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REVIEW ARTICLE

Effects of novel glucose-lowering drugs on the COVID-19 patients with diabetes: A network meta-analysis of clinical outcomes

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Abstract

Objective This study aimed to assess the effects of sodium-glucose co-transporter inhibitors (SGLT2i), glucagon-like peptide-1 receptor agonists (GLP-1RA), and dipeptidyl peptidase-4 inhibitors (DPP4i) on individuals subjected to diabetes and COVID-19.

Methods PubMed, Embase, Web of Science, and Cochrane Library were systematically searched to cover studies (except for case reports and review studies) published until August 30, 2022. The primary outcome was the mortality of people with diabetes and COVID-19. The secondary outcomes comprised the requiring intensive care unit (ICU) admission and mechanical ventilation. Two reviewers independently screened studies, abstracted data, and assessed risk-of-bias. Furthermore, the network meta-analyses (NMA) were conducted.

Results A total of 12 trials were involved in the analysis. The OR and 95% CI of mortality for SGLT2i compared with SGLT2i + GLP-1RA and DPP4i reached 0.41 (0.17,0.97) and 0.69 (0.49,0.98), respectively. The OR and 95% CI of requiring mechanical ventilation for SGLT2i compared with the DPP4i reached 0.85 (0.75,0.97).

Conclusions As revealed by the result of this study, SGLT2i is associated with the lower mortality rate in people with diabetes and COVID-19 among novel glucose-lowering drugs. And SGLT2i is linked to lower requiring mechanical ventilation. These findings can have a large impact on clinicians' decisions amid the COVID-19 pandemic.

Keywords COVID-19 · Diabetes · SGLT2 inhibitors · GLP-1 agonist · DPP-4 inhibitors

Introduction

Since the end of 2019, SARS-CoV-2 has emerged as a novel disease-causing microorganism leading to the COVID-19 pandemic. By the end of October 2022, more than 622 million people had been infected with SARS-CoV-2 globally, approximately 6 million of whom died [1]. The COVID-19 pandemic was superimposed on the pre-existing diabetes pandemic, creating a large population of people with diabetes and COVID-19.

Existing research has suggested that diabetes is an independent risk factor for worse outcomes and in-hospital mortality in COVID-19 patients [2–5]. In addition, other co-morbidities common to patients with diabetes, such as cardiovascular disease (CVD) and obesity, put COVID-19 patients at greater risk of poor clinical outcomes [6, 7]. Chronic hyperglycemia can impair innate and humoral immunity. In addition, diabetes is correlated with chronic, low-grade inflammatory states that affect glucose regulation and peripheral insulin sensitivity [8]. There is a two-way correlation between COVID-19 and diabetes. Diabetics are at an increased risk of complications when infected with COVID-19; besides, SARS-CoV-2 may serve as a diabetic agent by binding to ACE2 in pancreatic β cells, thus resulting in acute dysfunction and altered glucose regulation [9]. All approved oral antidiabetic agents can be safe in T2DM patients and COVID-19 [10], whereas no conclusive data have been available to indicate a mortality benefit with any class of the above-mentioned drugs in the absence of large randomized controlled trials. However, the metabolic management of patients should be optimized to improve outcomes and reduce the burden on health systems.

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Whether commonly used glucose-lowering agents in diabetes patients affect COVID-19 patient prognosis should be determined since the mechanism of action of glucose-lowering drugs may affect the natural course of SARS-CoV-2 infection. Moreover, insights should be gained into whether the above-described drugs are harmful, neutral, or beneficial for COVID-19 patients. Besides, a relatively beneficial treatment option should be urgently selected from the many available for people with diabetes and COVID-19. Existing research has reported that antidiabetic drugs exert antidiabetic effects and anti-inflammatory and immunomodulatory effects [2, 11]. Numerous studies have investigated the effects of antidiabetic drugs on the clinical outcomes of COVID-19 diabetes patients. Several paired meta-analyses have examined the effects of specific antidiabetic agents on COVID-19 mortality and serious adverse outcomes, which comprise metformin, dipeptidyl peptidase 4 inhibitors (DPP4i), sulfonylureas, as well as insulin and glucagon-like peptide-1 receptor agonists (GLP-1RA) [11–13]. However, the above-mentioned studies only compared patients who used specific antidiabetic drugs with non-users. The risk of death between different antidiabetic drugs in the above-described patients remains unclear.

