within each group. All statistical analyses were performed using SAS ver. 9.4 (SAS Institute Inc., Cary, NC, USA), and P-values less than 0.05 were considered statistically significant.

### RESULTS

#### Patient disposition and baseline characteristics

After PSM, 1,400 patients (700 patients in each group) were included in the analysis. The characteristics of groups A and B before and after PSM are compared in Table 1. The ASDs of all covariates were below 0.1, indicating that the two groups were sufficiently balanced after PSM (Table 1).

#### Comparison of the primary outcome HDL-C

In the posttreatment comparison conducted using the Student t-test, group A showed significantly higher HDL-C levels (51.4±12.92 vs. 49.1±12.15 mg/dL, P<0.001) than group B. When comparing the pretreatment and posttreatment HDL-C levels within each group, a significant increase was found in group A (49.54±20.03 to 51.6±12.92 mg/dL, P=0.007), whereas no significant change was observed in group B (49.14±13.52 to 49.1±2.15 mg/dL, P=0.937) (Table 2).

#### Changes in the secondary outcomes

In the posttreatment comparison conducted using the Student t-test, group A showed significantly lower TG levels than group B (120.51 mg/dL, 95% confidence interval).

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**Table 1. Continued**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before PSM</th>
<th>After PSM</th>
<th>ASD</th>
<th>Before PSM</th>
<th>After PSM</th>
<th>ASD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A (n=700)</td>
<td>Group B (n=45,850)</td>
<td>ASD</td>
<td></td>
<td>Group A (n=700)</td>
<td>Group B (n=700)</td>
<td>ASD</td>
</tr>
<tr>
<td>LDL-C (mg/dL)</td>
<td>96.20±51.49</td>
<td>100.30±44.32</td>
<td>0.0854</td>
<td>94.90±36.15</td>
<td>95.62±37.01</td>
<td>0.0199</td>
</tr>
<tr>
<td>Aspartate aminotransferase (U/L)</td>
<td>26.84 (25.41–27.83)</td>
<td>28.22 (28.03–28.34)</td>
<td>0.1097</td>
<td>28.79 (26.98–30.05)</td>
<td>29.08 (27.22–30.38)</td>
<td>0.0043</td>
</tr>
<tr>
<td>Alanine aminotransferase (U/L)</td>
<td>29.08 (27.25–30.35)</td>
<td>31.50 (31.24–31.67)</td>
<td>0.1366</td>
<td>26.58 (25.16–27.56)</td>
<td>26.84 (25.50–27.77)</td>
<td>0.0203</td>
</tr>
<tr>
<td>Triglyceride (mg/dL)</td>
<td>141.17 (132.47–147.26)</td>
<td>148.41 (147.27–149.18)</td>
<td>0.083</td>
<td>141.17 (132.45–147.26)</td>
<td>141.17 (132.31–147.37)</td>
<td>0.0047</td>
</tr>
<tr>
<td>rGTP (IU/L)</td>
<td>37.34 (34.26–39.53)</td>
<td>38.86 (38.47–39.12)</td>
<td>0.0578</td>
<td>37.34 (34.26–39.53)</td>
<td>36.97 (34.07–39.02)</td>
<td>0.0085</td>
</tr>
<tr>
<td>GFR (mL/min/1.73 m²)</td>
<td>90.41±25.79</td>
<td>91.16±29.32</td>
<td>0.0272</td>
<td>90.41±25.82</td>
<td>91.31±25.59</td>
<td>0.0350</td>
</tr>
<tr>
<td>Fatty liver index</td>
<td>49.39±26.90</td>
<td>52.96±26.69</td>
<td>0.1332</td>
<td>49.39±26.89</td>
<td>49.99±26.29</td>
<td>0.0254</td>
</tr>
<tr>
<td>Diabetes mellitus duration (yr)</td>
<td>9.05±4.06</td>
<td>7.07±4.72</td>
<td>0.4497</td>
<td>9.05±4.07</td>
<td>9.29±4.10</td>
<td>0.0586</td>
</tr>
<tr>
<td>Previous index date (day)</td>
<td>353.92±230.97</td>
<td>347.79±230.95</td>
<td>0.0265</td>
<td>354.09±230.94</td>
<td>345.30±223.00</td>
<td>0.0387</td>
</tr>
<tr>
<td>Next index date (day)</td>
<td>330.82±215.76</td>
<td>329.50±214.20</td>
<td>0.0061</td>
<td>330.71±216.06</td>
<td>345.45±226.62</td>
<td>0.0666</td>
</tr>
</tbody>
</table>

Values are presented as number (%), mean±standard deviation, or geometric mean (95% confidence interval).

