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Baseline characteristics and risk factors for short-term outcomes in 132 COVID-19 patients with diabetes in Wuhan China: A retrospective study

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ABSTRACT

Aims: To investigate the clinical characteristics, laboratory findings and high- resolution CT (HRCT) features and to explore the risk factors for in-hospital death and complications of coronavirus disease 2019 (COVID-19) patients with diabetes.

Methods: From Dec 31, 2019, to Apr 5, 2020, a total of 132 laboratory-confirmed COVID-19 patients with diabetes from two hospitals were retrospectively included in our study. Clinical, laboratory and chest CT data were analyzed and compared between the two groups with an admission glucose level of ≤11 mmol/L (group 1) and >11 mmol/L (group 2). Logistic regression analyses were used to identify the risk factors associated with in-hospital death and complications.

Results: Of 132 patients, 15 died in hospital and 113 were discharged. Patients in group 2 were more likely to require intensive care unit care (21.4% vs. 9.2%), to develop acute respiratory distress syndrome (ARDS) (23.2% vs. 9.2%) and acute cardiac injury (12.5% vs. 1.3%), and had a higher death rate (19.6% vs. 5.3%) than group 1. In the multivariable analysis, patients with admission glucose of >11 mmol/l had an increased risk of death (OR: 7.629, 95%CI: 1.391–37.984) and in-hospital complications (OR: 3.232, 95%CI: 1.393–7.498). Admission d-dimer of ≥1.5 μg/mL (OR: 6.645, 95%CI: 1.212–36.444) and HRCT score of ≥10 (OR: 7.792, 95%CI: 2.195–28.958) were associated with increased odds of in-hospital death and complications, respectively.

Conclusions: In COVID-19 patients with diabetes, poorly-controlled blood glucose (>11 mmol/L) may be associated with poor outcomes. Admission hyperglycemia, elevated d-dimer and high HRCT score are potential risk factors for adverse outcomes and death.

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1. Introduction

Since the late of December 2019, a newly recognized novel coronavirus disease (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread rapidly in China and around the world [1]. According to the report of World Health Organization on May 18, 2020, the total number of confirmed cases has risen sharply to 4,618,821 in more than 110 countries, with 311,847 (6.8%) deceased cases [2]. The population is generally susceptible to SARS-CoV-2 infection. However, several epidemiological studies had described that older adults and those with certain underlying diseases are more vulnerable to the disease, with diabetes mellitus (DM) being one of the most frequent comorbidities [1,3,4].

It has been estimated that 463 million adults are living with diabetes worldwide [5], and those individuals are at a higher risk of infection and may have worse outcomes than the population without diabetes once infected [6,7]. Previous studies demonstrated that diabetes was an independent risk factor for mortality in patients with Severe Acute Respiratory Syndrome coronavirus (SARS-CoV), Pandemic Influenza A (H1N1) and Middle East Respiratory Syndrome coronavirus (MERS-CoV) [8–10]. Angiotensin-converting enzyme 2 (ACE2) is a functional receptor for SARS-CoV that is expressed in pancreatic islets, among others, which can aggravate the diabetes progression [11]. Notably, SARS-CoV-2 can also bind to the target cells through ACE2 and the affinity is 10–20 times higher than SARS-CoV [12]. Therefore, COVID-19 patients with diabetes might have higher disease severity and poor prognosis. However, the available information regarding COVID-19 patients with diabetes is inadequate at present.

Hence, this study aimed to analyze the detailed clinical characteristics, laboratory findings and HRCT features and to explore the risk factors for in-hospital death and complications of COVID-19 patients with diabetes.

2. Materials and methods

2.1. Patients

This was a retrospective cohort study carried out at two hospitals in Hubei province, China (Wuhan Union hospital of Tongji Medical College and Jinyintan Hospital). All patients with pre-existing diabetes who were diagnosed with SARS-CoV-2 pneumonia according to WHO interim guidance [13], and those who died or were discharged from hospital between Dec 31, 2019, and Apr 5, 2020, were included in this study. The study was approved by the institutional review boards of the two hospitals. Informed consent was waived for this retrospective study.

2.2. Data collection

All admission data were obtained from patients' electronic medical records and were reviewed by two physicians (Jin Gu and Yue Cui). Information extracted included demographic data, exposure history, comorbidities, symptoms, treatments, in-hospital complications, outcomes, laboratory results and chest CT images. Based on the fasting blood glucose (FBG) levels on admission, two groups of patients were designated: group 1 (with FBG $\leq$ 11 mmol/L) and group 2 (with FBG > 11 mmol/L).