Sodium-glucose co-transporter inhibitors (SGLT2i), GLP-1RA, and DPP4i have been confirmed as novel glucose-lowering agents for the management of diabetes [14]. Novel glucose-lowering medications may reduce adverse COVID-19 outcomes for their anti-inflammatory properties, whereas rare research has systematically investigated the potential role of different pharmacological classes in adverse COVID-19 outcomes thus far [15]. Previous research has reported that DPP4i plays a beneficial role in T2DM patients hospitalized for COVID-19 [15, 16]. SGLT2i and GLP-1RA exhibit several anti-inflammatory properties, which may be correlated with better outcomes [15, 17]. In contrast, safety concerns have been raised for SGLT2i and GLP-1RA since they up-regulate ACE2 expression, such that SARS-CoV-2 binding to the cells is mediated [18]. However, RAAS inhibitor drugs, which also up-regulate ACE2 expression, do not appear to be correlated with an increased risk of incident COVID-19 or worse outcomes in prevalent COVID-19 [19]. There are no independent studies assessing the effects of the three novel hypoglycemic agents in people with diabetes and COVID-19. Accordingly, no clear consensus has been reached on using the above three agents in the above-mentioned patients. On that basis, this knowledge gap was filled through network meta-analyses (NMA) and the assessment of three novel glucose-lowering drugs (i.e., SGLT2i, GLP-1RA, and DPP4i) on mortality and morbidity of severe disease in people with diabetes and COVID-19. Mortality in people with diabetes and COVID-19 served as the primary outcome. In terms of the secondary outcome of this study, the incidence of severe disease (requiring intensive care unit admission; mechanical ventilation) in people with diabetes and COVID-19 was also assessed.

Methods

The PROSPERO registration number was CRD42022355190. Our meta-analysis was consistent with the PRISMA statement and also the network meta-analysis extension statement of PRISMA (Sup. Table 1).

Searching strategy

PubMed, Embase, Web of Science, and Cochrane Library were systematically searched for relevant studies up to August 30, 2022, and our search was limited to the English language. Search terms comprised novel glucose-lowering drugs (e.g., SGLT2i, GLP-1RA, and DPP4i), diabetes, and COVID-19. The detailed and complete search strategy is presented in Sup. Table 2. Imported the retrieved studies into EndnoteX9 and extracted them by filtering their titles and abstracts. Duplicate studies and multiple reports using the same data were removed. After initial screening, ineligible studies were excluded by reading the complete text, and the final remaining studies were covered.

Inclusion criteria

Study type that conformed to the requirements of the non-randomized trials and observational studies. The study subjects were adults (aged ≥ 18 years) with diabetic COVID-19. Intervention measures are novel glucose-lowering drugs (e.g., SGLT2i, GLP-1RA, and DPP4i). All the covered literature should report any one of the primary or secondary outcome indicators, the primary outcome was the mortality of people with diabetes and COVID-19, and the secondary outcomes were the requiring intensive care unit (ICU) admission and mechanical ventilation. Studies published in English were searched.

Exclusion criteria

Exclusion criteria are presented as follows: case reports, review studies and abstracts, duplicate publications in the literature, literature for which complete data could not be extracted, animal studies, non-adult patient, and non-English language studies.

Data extraction

The relevant data were extracted by two independent evaluators (Y Y, LZ) using a predetermined data collection form following the inclusion criteria. The primary data extracted comprised study characteristics (e.g., first author, publication date, country, and study design), characteristics of the patient (e.g., sample size, mean age,

and proportion of males), as well as study outcome data. Any disagreements in the data extraction process would be resolved through discussions with a third reviewer (CL).

Risk of bias assessment

The risk of bias assessment was conducted by two independent authors using the Newcastle–Ottawa Scale (NOS) [20]. Any disagreements during the risk of bias assessment would be resolved by discussion.

Statistical analysis

The ratio (OR) and 95% confidence interval served as the effect size indicators for the dichotomous variables (e.g., mortality, requiring intensive care unit admission, and mechanical ventilation). The heterogeneity between studies was estimated through the I^2 test. After the exclusion of effects exerted by significant clinical heterogeneity, the random-effects model was employed for the meta-analysis. The network meta-analyses (NMA) were conducted using STATA 16.0 software based on a frequency-based random effects model, in which the study outcome measures were networked by the group command. Data processing, network evidence plots, funnel plots, forest plots, and surface area under the cumulative rankograms (SUCRA) were completed sequentially. The area enclosed by the curve and the horizontal axis in the SUCRA plot can indicate the percentage of treatment effectiveness (SUCRA value), which is ranked without any uncertainty. The ranking of the treatment modality will be improved with the rise of the SUCRA value. Publication bias of the relevant literature was assessed using funnel plots. $P<0.05$ indicated a difference that achieved statistical significance.

