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ORIGINAL PAPER

Short- and long-term prognosis of glycemic control in COVID-19 patients with type 2 diabetes

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Summary

Background and aim: To systematically evaluate the associations between glycemic control and short- to long-term outcomes in coronavirus disease 2019 (COVID-19) patients with type 2 diabetes (T2D).
Design and methods: A multi-center prospective cohort study including 574 COVID-19 patients with T2D was conducted in Wuhan, China. All patients were followed-up 1 year after hospital discharge using a uniformed questionnaire including self-reported symptoms, and the chronic obstructive pulmonary disease assessment test items.
Results: Of the 574 patients, 443 (77.2%) had well-controlled blood glucose. Glycemic control was significantly associated with decreased risk of death [odds ratio (OR) 0.24, 95% confidence interval (CI) 0.10–0.57], intensive care unit admission (OR 0.22, 95% CI 0.10–0.49), invasive mechanical ventilation (OR 0.25, 95% CI 0.08–0.72), disease progression (OR 0.25, 95% CI 0.11–0.55), and composite outcome (OR 0.26, 95% CI 0.14–0.49). The top five long-term sequelae include fatigue (31.5%), sweating (21.2%), chest tightness (15.1%), anxiety (12.2%), myalgia (10.6%) and short breath (6.4%). Glycemic control was associated with decreased risk of respiratory sequelae (OR 0.42, 95% CI 0.18–0.99; $P = 0.048$).
Conclusions: Glycemic control was significantly associated with short-term outcomes in COVID-19 patients with T2D and showed a significant association with long-term respiratory sequelae. The management and control of blood glucose has a positive impact on prognosis of COVID-19.

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Introduction

Type 2 diabetes (T2D) has been identified as the second most common comorbidity of coronavirus disease 2019 (COVID-19), and patients with T2D are at increased risk of severe COVID-19 complications and worse prognosis.[1–3] In a multicenter national study in China, T2D was present in 8.2% of patients, and the severe group had a higher proportion of T2D (23.7% vs. 6.8%).[4] Living systematic review and meta-analyses showed that diabetes was independently associated with increased risk of in-hospital severity and death of COVID-19.[5,6]

To date, no study has yet systematically evaluated whether glycemic control contributes to the short-term prognosis of COVID-19, as well as the long-term outcomes of survivors of COVID-19 with T2D. Current evidence focused on the comparisons between pre-existing T2D group and control group to explore the risk factor ordinarily.[2,3,5] However, T2D is a highly complex and heterogeneous disease, for which studies have found that different glycemia status (e.g. glycemic control rate) could result in different outcomes.[6,7] Even different antidiabetic medications can cause very different treatment outcomes of COVID-19 although the results might be biased.[8–13] More attention should be focused on the glycemia status, and only effective glycemic control is crucial for COVID-19 patients with T2D.[14]

In this study, we aimed to present the short- to long-term outcomes of COVID-19 patients with T2D, and systematically evaluate whether glycemic control contributes to the short-term prognosis of COVID-19, and long-term outcomes of survivors of COVID-19 with T2D in a multi-center prospective cohort study in Wuhan, China.

Materials and methods

Study design and patients

Included in this multi-center prospective cohort study were all laboratory-confirmed COVID-19 patients with T2D, who were admitted to the two designated hospitals in Wuhan, China (Huoshenshan Hospital and Taikang-Tongji Hospital) between 12 February and 10 April 2020.[2,15,16] Baseline information, including demographic characteristics, coexisting disorders, clinical symptoms and laboratory findings were collected from electronic medical record system and validated by a telephone interview. All discharged patients met the uniform discharge criteria of the World Health Organization (WHO) interim guidance.[17] Follow-up data were obtained from telephone interviews by two trained physicians between 1 March 2021 and 20 March 2021, using a uniformed questionnaire including self-reported symptoms, and the chronic obstructive pulmonary disease (COPD) assessment test (CAT) score items (Supplementary Table 1). Patients were asked to report any persistent or emerging symptoms, respectively. The patient's current symptoms are carefully distinguished from their pre-disease status or other underlying diseases that are not associated with infection of COVID-19. All survey data were double entered and validated using EpiData (version 3.1, EpiData Association, Odense, Denmark) software, and disputes were arbitrated by the expert committees composed of experts of respiratory and critical care medicine, and epidemiology. This study was approved by the institutional review board of Daping Hospital of Army Medical University (Ethics number 202153), and verbal informed consent was obtained from all patients or their legal guardians prior to the follow-up.