2.3. Outcomes and definitions

The primary outcomes included an intensive care unit (ICU) entry and in-hospital death. The secondary outcomes were any in-hospital complications, including SARS-CoV-2-related ARDS, acute cardiac injury, acute kidney injury and secondary infection. ARDS was diagnosed based on the WHO guidance for COVID-19 [13]. Acute cardiac injury was identified if the serum high-sensitivity cardiac troponin I level was above the upper limit of the 99th percentile reference [14]. Acute kidney injury was diagnosed according to the clinical practice guidelines of KDIGO [15]. Secondary infection was identified if the patient had a positive culture of a new pathogen obtained from the lower respiratory tract specimens or blood samples after admission [14].

2.4. Chest CT protocol and evaluation

Chest CT scans were obtained using either of the following CT scanners: SOMATOM Definition AS+, SOMATOM Spirit, or SOMATOM Perspective (Siemens Healthineers, Forchheim, Germany). The parameters used for the scanning protocol were as described in our previous study [16]. All initial CT images were assessed by three radiologists (Heshui Shi, Jin Gu and Yanqing Fan) with more than 15 years of experience in thoracic radiology. The predominant three CT findings included ground glass opacity (GGO), crazy-paving pattern and consolidation, and any other CT characteristics were described on the basis of previous studies on COVID-19 patients [16,17]. The extent of pulmonary involvement of all of these abnormalities in each lung lobe was evaluated using a semi-quantitative scoring system [18]. CT score for each of the three findings at each of the 5 lung lobes was scored from 0 to 5, with a total score of 0–25. Each lobe was scored as follows: 0, no involvement; 1, $\leq$5% involvement; 2, 6–25% involvement; 3, 26–49% involvement; 4, 50–75% involvement; 5, >75% involvement.

2.5. Statistical analysis

The Kolmogorov–Smirnov test was used to check the normality. Data were expressed as the mean ± SD, median (IQR) and n (%) for normally, non-normally continuous variables and categorical variables, respectively. Differences between two groups stratified by FBG were assessed using independent-sample Student's *t* test, Mann-Whitney test, χ^2 test, or Fisher's exact test, as appropriate. Univariate and multivariate logistic regression models were used to explore the risk factors associated with in-hospital death and complications. A two-sided p value <0.05 was considered statistically significant. Analyses were performed using SPSS software version 21 (IBM, Chicago, IL, USA).

3. Results

3.1. Demographics and clinical characteristics

From Dec 31, 2019, to Apr 5, 2020, a total of 154 consecutive confirmed COVID-19 patients with diabetes were admitted to hospital. Of these, 12 were excluded due to the lack of serum glucose test results and 10 were excluded because of missing CT images or other key information in their medical records. Thus, 132 patients (85 from Wuhan Union hospital of Tongji Medical College and 47 from Jinyintan Hospital) were eventually included in this study.

The baseline clinical characteristics of all patients and the subgroups (stratified by the levels of FBG) are presented in Table 1. For the study cohort, the median age was 65 years (IQR, 57–71) and 70 (53%) patients were male. 130 patients (98.5%) were type 2 diabetes and the median disease duration was 8.5 years (IQR, 4–11.75). The most common symptoms at onset were fever (107, 81.1%) and cough (87, 65.9%), followed by shortness of breath (42.4%) and sputum (35.6%). The median time from onset of symptoms to hospital admission was 10 days (IQR, 7.0–16.0). More than half of the patients had at least one other comorbidity, with hypertension being the most common (64.4%), followed by cardiovascular (13.6%) and cerebrovascular diseases (9.1%). Among 132 patients, 39 (29.3%) patients received high flow nasal cannula oxygen therapy, 10 (7.6%) patients needed noninvasive respiratory support and 5 (3.8%) patients required endotracheal intubation. In addition, most of the patients received antiviral (99.2%) and antibiotic treatments (85.6%), and some patients have taken corticosteroids (29.5%), intravenous immunoglobulin (22.7%) and antifungal agents (11.4%).

Compared with group1, patients in group 2 were more likely in need of systematic corticosteroid treatment, and had more fever, more sputum, longer disease duration and lower oxygen saturation, but had no significant differences in age, gender and some other characteristics (Table 1).