Results

Literature search and screening

In this study, 378 studies were initially searched. 12 studies were finally covered after a hierarchical screening process. Figure 1 illustrates the selection of the literature.

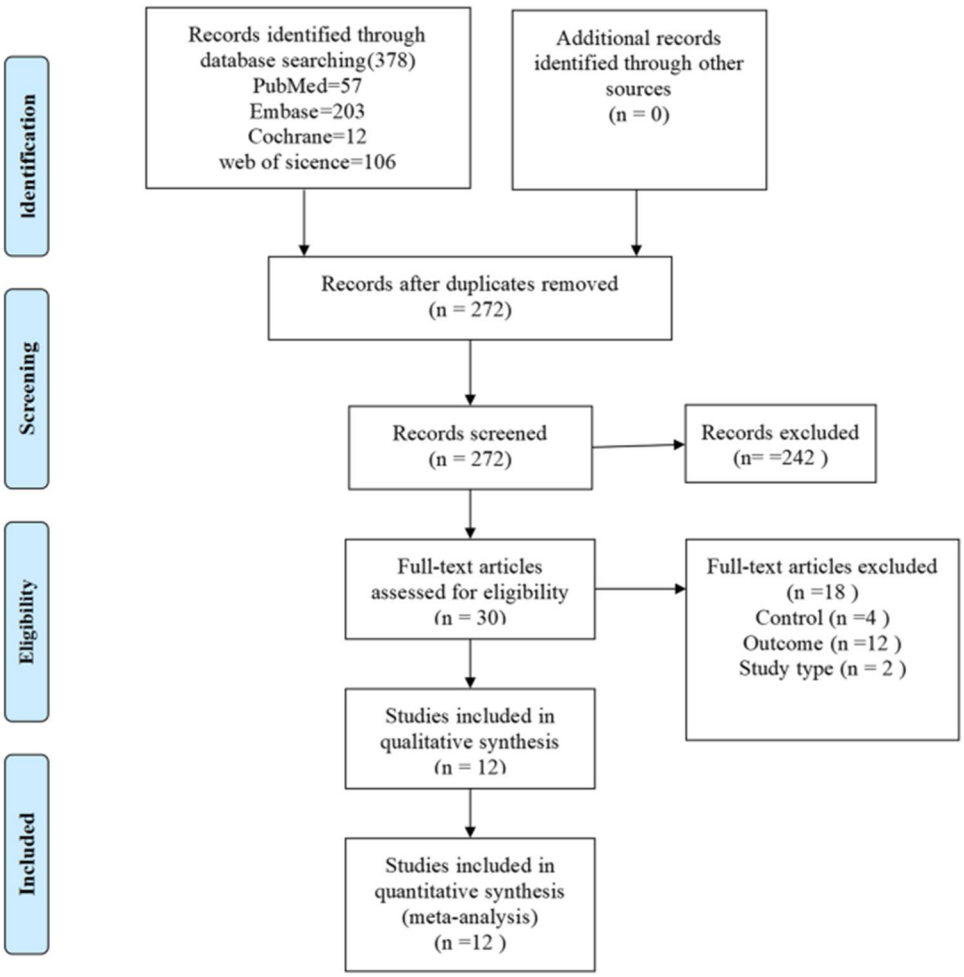

Fig. 1 The flow diagram of study selection

Basic characteristics of involved literature

A total of 12 studies were covered in the literature [21–32], including 52148 patients. A total of seven retrospective cohort studies, three cross-sectional studies, one combined prospective and retrospective cohort study, and one Case series were involved. Table 1 lists the characteristics of the included studies.

Bias risk assessment of involved literature

The Newcastle–Ottawa Quality Assessment measured studies' quality. The quality scores of the studies ranged from seven to eight stars (Sup. Table 3).

Outcome indicators

Mortality

Evidence network A total of 12 studies reported mortality rates for five treatment regimens involving novel hypoglycemic agents in people with diabetes and COVID-19. The dot size indicates the size of the sample using the intervention and the thickness of the line shows the number of trials (Fig. 2A). The closed-loop inconsistency factor (IF) approached 1, as indicated by the result of the consistency test, and the lower limit of 95% CI covered 0, suggesting no significant inconsistency. Sup. Fig. 1 presents the results of the consistency test.

Publication bias As depicted in the funnel plot, most of the scatter points laid on either side of the vertical line, and they were essentially symmetric, probably exhibiting some publication biases (Fig. 3A).