PSM, propensity score matching; SGLT2-i, sodium-glucose cotransporter-2 inhibitors; TZD, thiazolidinedione; ASD, absolute standardized difference; GLP-1, glucagon-like peptide-1; DPP4-i, dipetidyl peptidase-4 inhibitors; AGI, alpha-glucosidase inhibitors; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; rGTP, gamma-glutamyl transpeptidase; GFR, glomerular filtration rate.
**Table 2.** Effect of sodium-glucose cotransporter-2 inhibitors with or without thiazolidinedione treatment in propensity score-matched type 2 diabetes patients (n=1,400)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pretreatment</th>
<th>Posttreatment</th>
<th>P-value</th>
<th>P-value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDL cholesterol (mg/dL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group A</td>
<td>49.54±20.03</td>
<td>51.60±12.92</td>
<td>0.007</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Group B</td>
<td>49.14±13.52</td>
<td>49.10±12.15</td>
<td>0.937</td>
<td></td>
</tr>
<tr>
<td>Triglyceride (mg/dL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group A</td>
<td>141.53 (135.71–147.60)</td>
<td>120.51 (115.60–125.62)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Group B</td>
<td>141.15 (135.21–147.34)</td>
<td>135.59 (129.98–141.43)</td>
<td>0.056</td>
<td></td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group A</td>
<td>176.01±44.08</td>
<td>167.40±41.49</td>
<td>&lt;0.001</td>
<td>0.131</td>
</tr>
<tr>
<td>Group B</td>
<td>176.48±41.25</td>
<td>165.85±40.71</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>LDL cholesterol (mg/dL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group A</td>
<td>94.90±36.15</td>
<td>88.23±36.05</td>
<td>&lt;0.001</td>
<td>0.054</td>
</tr>
<tr>
<td>Group B</td>
<td>95.62±37.01</td>
<td>86.13±33.76</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

Values are presented as mean±standard deviation or geometric mean (95% confidence interval). The Student t-test was used to compare posttreatment differences between groups A and B. Pretreatment values after propensity score matching were assumed to be the same.

HDL, high-density lipoprotein; LDL, low-density lipoprotein.

<sup>a</sup>Student t-test.
tival [CI] 115.6–126.62 mg/dL vs. 135.59 mg/dL, 95% CI 129.98–141.43 mg/dL; P<0.001). When comparing the pre-
treatment and posttreatment TG levels within each group, a
significant decrease was observed in group A (141.53 mg/
dl [95% CI, 135.71–147.6 mg/dL] to 120.51 mg/dL [95% CI, 115.6–125.62 mg/dL]; P<0.001), but not in group B (141.15
mg/dL [95% CI, 135.7–147.6 mg/dL] to 135.59 mg/dL [95% CI, 129.98–141.43 mg/dL]; P=0.056).

No statistically significant differences were found between
groups A and B in the posttreatment comparisons of TC lev-
els (167.4±41.49 mg/dL vs. 165.85±40.71 mg/dL, P=0.479)
and LDL-C levels (88.23±36.05 mg/dL vs. 86.13±33.76 mg/
dl, P=0.261) using the Student t-test. However, both groups
showed significant decreases in these parameters in com-
parisons between pretreatment and posttreatment values.
TC levels decreased from 176.01±44.08 to 167.4±41.49
mg/dL (P<0.001) in group A and from 176.48±41.25 to
165.85±40.71 mg/dL (P<0.001) in group B. LDL-C levels
decreased from 94.9±36.15 to 88.23±36.05 mg/dL (P<0.001)
in group A and from 95.6±37.01 to 86.13±33.76 mg/dL
(P<0.001) in group B (Table 2).

**DISCUSSION**

In this study, we tried to determine whether dyslipidemia
could be improved by using TZD in combination with
SGLT2-i. Although our study was an observational study,
we tried to reduce the differences between the groups by
using PSM, and our real-world data might be useful consid-
ering that no clinical trial data regarding this question are
available yet.