3.2. Laboratory findings

On admission-laboratory test results of all patients and the subgroups are presented in Table 2. In all patients, there were abnormal routine blood indices, including, among others, decreased absolute lymphocyte count (76, 57.6%) and increased platelet count (63, 47.7%), and abnormal coagulation profile including increased d-dimer (62, 47%) and fibrinogen (55, 41.7%). Some patients had an abnormal liver function, including increased alanine aminotransferase (ALT; 35, 26.5%) and aspartate aminotransferase (AST; 36, 27.3%). Some patients had abnormal myocardial enzymes, including elevated lactate dehydrogenase (LDH; 62, 47%), high-sensitivity troponin I (22, 16.7%) and decreased creatine kinase (33, 25%). Regarding the inflammation-related biomarkers, more than half of the patients had an increased serum ferritin (87, 65.9%), interleukin-6 (IL-6; 71, 53.8%), erythrocyte sedimentation rate (ESR; 98, 74.2%), C-reactive protein (CRP; 94, 71.2%) and serum amyloid protein A levels (SAA; 85, 64.4%).

Compared with group 1, patients in group 2 had lower absolute lymphocyte count (0.73 [IQR, 0.58–0.97] vs. 1.05 [IQR, 0.69–1.32]; p = 0.007), and higher d-dimer (1.72 [IQR, 0.72–3.39] vs. 1.51 [IQR, 0.35–2.57]; p = 0.039), IL-6 (10.77 [IQR, 8.05–15.50] vs. 8.64 [IQR, 6.74–12.25]; p = 0.032), ESR (61.61 ± 25 .93 vs. 49.28 ± 27.59; p = 0.025) and CRP (66.59 [IQR, 27.50–128.80] vs. 33.29 [IQR, 5.35–97.75]; p = 0.004) (Table 2).

3.3. The initial HRCT score and features

All patients had abnormal CT imaging features as presented in Table 3. 119 (90.2%) patients had bilateral lung involvement; 70 (53%) patients showed both central and peripheral distribution, and 87 (65.9%) patients showed diffuse involvement (Fig. 1, A-C). The most frequent CT characteristics were ground glass opacity (GGO; 80, 60.6%) (Fig. 1, D,E), air bronchogram (95, 72%), interlobular septal thickening (84, 63.9%) and crazy-paving pattern (39, 29.5%), followed by pleural effusion (23, 17.4%) and bronchiolar dilatation (21, 15.9%). Other less common features on CT included round cystic changes, pericardial effusion and lymphadenopathy. Tree in bud signs and cavitation were not observed in any of the patients.

According to the semi-quantitative scoring system, the median total CT score of the pulmonary involvement was 11.5 (IQR, 6–18). Compared with group 1, patients in group 2 had higher total CT score (14.5 [IQR, 9–20] vs. 9.5 [IQR, 5–17]; p = 0.010) (Fig. 1, F). CT score of the bilateral upper lobes and right lower lobe in group 2 patients were also greater than patients in group 1. There were no significant differences in baseline CT characteristics mentioned above.

3.4. Clinical complications and outcomes

Among 132 patients, there were 31 patients (23.5%) with at least one complication; 20 (15.2%) patients developed ARDS, 8 (6.1%) patients had acute cardiac injury, 8 (6.1%) patients had secondary infection, and 2 (1.5%) patients with acute renal injury. The median time from onset of symptoms to ARDS was 14 days (IQR, 9–23). For the primary outcome, 19 (14.4%) patients were admitted to ICU, and 15 (11.4%) patients died. The median time from onset of symptoms to ICU admission was 15 days (IQR, 10–21), whereas the median duration to death and discharge was 21 days (IQR, 16–28) and 33 days (IQR, 24–49), respectively (Table 1).

Compared with group 1, patients in group 2 had a higher death rate (19.6% vs. 5.3%, p = 0.010), were more likely to require ICU care (21.4% vs. 9.2%, p = 0.048) and to have more in-hospital complications, including ARDS (23.2% vs. 9.2, p = 0.027) and acute cardiac injury (12.5% vs. 1.3%, p = 0.010).

3.5. Prognostic factors

The risk factors associated with in-hospital death and complications are shown in Supplemental Table S1. According to univariable analysis, the admission glucose, absolute lymphocyte count and d-dimer were associated with an increased risk of in-hospital death and complications. Total CT score of the pulmonary involvement, white blood cell

Table 1 – Demographics, and baseline clinical characteristics of COVID-19 patients with diabetes.