Network meta-analysis Mortality was reported in 12 studies involving five treatment regimens, and network comparisons among the above-mentioned regimens yielded ten pairwise comparisons, of which two were statistically significant. The OR and 95% CI for SGLT2 compared with SGLT2i + GLP-1RA and DPP4i reached 0.41 (0.17,0.97) and 0.69 (0.49,0.98), respectively, as shown in Fig. 4A. The forest plots shown in Sup. Fig. 2.

SUCRA probability ranking The ranking of the five treatment options involving novel hypoglycemic agents, based on the area under the SUCRA curve, was as follows: SGLT2i > GLP-1RA > DPP4i > non-DPP4i > SGLT2i + GLP-1RA (Fig. 5A).

ICU

Evidence network Three studies report the endpoint of four treatment regimens involving novel hypoglycemic agents in people with diabetes and COVID-19 requiring intensive care unit (ICU) admission. The dot size indicates the size of the sample using the intervention, and the thickness of the line represents the number of trials, forming a closed loop (Fig. 2B).

Network meta-analysis Three studies reported requiring ICU admission involving four treatment options, and network comparisons among the above-described treatment options yielded a total of six pairwise comparisons, none of which were statistically significant (Fig. 4B). The forest plots shown in Sup. Figure 2.

SUCRA probability ranking Based on the area under the SUCRA curve, the four treatment options involving novel hypoglycemic agents were ranked as follows: SGLT2i > DPP4i > non-DPP4i > GLP-1RA (Fig. 5B).

Table 1 Characteristics of the included studies

Study	Study type	Sample	Age (years)	Male (%)	Metformin (%)	Statin (%)	Mortality (%)
Silverii (2021)[21]	Cross-sectional study	159	73.31 ± 12.66	NA	NA	NA	35.06%
Noh (2021)[22]	Retrospective cohort study	586	NA	NA	NA	NA	11.98%
Kahkoska (2021)[23]	Retrospective cohort study	12446	58.6 ± 13.1	46.60%	61.60%	27.20%	3.40%
Ramos-Rincón (2021)[24]	Cross-sectional study	2763	86 (82.7–88.9)	47.09%	53.50%	49.20%	48.70%
Orioli (2021)[25]	Retrospective cohort study	73	69 ± 14	52.00%	66.20%	35.60%	15.00%
Israelsen (2021)[26]	Prospective cohort study	616	59 (51–70)	53.00%	58.90%	50.00%	3.41%
Sourij (2020)[27]	Prospective and Retrospective cohort study	238	71.1 ± 12.9	63.60%	32.30%	NA	24.40%
Nyland (2021)[28]	Retrospective cohort study	29516	60.9 ± 15.0	48.20%	NA	NA	6.50%
Elibol (2021)[29]	Cross-sectional study	432	63.3 ± 10.3	45.60%	NA	NA	21.00%
Pérez-Belmonte (2020)[30]	Retrospective cohort study	2666	74.9 ± 8.4	61.90%	60.80%	58.00%	36.85%
Zhou (2020)[31]	Retrospective cohort study	2563	63 (55–67)	46.68%	NA	NA	2.93%
Mirani (2020)[32]	Case series	90	71 (64–78)	72.20%	76.67%	NA	42.22%

NA means Not Applicable

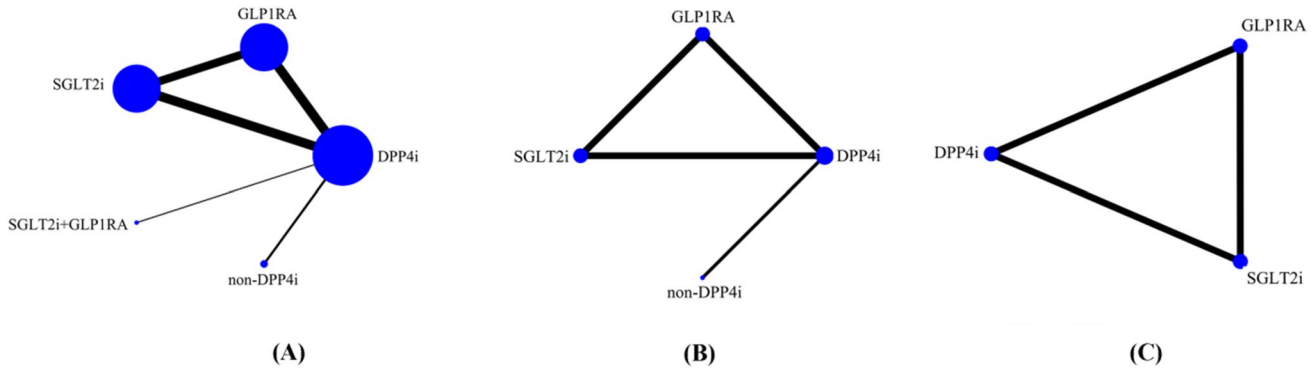

Fig. 2 Network diagrams of outcome indicators: (**A**) Mortality (**B**) ICU (**C**) Mechanical ventilation