Definition and outcomes

Disease severity at admission was defined by the WHO guideline for COVID-19. Identification of T2D was based on an ICD-10 code for a diagnosis of T2D in the electronic medical record. Well-controlled blood glucose was defined as glycemic variability upon admission lower than 10.0 mmol/l, while the poorly controlled blood glucose was defined when exceeding 10.0 mmol/l according to the guideline for the prevention and treatment of T2D in China (2020 edition).[18] Intensive care unit (ICU) admission, the need for invasive mechanical ventilation, in-hospital death and disease progression are short-term outcomes in our study. Disease progression was defined as the occurrence of a progression in a disease category during hospitalization. The short-term composite outcome is defined as a composite endpoint of the need for ICU admission, mechanical ventilation, in-hospital death or disease progression. Post-sequelae and CAT scoring 1 year after discharge were the primary indicator of long-term outcomes. Post-sequelae includes any one of systemic sequelae, respiratory sequelae, cardiovascular sequelae, neurological sequelae and digestive sequelae, while emerging sequelae were defined as symptoms that were not observed during hospitalization but were reported in follow-up. Meanwhile, CAT was commonly used to assess symptom burden of COVID-19 patients, and CAT scores $\geq$ 10 was recommended as the threshold for maintenance treatment in COPD.[19]

Statistical analysis

Demographic characteristics and clinical consequences in patients were presented as median [interquartile range (IQR)] for continuous variables and expressed as counts and percentages for categorical variables. Means of continuous data from two groups were compared using the Mann–Whitney U test. The frequencies of categorical variables were compared using the Chi-squared test or Fisher's exact test (when one or more of the cell counts in a 2×2 table is less than 5). Survival curve was conducted by the Kaplan–Meier method. We also used a logistic regression model to find risk factors for the short- to long-term outcomes of COVID-19 patients with T2D. All variables associated with endpoints were included in the univariate regression model, and variables with $P < 0.1$ in univariate analyses were entered into the multivariate regression models. To reduce the effects of selection bias and confounding factors caused by loss of follow-up in prognosis comparison, propensity score matching (PSM) was performed to create comparable groups. We evaluated the stability of the results by comparing the differences between totally enrolled patients and patients selected by PSM. The factors for propensity score calculation include age, sex, disease severity at admission and clinical symptoms with statistically significant differences, and 1:1 matching was performed using a 0.1 caliper width. All analyses were done with R software (Institute for Statistics and Mathematics, Vienna, Austria), version 4.0.2. The reported statistical significance levels were all two-sided, and $P < 0.05$ was considered to indicate statistical significance.

Results

Baseline characteristics

A total of 574 COVID-19 patients with T2D were included in this study (Table 1 presented the baseline characteristics). Of them, 443 (77.2%) had well-controlled blood glucose, while 131 (22.8%)

Table 1. Baseline characteristics

Variables	Total ($N = 574$)	Poorly controlled ($N = 131$)	Well-controlled ($N = 443$)	P-value
Age (years), median (IQR)[a]	65 (58–72)	63 (57–71)	65 (58–72)	0.269
17–65	301 (52.4%)	68 (51.9%)	210 (47.4%)	0.372
≥66	281 (47.6%)	63 (48.1%)	233 (52.6%)	
Sex				
Male	311 (54.2%)	74 (56.5%)	237 (53.5%)	0.551
Female	263 (45.8%)	57 (43.5%)	206 (46.5%)	
Severity at admission				
Non-severe	342 (59.6%)	70 (53.4%)	272 (61.4%)	0.106
Severe	262 (40.4%)	61 (46.6%)	171 (38.6%)	
Coexisting disorders				
Hypertension	352 (61.3%)	78 (59.5%)	274 (61.9%)	0.683
Coronary heart disease	83 (14.5%)	15 (11.5%)	68 (15.3%)	0.322
Cardiovascular disease	111 (19.3%)	23 (17.6%)	88 (19.9%)	0.616
Cerebrovascular disease	60 (10.5%)	13 (9.9%)	47 (10.6%)	0.873
Tumor	25 (4.4%)	7 (5.3%)	18 (4.1%)	0.625
Chronic kidney disease	33 (5.7%)	9 (6.9%)	24 (5.4%)	0.670
COPD	4 (0.7%)	0 (0%)	4 (0.9%)	1.000
Symptoms				
Myalgia	148 (26.0%)	41 (31.3%)	107 (24.2%)	0.112
Chill	15 (2.6%)	1 (0.8%)	14 (3.2%)	0.210
Fatigue	327 (57.0%)	79 (60.3%)	248 (56.0%)	0.422
Cough	401 (69.9%)	99 (75.6%)	302 (68.2%)	0.129
Sore throat	29 (5.1%)	6 (4.6%)	23 (5.2%)	0.827
Hemoptysis	3 (0.5%)	0 (0%)	3 (0.7%)	1.000
Expectoration	118 (20.6%)	28 (21.4%)	90 (20.3%)	0.806
Nasal congestion	6 (1.0%)	2 (1.5%)	4 (0.9%)	0.624
Anorexia	306 (53.5%)	72 (55.0%)	234 (52.8%)	0.691
Diarrhea	33 (5.7%)	9 (6.9%)	24 (5.4%)	0.670
Nausea	11 (1.9%)	4 (3.1%)	7 (1.6%)	0.283
Vomiting	13 (2.3%)	3 (2.3%)	10 (2.3%)	1.000
Dizziness	17 (3.0%)	5 (3.8%)	12 (2.7%)	0.557
Headache	15 (2.6%)	4 (3.1%)	11 (2.5%)	0.756
Chest tight	184 (32.1%)	36 (27.5%)	148 (33.4%)	0.241
Short breath	259 (45.1%)	69 (52.7%)	190 (42.9%)	0.057
Dyspnea	63 (11.0%)	19 (14.5%)	44 (9.9%)	0.097