	All patients (n = 132)	Group 1 (n = 76)	Group 2 (n = 56)	*p* value
Age, years	65(57–71)	65(58–71)	65(56–71)	0.841
≥65	71(53.8)	42(55.3)	29(51.8)	0.692
<65	61(46.2)	34(44.7)	27(48.2)	–
Sex				
Male	70(53)	44(57.9)	26(46.4)	0.192
Female	62(47)	32(42.1)	30(53.6)	–
Diabetes Type				
Type 2 diabetes	130(98.5)	75(98.7)	55(98.2)	1.000
Type 1 diabetes	2(1.5)	1(1.3)	1(1.8)	–
Diabetes duration, year	8.5(4–11.75)	6(2–11)	10(5–12)	0.033
Exposure				
Exposure to Huanan seafood market	10(7.6)	6(7.9)	4(7.1)	1.000
Exposure to patients*	20(15.2)	14(18.4)	6(10.7)	0.222
Other comorbidities				
Any	88(66.7)	48(63.2)	40(71.4)	0.319
Hypertension	85(64.4)	46(60.5)	39(69.6)	0.324
Cardiovascular disease	18(13.6)	14(18.4)	4(7.1)	0.062
Cerebrovascular disease	12(9.1)	6(7.9)	6(10.7)	0.578
Chronic pulmonary disease	6(4.5)	2(2.6)	4(7.1)	0.401
Chronic kidney disease	4(3)	3(3.9)	1(1.8)	0.637
Chronic liver disease	4(3)	1(1.3)	3(5.4)	0.311
Malignancy	3(2.3)	1(1.3)	2(3.6)	0.574
Signs and symptoms				
Fever	107(81.1)	57(75)	50(89.3)	0.038
Maximum temperature, °C	38(37.43–38.8)	38(36.8–38.8)	38(37.5–38.8)	0.331
≤37.3	32(24.2)	23(30.3)	9(16.1)	0.060
37.3–38	42(31.8)	20(26.3)	22(39.3)	0.114
38.1–39	46(34.8)	28(36.8)	18(32.1)	0.476
≥39.1	12(9.1)	5(6.6)	7(12.5)	0.242
Cough	87(65.9)	46(60.5)	41(73.2)	0.154
Shortness of breath	56(42.4)	28(36.8)	28(50)	0.166
Sputum	47(35.6)	21(27.6)	26(46.4)	0.026
Fatigue	44(33.3)	22(28.9)	22(39.3)	0.213
Chest tightness	16(12.1)	8(10.5)	8(14.3)	0.513
Dyspnea	14(10.6)	6(7.9)	8(14.3)	0.239
Myalgia	9(6.8)	3(3.9)	6(10.7)	0.240
Diarrhea	9(6.8)	7(9.20	2(3.6)	0.357
Pharyngalgia	5(3.8)	3(3.9)	2(3.6)	1.000
Dizziness	4(3.0)	2(2.6)	2(3.6)	1.000
Nausea	3(2.3)	3(3.9)	0(0)	0.262
Abdominal pain	2(1.5)	2(2.6)	0(0)	0.508
Vomiting	0(0)	0(0)	0(0)	–
Heart rate, bpm	89(80–98)	88(80–98)	90(81–100)	0.305
Respiratory rate	21(20–43)	21(20–23)	22(20–24)	0.570
Systolic blood pressure, mmHg	80(74–87)	80(74–87)	80(73–87)	0.906
Diastolic blood pressure, mmHg	130.1 ± 15.72	128.5 ± 15.48	132.27 ± 15.91	0.174
Oxygen saturation (%)	95(90–97)	97(92–98)	93(88–96)	0.004
Treatment				
High flow nasal cannula oxygen	39(29.3)	20(26.3)	19(33.9)	0.343
Mechanical ventilation				
Non-invasive	10(7.6)	5(6.6)	5(8.9)	0.864
Invasive	5(3.8)	2(2.6)	3(5.4)	0.650
Antiviral treatment	131(99.2)	64(84.2)	49(87.5)	0.423
Antibiotic treatment	113(85.6)	65(85.5)	52(92.9)	0.190
Glucocorticoids	39(29.5)	17(22.4)	22(39.3)	0.053
Intravenous immunoglobulin therapy	30(22.7)	16(21.1)	14(25)	0.593
Antifungal therapy	15(11.4)	7(9.2)	8(14.3)	0.364
Duration from onset of symptoms to, median (IQR), days				
Hospital admission	10(7–16)	11(7–18)	10(7–15)	0.469
ARDS	14(9–23)	18(9–24)	14(8–220)	0.736
ICU	15(10–21)	18(11–24)	12(10–19.75)	0.213
Death	21(16–28)	24.5 (14.25–40.75)	21(16–22)	0.639
Discharge	33(24–49)	32.5 (22.5–48.5)	33(25–50)	0.847
Complications				
Any	31(23.5)	11(14.5)	20(35.7)	0.004
ARDS	20(15.2)	7(9.2)	13(23.2)	0.027
Acute cardiac injury	8(6.1)	1(1.3)	7(12.5)	0.010
Secondary infection	8(6.1)	4(5.3)	4(7.1)	0.722
Acute renal injury	2(1.5)	1(1.3)	1(1.8)	1.000
Clinical outcomes				
ICU Admission	19(14.4)	7(9.2)	12(21.4)	0.048
Death	15(11.4)	4(5.3)	11(19.6)	0.010

Data are expressed as n (%) or mean (SD) or median (IQR). The *p* values reflect comparisons between group 1 and group 2.
ARDS, acute respiratory distress syndrome; ICU, intensive care unit.
* Patients who have confirmed SARS-CoV-2 infection.