Mechanical ventilation

Evidence network Two studies report the endpoint of three treatment regimens involving novel hypoglycemic agents in people with diabetes and COVID-19 requiring mechanical ventilation. The dot size indicates the size of the sample using the intervention, and the thickness of the line represents the number of trials, forming a closed loop (Fig. 2C).

Publication bias The funnel plot indicates that most scatter points are located in the middle or on one side of the vertical line (Fig. 3B). They are not symmetrical, suggesting the presence of publication bias.

Network meta-analysis Requiring mechanical ventilation was reported in 2 studies involving three treatment regimens, and network comparisons among the above-mentioned regimens yielded a total of 3 pairwise comparisons, of which one was statistically significant. The OR and 95% CI for SGLT2i compared with the DPP4i group reached 0.85 (0.75,0.97) (Fig. 4C). The forest plots are presented in Sup. Fig. 2.

SUCRA probability Ranking The ranking of the three therapeutic regimens involving novel hypoglycemic agents following the area under the SUCRA curve follows a descending order as follows: SGLT2i > GLP-1RA > DPP4i (Fig. 5C).

Discussion

In this study, the correlation between three novel glucose-lowering drugs and outcome indicators (mortality, requiring ICU admission, and requiring mechanical ventilation) in people with diabetes and COVID-19 was assessed. A total of 12 studies and three antidiabetic drugs (i.e., DPP4i, SGLT2i, and GLP-1RA) were covered in the analysis. As indicated by the results, in people with diabetes and COVID-19, mortality was significantly lower in the SGLT2i treatment group compared with the DPP4i group and the SGLT2i + GLP-1RA group. Requiring mechanical ventilation was significantly reduced in the SGLT2i group compared with the DPP4i

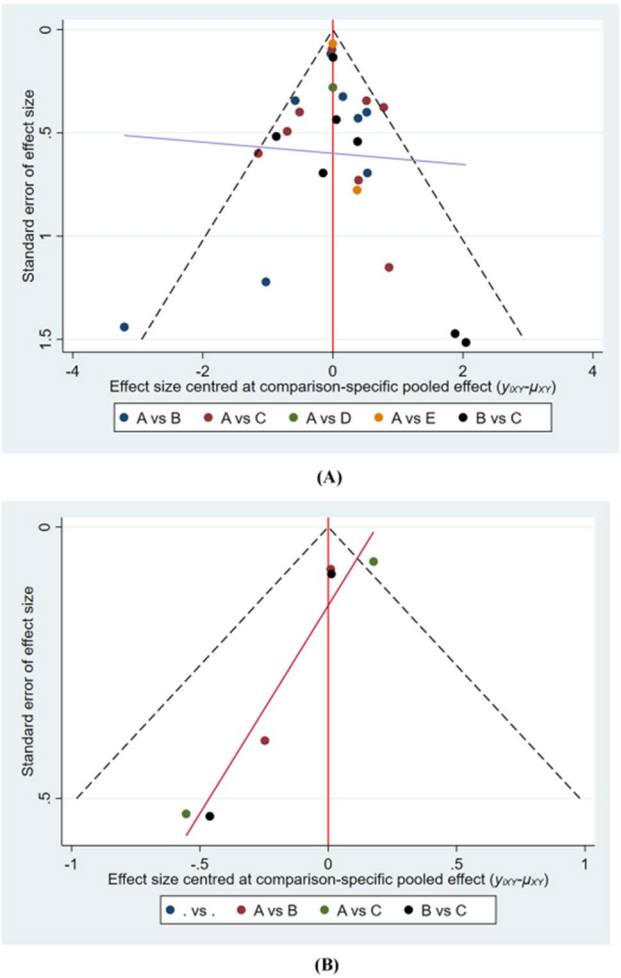

Fig. 3 Funnel plot outcome indicators: (**A**) Mortality (**B**) ICU. A: DPP4i, B:GLP1RA, C: SGLT2i