[a]Age was treated as a continuous variable in this table.

had poorly controlled blood glucose (Figure 1). The median age of the eligible patients was 65.0 (IQR 58.0–72.0) years old, with 311 (54.2%) being male. A total of 262 (40.4%) patients were categorized as severe. There was no significant difference in age, sex, disease severity and clinical symptoms at baseline (all P values >0.05).

Associations of glycemic control with short-term outcomes of COVID-19

As shown in Table 2, totally 24 deaths, 29 ICU admissions, 15 invasive mechanical ventilation, 27 disease progression and 51 composite outcomes occurred during hospitalization. As expected, the percentages of all short-term outcomes in the well-controlled group were significantly lower, compared with those in the poorly controlled group ($P < 0.05$) (Figure 2). Glycemic control was significantly associated with decreased risk of death [odds ratio (OR) 0.24, 95% confidence interval (CI) 0.10–0.57], ICU admission (OR 0.22, 95% CI 0.10–0.49), invasive mechanical ventilation (OR 0.25, 95% CI 0.08–0.72), disease progression (OR 0.25, 95% CI 0.11–0.55) and composite outcome (OR 0.26, 95% CI 0.14–0.49), after adjusted for disease severity at admission, age and sex (Table 2). Survival curve also showed that there was a significant difference in terms of survival rate between the two groups ($P < 0.001$) (Figure 3). We also explored the risk factors of the short-term composite outcome using a multivariate logistic regression model and identified that glycemic control (OR 0.23, 95% CI 0.12–0.43), disease severity at admission (OR 2.03, 95% CI 1.04–3.97), dyspnea (OR 4.35, 95% CI 2.14–8.81) and cardiovascular disease (OR 3.84, 95% CI 1.97–7.48), were independently associated with the composite outcome (Table 3).

Associations of glycemic control with long-term outcomes of COVID-19

Patients included in this study were further followed-up 1 year after hospital discharge. As shown in Figure 4, of the 574 COVID-19 patients with T2D, 263 were not available because of death during hospitalization ($n = 24$) or decline to participate ($n = 136$) or unable to be contacted ($n = 103$). Hence, 311 (54.2%) patients with complete follow-up data were enrolled. The median (IQR) age of the enrolled participants was 63.0 (53.0–70.0) years, with 163 (52.4%) men and 148 (47.6%) women. The median (IQR) time from discharge to follow-up was 362.0 (357.0–370.0) days. Of the 311 eligible patients, 153 patients (49.2%) report at least one sequelae at follow-up (Table 4). The top five post-sequelae include fatigue (31.5%), sweating (21.2%), chest