An increase in HDL-C levels was observed only in pa-
patients who were prescribed SGLT2-i and TZD (group A),
who had higher posttreatment HDL-C levels than patients
who were prescribed SGLT2-i only (group B). These results
suggest that the combination of TZD and SGLT2-i might
be helpful for the improvement of HDL-C. Many previous
studies have confirmed that TZD significantly increases
HDL-C levels [12,15,16,24]. Although it has been accepted
that the increase in HDL-C levels with TZD treatment is
entirely due to an increase in the HDL3 subfraction, the
mechanism by which TZD induces alterations in the HDL3
subfraction remains unclear [25].

SGLT2-i medications are generally considered to improve
HDL-C, but unexpectedly, the present study using NHIS
data found no increase in HDL-C levels with SGLT2-i treat-
ment. A possible explanation might be that previous studies
inconsistent results were reported regarding the effects of
different SGLT2-i drugs on HDL-C levels [22–24], which
is relevant since group B in our real-world study used various
types of SGLT2-i (dapagliflozin, empagliflozin, and ipragli-
flozin). In addition, treatment persistence and/or adher-
ence might not have been optimal in this study population
compared to a clinical trial. Limitations of insurance bene-
fits for SGLT2-i and TZD may also be a factor (Fig. 2).

TG is also an important aspect of diabetic dyslipidemia
and a substantial risk factor for atherosclerotic CVD in
patients with T2D [26]. In patients who were prescribed
SGLT2-i and TZD (group A), the posttreatment TG levels
were lower than in those who were prescribed SGLT2-i only
(group B). This is in line with the results of previous studies
showing a decrease in TG with TZD treatment [15,27,28].

LDL-C and TC levels decreased after treatment within
groups A and B, but the posttreatment comparison be-
tween groups A and B did not yield significant results. TZD
showed a consistent LDL-C reduction effect [15,28], while
SGLT2-i slightly increased LDL-C levels [14], although
differences were observed depending on the specific drugs or
doses. Variations in the types and doses of SGLT2-i were
not considered in this study, but should be investigated in
future research.

There are several limitations of this study. First, the Na-
tional Health Insurance Research Database (NHIRD) was
created for entitlement and reimbursement management;
therefore, it lacks clinical information, such as why patients
were prescribed specific antidiabetic drugs. While we tried
to balance the two groups with PSM, there could have still
been some unmeasured confounders. Second, the number
of patients in each group was small, at 700. Currently, the
reimbursement of oral antidiabetic drugs is limited to two
drugs, and the patient must pay for a third drug. As most
people are prescribed metformin as the first-line drug, the
number of patients who were prescribed both SGLT2-i and
TZD is limited. Therefore, although this was a nationwide
study, the sample size was only 700 patients and a more
detailed analysis was not possible. Third, our endpoint of
the lipid profile is only a proxy marker of CVD. Fourth, in-
formation about the concomitant use of anti-hyperlipidem-
ic drugs was lacking. Further research is needed to clarify
whether improving the lipid profile could lead to a reduced

---

**Table 2**

<table>
<thead>
<tr>
<th>Drug Combination</th>
<th>Posttreatment TG Level (mg/dL)</th>
<th>Pre-treatment TG Level (mg/dL)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGLT2-i only</td>
<td>141.15±36.05</td>
<td>167.4±41.49</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TZD and SGLT2-i</td>
<td>88.23±36.05</td>
<td>167.4±41.49</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

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**References**

[12,15,16,24]
risk of coronary artery disease.

In conclusion, our study results suggest that a combination of SGTL2-i and TZD might be more effective for improving dyslipidemia than SGTL2-i alone in T2D patients. Our findings are consistent with the recommendations for using TZD in the American Diabetes Association guidelines for T2D patients with a higher CVD risk, but further studies are needed to confirm these findings.

ARTICLE INFORMATION

Ethical statements
This study was approved by the Institutional Review Board of Sungkyunkwan University (No. 2021-05-017). Participants who underwent national health checkup examinations provided written informed consent for the use of their data for research purposes. All personal information was deleted, and only de-identified data were included in the analysis.

Conflicts of interest
The authors have no conflicts of interest to declare.

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None.

Author contributions
Conceptualization: TP, KH, DS; Data curation: KH, TP; Formal analysis: KH, TP; Methodology: DS, TP, KH; Project administration: DS, TG, HK; Supervision: DS; Validation: DS, TP, KH, JP; Writing—original draft: TP, KH, DS, JP; Writing—review & editing: TP, JP, KH, DS.

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