SGLT2i	1.11 (0.74,1.65)	**1.44 (1.02,2.04)**	1.92 (0.99,3.75)	**2.46 (1.03,5.88)**
0.90 (0.60,1.34)	GLP1RA	1.30 (0.92,1.84)	1.73 (0.89,3.37)	2.22 (0.93,5.30)
0.69 (0.49,0.98)	0.77 (0.54,1.09)	DPP4i	1.34 (0.76,2.35)	1.71 (0.77,3.80)
0.52 (0.27,1.01)	0.58 (0.30,1.12)	0.75 (0.43,1.32)	non-DPP4i	1.28 (0.48,3.40)
0.41 (0.17,0.97)	0.45 (0.19,1.07)	0.58 (0.26,1.30)	0.78 (0.29,2.07)	SGLT2i+GLP1RA

(A)

SGLT2i	1.09 (0.35,3.36)	1.29 (0.20,8.26)	1.67 (0.53,5.26)
0.92 (0.30,2.82)	DPP4i	1.18 (0.27,5.17)	1.53 (0.49,4.77)
0.78 (0.12,4.99)	0.85 (0.19,3.73)	non-DPP4i	1.30 (0.20,8.40)
0.60 (0.19,1.88)	0.65 (0.21,2.04)	0.77 (0.12,4.98)	GLP1RA

(B)

SGLT2i	1.08 (0.91,1.27)	**1.17 (1.04,1.33)**
0.93 (0.79,1.10)	GLP1RA	1.09 (0.94,1.26)
0.85 (0.75,0.97)	0.92 (0.79,1.07)	DPP4i

(C)

Fig. 4 Results from the NMA showing the effect of each of the interventions: (**A**) Mortality (**B**) ICU (**C**) Mechanical ventilation. The values in bold font represent statistically significant differences

group among diabetes and COVID-19 patients. As revealed by the above result, SGLT2i, among the three new hypoglycemic agents, is correlated with lower mortality and required mechanical ventilation in diabetes and COVID-19 patients.

SGLT2i is a unique class of glucose-lowering drugs primarily employed for the treatment of T2DM. The above class of drugs works by impairing the ability of the kidneys to absorb and filter glucose [33]. This drug exerts significant cardiorenal protective effects, especially in people subjected to atherosclerosis, heart failure, and decreased renal function [2, 34]. Moreover, existing research has suggested that this class of drugs can inhibit inflammation and fibrosis [34, 35]. An existing RCT study reported a lower but nonsignificant mortality rate in patients with diabetes administrated with dapagliflozin [36]. In COVID-19, SGLT2i reverses acid–base cytokine homeostasis by reducing lactate accumulation under the occurrence of hypoxemia and hypoxia, such that the decrease in cytoplasmic pH can be inhibited, and cellular damage can be prevented during cytokine storms [37]. The multiple effects of SGLT2i may be of potential benefit to COVID-19 patients, and SGLT2i may play a role in the future management of COVID-19[34, 38]. A previous meta-analysis has indicated that mortality is significantly lower in SGLT2i users compared with COVID-19 patients without SGLT2i [39, 40]. This study drew a conclusion that among with people with diabetes and COVID-19, mortality was significantly lower in the SGLT2i group compared with the DPP4i group and the SGLT2i + GLP-1RA group. Notably, there may be some controversy about the fact that the mortality rate of the SGLT2i group is lower than that of SGLT2i + GLP-1RA, the main possible reason for the result is that patients on both SGLT2i and GLP-1RA may have more severe diabetes and are associated with more mortality. Further relevant in vivo or in vitro model validation should be performed. Moreover, it is recommended that more standardized randomized controlled double-blind trials are needed in the future to provide a stronger basis for the safety and efficacy of novel glucose-lowering drugs for COVID-19 patients with diabetes. Requiring mechanical ventilation was significantly reduced in the SGLT2i group compared with the DPP4i group.

GLP-1 is generated by L cells in the distal ileum and proximal colon, binding to receptors in the pancreas, kidney, lung, gastrointestinal tract, as well as peripheral nervous system. Moreover, it is capable of stimulating insulin production, inhibiting glucagon release while delaying gastric emptying. GLP-1RA is another hypoglycemic agent that significantly reduces hospitalization, respiratory complications, and mortality in patients with diabetes [28]. In general, GLP-1RA acts on GLP-1 receptors in the lung epithelium and immune cells. GLP-1RA is capable of lowering blood glucose while controlling inflammation-induced lung damage and reducing major cardiovascular complications [2, 41]. Existing research [42] reported that GLP-1RA is capable of improving pulmonary function in patients with diabetes. In COVID-19, GLP-1RA is conducive to reducing cytokine-induced lung injury by interfering with the NF-kB pathway, or exerting anti-inflammatory effects [43, 44]. Two meta-analyses have confirmed the benefit of GLP-1RA in managing COVID-19, mainly in terms of lower mortality in GLP-1RA users compared with non-users [34, 38]. However, no correlation between GLP-1RA and mortality was identified in this study. The possible reason for this result is that the number of included studies in this study was limited and only compared among new hypoglycemic drugs.