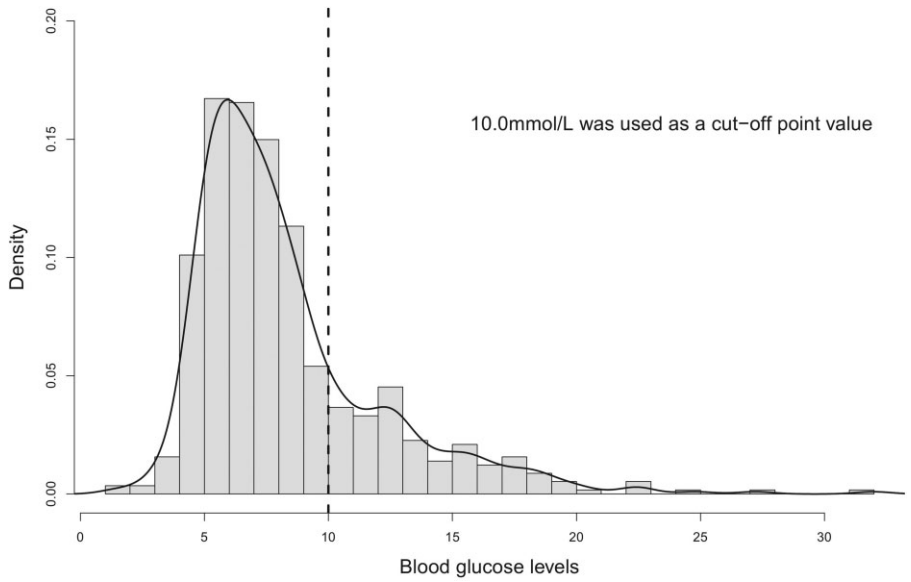

Figure 1. Distribution of the blood glucose level among the poorly controlled group and the well-controlled group.

Table 2. Associations of glycemic control with short-term outcomes of COVID-19

Endpoints	Poorly controlled ($N = 131$)	Well-controlled ($N = 443$)		OR (95% CIs)[a]	*P*-value
Death	13 (9.9%)	11 (2.5%)	Unadjusted	0.23 (0.10–0.53)	0.001
			Adjusted[b]	0.24 (0.10–0.57)	0.001
ICU admission	16 (12.2%)	13 (2.9%)	Unadjusted	0.22 (0.10–0.57)	<0.001
			Adjusted	0.22 (0.10–0.49)	<0.001
Invasive mechanical ventilation	8 (6.1%)	7 (1.6%)	Unadjusted	0.25 (0.09–0.69)	0.009
			Adjusted	0.25 (0.08–0.72)	0.010
Disease progression	14 (10.7%)	13 (2.9%)	Unadjusted	0.25 (0.12–0.55)	0.001
			Adjusted	0.25 (0.11–0.55)	0.001
Composite outcome[c]	25 (19.1%)	26 (5.9%)	Unadjusted	0.26 (0.15–0.48)	<0.001
			Adjusted	0.26 (0.14–0.49)	<0.001

[a]The uncontrolled group was used as the benchmark for comparison.
[b]Adjusted for disease severity at admission, age and sex.
[c]Composite outcome is defined as a composite endpoint of ICU admission, the need for invasive mechanical ventilation, in-hospital death and disease progression.

tightness (15.1%), anxiety (12.2%), myalgia (10.6%) and short breath (6.4%). Of them, fatigue, chest tightness, myalgia and short breath are persistent symptoms, although the prevalence rate dropped sharply (Supplementary Table 2 and Figure 5). Sweating and anxiety are emerging sequelae (Supplementary Table 2 and Figure 5). The median of CAT score was 2 (0–5) in all patients, while a total of 26 patients (8.4%) had CAT scores ≥10 (Table 4).

We then evaluated the associations of glycemic control with different long-term outcomes COVID-19, including systemic sequelae, neurological sequelae, cardiovascular sequelae, respiratory sequelae, digestive sequelae, emerging sequelae and CAT score ≥ 10. We found glycemic control was associated with decreased risk of respiratory sequelae (OR 0.42, 95% CI 0.18–0.99; $P = 0.048$) (Table 5), and blood glucose levels were significantly associated with increased risk of respiratory sequelae (OR for per unit: 1.11, 95% CI 1.02–1.21; $P = 0.017$) (Supplementary Table 3).

As the patients lost to follow-up before were a little older than those enrolled ($P < 0.001$, Supplementary Table 4), PSM was conducted to evaluate the lost to follow-up bias in the sensitivity analysis. Totally, 189 patients in the enrolled population were matched successfully with those lost to follow-up, and the baseline characteristics were comparable (Supplementary Table 4). We then compared the post-sequelae 1 year after hospital discharge between totally enrolled patients ($n = 311$) and those selected by PSM ($n = 189$) and did not find any significant difference in the long-term outcomes (Supplementary Table 5, all $P > 0.05$). This indicates the loss to follow-up bias was negligible, and the enrolled patients were representative.