An enzyme termed DPP-4 rapidly degrades GLP-1, i.e., DPP4i targets, a process that maintains the function of GLP-1 for more extended periods. DPP-4 is abundantly expressed

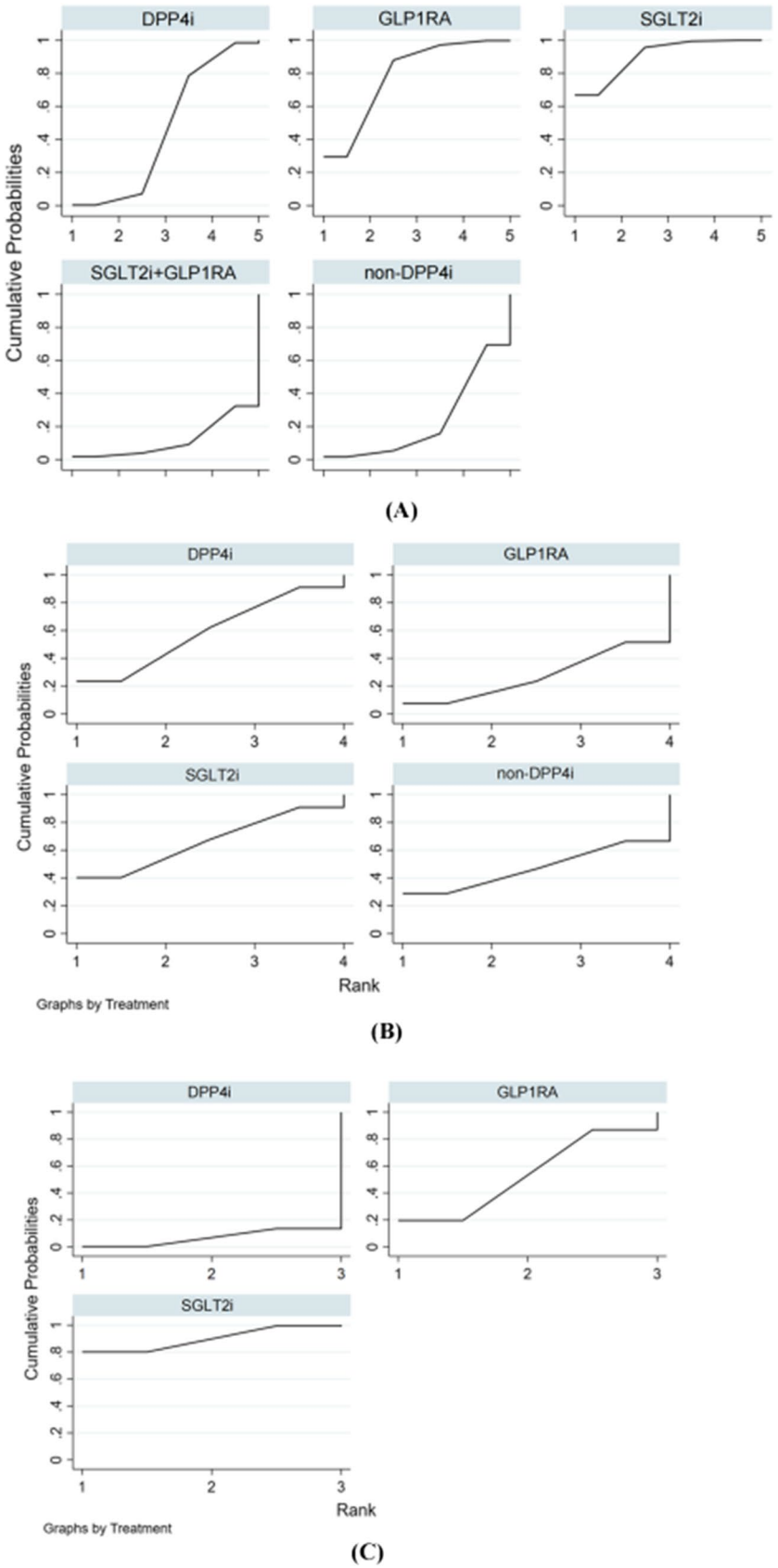

Fig. 5 Curve diagram of SUCRA of outcome indicators: (**A**) Mortality (**B**) ICU (**C**) Mechanical ventilation