Discussion

In this prospective cohort study, we systematically evaluated the associations between glycemic control and short- to long-term outcomes of COVID-19 patients with T2D. Of the 574 patients, 443 (77.2%) had well-controlled blood glucose. For short-term outcomes, glycemic control was significantly associated with decreased risk of death, ICU admission, invasive mechanical ventilation, disease progression and composite outcome. For long-term outcomes, glycemic control was

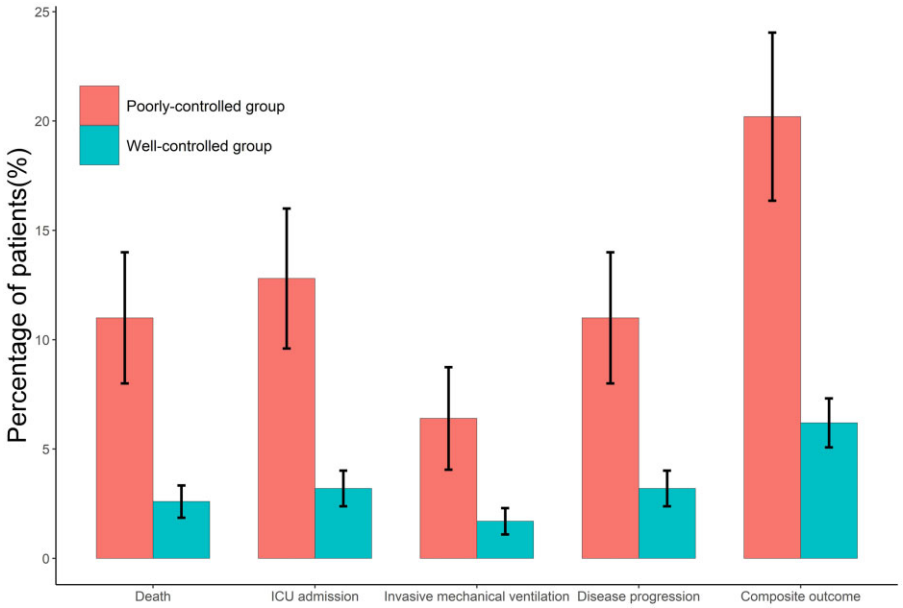

Figure 2. The comparison of percentage of the short-term outcomes between the poorly controlled group and the well-controlled group. Outcomes are shown on the x-axis, and the percentage of patients in each outcome group is shown on the y-axis.

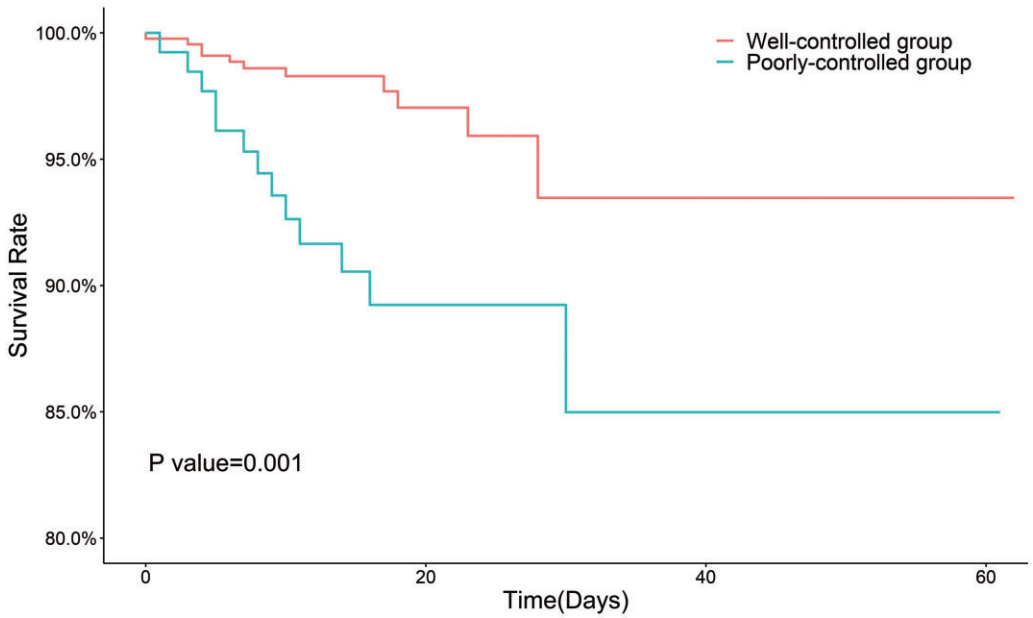

Figure 3. Kaplan–Meier survival curves for the poorly controlled group and the well-controlled group. The two survival curves to compare the survival probability at different point of time of the two groups.

significantly associated with decreased risk of respiratory sequelae. Taken together, our study verified that glycemic control was significantly associated with short-term outcomes in COVID-19 patients with T2D and showed a significant association with long-term respiratory sequelae.

It is known that hyperglycemic environment is detrimental to the clinical prognosis of COVID-19. However, whether glucose-lowering drugs affect the prognosis of COVID-19 patients with T2D is still inconclusive.[14] Currently, several glucose-lowering drugs were mainly used in COVID-19 patients, including metformin, insulin, sodium-glucose cotransporter 2 (SGLT2) inhibitor, sulfonylureas and dipeptidyl peptidase 4 (DPP4) inhibitors and a combination of such drugs would be used depending on the clinical practice.[20,21] According to a national study in England, metformin, SGLT2 inhibitors and sulfonylureas were associated with reduced risks of the COVID-19-related mortality, while insulin and DPP4 inhibitors were associated with increases in risk.[22] A study conducted in Wuhan, China also reported that insulin treatment was associated with increased mortality in COVID-19 patients with T2D.[23] However, another study in Wuhan found metformin was associated with increased incidence of acidosis and was not associated with increased 28-day all-cause mortality.[8] A study in Korea impacted that DPP-4i in monotherapy or combination with

Table 3. Risk factors associated with the short-term composite outcome

Variables	Univariate			Multivariate		
	OR	95% CIs	P-value	OR	95% CIs	P-value
Sex						
Male	1					
Female	0.72	0.40–1.29	0.577			
Age						
17–65	1					
≥66	2.20	1.19–4.07	0.012			
Glycemic control	0.26	0.15–0.48	<0.001	0.23	0.12–0.43	<0.001
Disease severity at admission						
Non-severe	1					
Severe	3.28	1.79–6.03	<0.001	2.03	1.04–3.97	0.038
Symptoms						
Myalgia	1.17	0.62–2.20	0.626			
Fatigue	0.73	0.41–1.29	0.281			
Cough	1.06	0.56–1.98	0.862			
Sore throat	1.21	0.35–4.14	0.761			
Expectoration	1.46	0.76–2.78	0.255			
Nasal congestion	2.10	0.24–18.31	0.503			
Anorexia	1.10	0.62–1.96	0.737			
Diarrhea	1.370	0.46–4.04	0.570			
Nausea	2.36	0.50–11.22	0.280			
Chest tight	1.65	0.93–2.59	0.090			
Short breath	1.56	0.88–2.77	0.126			
Dyspnea	5.69	2.98–10.86	<0.001	4.35	2.14–8.81	<0.001
Coexisting conditions						
Hypertension	1.11	0.61–2.00	0.740			
Coronary heart disease	2.40	1.24–4.64	0.010			
Cardiovascular disease	4.29	2.38–7.73	<0.001	3.84	1.97–7.48	<0.001
Cerebrovascular disease	2.63	1.27–5.44	0.009			
Tumor	3.58	1.36–9.39	0.010			
Chronic kidney disease	3.75	1.60–8.80	0.002			
Chronic liver disease	2.63	0.95–7.29	0.063			

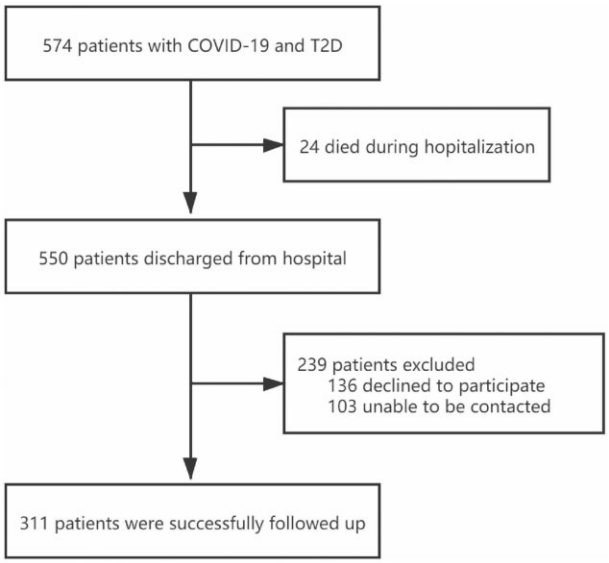

Figure 4. Flow chart of the follow-up of the enrolled COVID-19 patients with T2D.

renin–angiotensin system blockers shown protective effects against severe/lethal cases.[24] Even some research reported that there is no significant association between poor prognosis and glucose-lowering drugs in patients with COVID-19.[20,25] There is no clear indication to change prescribing of glucose-lowering drugs in COVID-19 patients to date, as these results may be biased by the glycemic control effect.