in various cells (e.g., lymphocytes, adipocytes, endothelial cells, and lung epithelial cells), and is also present on the surface of different immune cells [45, 46]. DPP-4 takes on a critical significance to regulating inflammatory and immune responses through its ability to regulate various cytokines, chemokines, as well as peptide hormones [47, 48]. Given the role of DPP4i in regulating T-cell activity [45], the use of DPP4i has raised concerns regarding increased susceptibility to infection. However, no evidence in large clinical trials has demonstrated that using DPP4i can elevate the risk of infection [49, 50]. Uncertain anti-inflammatory properties are caused by the effect of DPP4i, which attenuates the activation of inflammatory vesicles and reduces the levels of inflammatory biomarkers (e.g., IL-6, IL-18, and CRP) in human plasma in some studies [51, 52]. Several studies have suggested that DPP4i exerts no effect on inflammatory biomarkers at the human plasma level [53, 54]. Nevertheless, DPP4i can potentially enhance the activity of certain inflammatory networks by preventing the degradation of inflammatory factors by the DPP4 enzyme [55]. Since DPP4i is capable of modulating inflammatory responses via multiple pathways, we hypothesized that they may have beneficial effects on patients prone to cytokine storming under the infection with COVID-19 [56]. Besides, no consistent conclusions have been reached regarding the correlation between DPP4i use and mortality in patients with combined diabetes mellitus and COVID-19. Some research has suggested that DPP4i use shows a correlation with lower mortality [39, 57, 58], and some previous studies have suggested that DPP4i can lead to increased mortality in people with diabetes and COVID-19 [40, 59]. Existing meta-analyses [11, 50, 60–63] indicated that DPP4i does not significantly affect COVID-19-associated mortality, which may also be related to the uncertain anti-inflammatory properties of DPP4i. This study found that DPP4 use was correlated with higher mortality and mechanical ventilation compared with SGLT2 in patients with combined diabetes mellitus COVID-19.

For the mortality, the ranking of the five treatment options involving novel hypoglycemic agents, based on the area under the SUCRA curve, was as follows: SGLT2i > GLP-1RA > DPP4i > non-DPP4i > SGLT2i + GLP-1RA. Notely, In our study, the SUCRA value of ICU was SGLT2i > DPP4i > non-DPP4i > GLP-1RA, but there was no significant difference among their ORs. The SUCRA value seems unreasonable. However, this phenomenon is not uncommon and has been addressed in several previous studies [64]. In particular, a potential bias in SUCRA does exist in the calculation, as SUCRA does not take into account the magnitude of effect differences between treatments, such interventions with wider CIs or fewer events may yield higher SUCRA values compared to some interventions with nonsignificant ORs. Respecting the mechanical ventilation, the ranking of the three therapeutic regimens involving novel hypoglycemic agents following the area under the SUCRA curve follows a descending order as follows: SGLT2i > GLP-1RA > DPP4i.

In summary, SGLT2i was more likely to be conducive to treating people with diabetes and COVID-19 among the above interventions included. The top interventions could be selected for patients with different goals.

Limitations

This study has some limitations. Firstly, this study included only observational studies, such that conclusions should be drawn with caution. However, we recruited the largest number of participants from a variety of studies of fair quality, allowing our meta-analysis to have high internal validity. Secondly, additional primary data mining is required because of the complexity of current diabetes treatment protocols. Thirdly is that due to the high publication rate on the COVID-19 topic within the past three years, some studies might be missed that were not included in this study. Although this was inevitable, we minimized this problem by assigning two investigators to systematically search and select studies and consulting with another investigator when necessary to reach a final decision.

Conclusion

In brief, this study aimed to assess the correlation between three novel glucose-lowering drugs and outcome indicators (mortality, requiring ICU admission, and requiring mechanical ventilation) in people with diabetes and COVID-19. To be specific, SGLT-2i was more likely to be conducive to treating people with diabetes and COVID-19. The above-described results may have implications for the clinical management of diabetes with COVID-19 and may inform the development of clinical practice guidelines or future RCT trials.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s13410-023-01228-x.

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Author contributions YY and LZ contributed to conception and design of the study and organized the database. CL performed the statistical analysis. YY wrote the first draft of the manuscript. LZ wrote sections of the manuscript. TK reviewed and edited the manuscript. YW made a critical review, commentary, and revision of the manuscript. All authors have read and approved the final manuscript.

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Data Availability Data supporting the finding of this study are available within the article text and tables.

Declarations

Ethics approval and consent to participate Not applicable.

Conflict of interest The authors declare no conflict of interest.

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