Previous studies have demonstrated glycemic control is significantly associated with the risk of severe complications and death of severe acute respiratory syndrome (SARS) and middle east respiratory syndrome (MERS) with T2D.[26,27] For short-term outcomes, Klonoff *et al.*[28] reported that admission glucose was a strong predictor of death among patients directly admitted to the ICU, while Zhu *et al.*[23] verified that well-controlled blood glucose was associated with markedly lower mortality compared to individuals with poorly controlled blood glucose. These results verified our findings, which revealed that glycemic control was significantly associated with decreased risk of death, ICU admission, invasive mechanical ventilation, disease progression and composite outcome in COVID-19 patients with T2D. Therefore, proper control of blood glucose levels is important to improve the short-term prognosis of COVID-19 patients with T2D. The possible explanations for COVID-19 patients with poorly controlled blood glucose more likely to develop poor outcomes include, first, the hyperglycemic environment could exacerbate insulin resistance, leading to increased β-cell stress naturally and eventually β-cell exhaustion and local innate immune response.[29,30] Second, in poorly controlled patients, potentially high glycosylated angiotensin-converting enzyme 2 (ACE2) in various organs may also increase SARS-CoV-2 viral

Table 4. Comparison of long-term outcomes between the poorly controlled group and the well-controlled group

Endpoints	Total ($n = 311$)	Poorly controlled ($N = 75$)	Well-controlled ($N = 236$)	P-value
Any one of post-sequelae	153 (49.2%)	37 (49.3%)	116 (49.2%)	1.000
Systemic sequelae	101 (32.5%)	26 (34.7%)	75 (31.8)	0.672
Fatigue	95 (30.5%)	26 (34.7%)	69 (29.2%)	0.390
Myalgia	32 (10.3%)	7 (9.3%)	25 (10.6%)	0.831
Respiratory sequelae	25 (8.0%)	10 (13.3%)	15 (6.4%)	0.084
Dyspnea	10 (3.2%)	4 (5.3%)	6 (2.5%)	0.261
Cough	14 (4.5%)	6 (8.0%)	8 (3.4%)	0.111
Expectoration	10 (3.2%)	4 (5.3%)	6 (2.5%)	0.564
Sore throat	3 (1.0%)	1 (1.3%)	2 (0.8%)	0.482
Nasal congestion	1 (0.3%)	1 (1.3%)	0	0.241
Cardiovascular sequelae	56 (18.0%)	11 (14.7%)	45 (19.1%)	0.399
Edema	4 (1.3%)	0	4 (1.7%)	0.576
Chest tightness	44 (14.1%)	9 (12%)	35 (14.8%)	0.577
Short breath	18 (5.8%)	4 (5.3%)	14 (5.9%)	1.000
Palpitation	12 (3.9%)	3 (4.0%)	9 (3.8%)	1.000
Neurological sequelae	130 (41.8%)	32 (42.7%)	98 (41.5%)	0.894
Dizziness	12 (3.9%)	4 (5.3%)	8 (3.4%)	0.492
Headache	7 (2.3%)	2 (2.7%)	5 (2.1%)	0.676
Anxiety	38 (12.2%)	11 (14.7%)	27 (11.4%)	0.543
Sweating	66 (21.2%)	18 (24.0%)	48 (20.3%)	0.519
Smell reduction	7 (2.3%)	2 (2.7%)	5 (2.1%)	0.676
Taste change	8 (2.6%)	3 (4.0%)	5 (2.1%)	0.405
Digestive sequelae	8 (2.6%)	2 (2.7%)	6 (2.5%)	1.000
Diarrhea	1 (0.3%)	0	1 (0.4%)	1.000
Nausea	2 (0.6%)	0	2 (0.8%)	1.000
Vomiting	1 (0.3%)	0	1 (0.4%)	1.000
Anorexia	4 (1.3%)	2 (2.7%)	2 (0.8%)	0.247
CAT scores	2 (0–5)	2 (0–5)	2 (0–5)	0.528
CAT score $\geq$ 10	26 (8.4%)	6 (8.0%)	20 (8.5%)	1.000

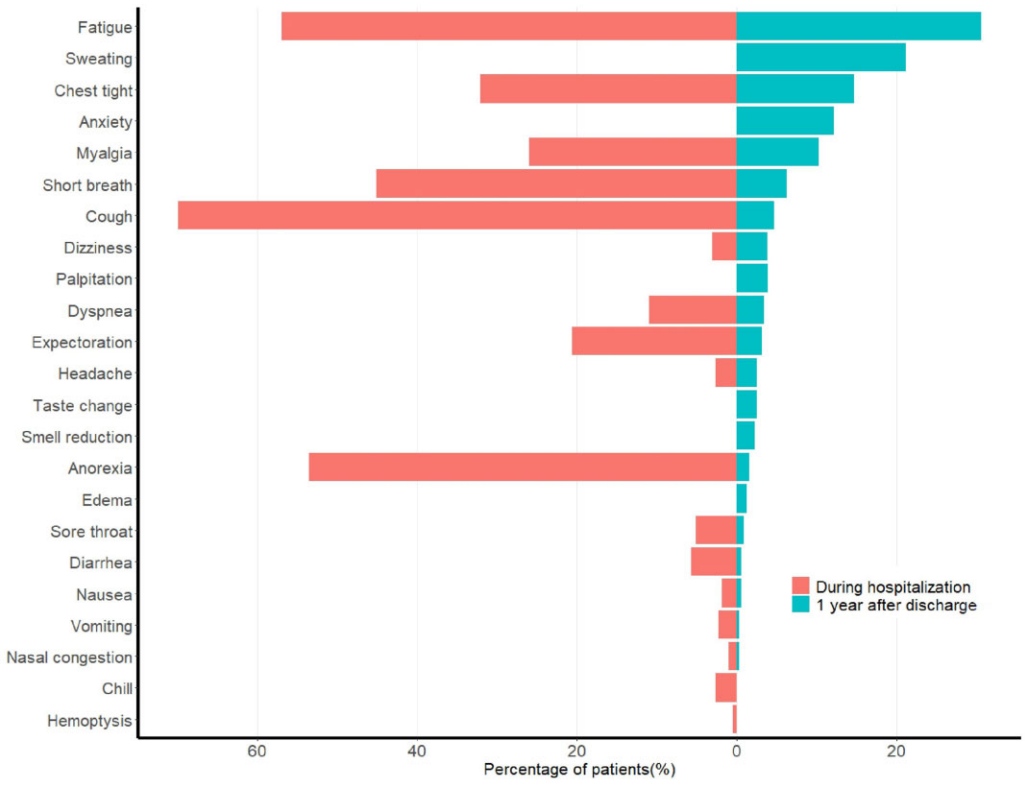

Figure 5. Clinical symptoms during hospitalization and 1 year after discharge.

Table 5. Evaluate the effect of glycemic control on different long-term outcomes

Endpoints	OR[a]	95% CIs	P-value
Any one of post-sequelae	1.0	0.59–1.69	0.995
Systemic sequelae	0.89	0.51–1.56	0.690
Respiratory sequelae	0.42	0.18–0.99	0.048
Cardiovascular sequelae	1.38	0.67–2.85	0.377
Neurological sequelae	0.97	0.57–1.66	0.913
Digestive system sequelae	0.86	0.17–4.42	0.860
Emerging sequelae	0.80	0.45–1.41	0.436
CAT score $\geq$ 10	1.01	0.41–2.09	0.980

Controlled blood glucose was defined when glycemic variability upon admission lower than 10.0 mmol/l.

[a]Adjusted for disease severity at admission, age and sex.

binding sites, leading to a higher propensity for COVID-19 infection and higher disease severity.[31]

In addition to short-term outcomes, we also followed-up the long-term outcomes of COVID-19 patients with T2D. After 1 year follow-up, the clinical symptoms of patients were greatly relieved, and 49.2% patients in our study reported at least one sequelae, consistent with results in other populations.[32,33] Among the top five long-term sequelae, sweating and anxiety are emerging sequelae, which indicated that the psychological comfort after hospital discharge of COVID-19 should not be neglected.[34] Our results indicated that glycemic control was significantly associated with decreased risk of respiratory sequelae, and blood glucose levels were significantly associated with increased risk of respiratory sequelae 1 year after hospital discharge. It can be interpreted that hyperglycemia-induced pulmonary connective tissue change, inflammatory response and microangiopathy are the most likely causative mechanisms leading to pulmonary function and respiratory symptoms.[35]

Our study also has several limitations. First, similar to other follow-up studies, a high rate of loss to follow-up possibly caused by individual willingness of patients not to be continuously concerned might bias the incidence of post-sequelae. However, the PSM suggests this bias might be limited. Second, because both the two hospitals (Huoshenshan Hospital and Taikang-Tongji Hospital) are emergency admission hospitals of COVID-19, glycemia was the only blood glucose parameter that was assayed and included in the data analyses, which could introduce unexpected confounding if another parameter, unmeasured but correlated to blood glucose concentration, were the actual driver of the shown effect. Third, long-term outcomes may have been influenced by a severe short-term outcome, and the glycemic control status might vary after hospital discharge. Fourth, telephone follow-up relied on self-reported symptoms may affect the accuracy of the long-term outcomes, although we performed rigorous quality control and repeat surveys of partial samples.

Conclusions

In conclusion, our study provides valuable clues that glycemic control was significantly associated with short-term outcomes in COVID-19 patients with T2D and showed a significant association with long-term respiratory sequelae. The management and control of blood glucose has a positive impact on the overall prognosis of COVID-19. Studies among different population and exploring relevant mechanisms are warranted to validate the results and popularize our findings.

Supplementary material

Supplementary material is available at *QJMED* online.

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