Table 2 – Laboratory findings of COVID-19 patients with diabetes.

	Normal range	All patients (n = 132)	Group 1 (n = 76)	Group 2 (n = 56)	*p* value
Routine blood test					
White blood cell count, $\times 10^9$/L	3.5–9.5	5.60(4.06–8.14)	5.51(4.03–7.29)	6.11(4.11–9.61)	0.225
Increased	–	21(15.9)	8(10.5)	13(23.2)	0.050
Decreased	–	16(12.1)	10(13.2)	6(10.7)	0.649
Neutrophil count, $\times 10^9$/L	1.8–6.3	4.44(2.65–8.15)	4.00(2.63–7.23)	6.76(2.85–9.62)	0.151
Lymphocyte count, $\times 10^9$/L	1.1–3.2	0.83(0.64–1.11)	1.05(0.69–1.32)	0.73(0.58–0.97)	0.007
Decreased	–	76(57.6)	37(48.7)	39(69.6)	0.017
Platelet count, $\times 10^9$/L	125–350	204(136–303)	200(141.5–283.5)	204.5(124–334.75)	0.796
Increased	–	63(47.7)	37(48.7)	26(46.4)	0.276
Decreased	–	24(18.2)	9(11.8)	15(26.8)	0.056
Haemoglobin, g/L	130–175	116.93 ± 17.73	116.19 ± 18.23	117.96 ± 17.17	0.608
Decreased	–	85(64.4)	48(63.2)	37(66.1)	0.502
Coagulation profile					
D-dimer, μg/L	<0.5	1.61(0.56–3.04)	1.51(0.35–2.57)	1.72(0.72–3.39)	0.039
Increase	_	62(47)	29(38.2)	33(58.9)	0.117
Prothrombin time, s	11–16	11.4(10.1–12.78)	11.2(10.10–12.60)	11.55(10.03–14.48)	0.438
Activated partial thromboplastin time, s	28.0–43.5	27.85(23.98–33.88)	29.30(25.15–36.35)	26.40(21.85–31.60)	0.137
Fibrinogen, g/L	2.0–4.0	4.84(3.98–6.60)	4.88(3.95–6.19)	4.70(4.05–7.40)	0.490
Increased	_	55(41.7)	30(39.5)	25(44.6)	0.908
Blood biochemistry					
Glucose, mmol/L	3.9–6.1	9.35(7.1–13.8)	7.34(6.30–8.80)	14.79(12.56–17.88)	<0.001
Glycosylated hemoglobin, %	4.0–6.0	7.65(6.93–8.88)	7.05(6.20–7.60)	8.80(7.63–9.38)	<0.001
Albumin, g/L	35–55	32.55(29.1–36.03)	31.9(30.2–36.78)	31.35(27.90–34.18)	0.077
Decreased	–	84(63.6)	43(56.6)	41(73.2)	0.103
Alanine aminotransferase, U/L	5–50	32.4 (15.75–56.25)	31(14–56)	37(17–61)	0.359
Increased	–	35(26.5)	19(25)	16(28.6)	0.957
Aspartate aminotransferase, U/L	15–40	35 (20.5–47.1)	35(18–49)	34.5 (22.03–47.15)	0.560
Increased	–	36(27.3)	24(31.6)	12(21.4)	0.107
Serum creatinine, μmol/L	57–111	66.5 (54.35–91.7)	72.6 (53.8–95.0)	64.9(55.2–87.48)	0.437
Creatine kinase, U/L	50–310	43(30–110)	51(26–110)	41.5(32–142.4)	0.896
Increased	–	5(3.8)	3(3.9)	2(3.6)	1.000
Decreased	–	33(25)	19(25)	14(25)	0.306
Lactate dehydrogenase, U/L	109–245	327.04 ± 140.32	307.41 ± 142.18	350.11 ± 136.51	0.159
Increased	–	62(47)	30(39.5)	32(57.1)	0.061
Myoglobin, ng/mL	<146.9	59.8(30.75–134.3)	65.75(35.78–144.18)	54.6(27.7–116.5)	0.511
High-sensitivity troponin I, pg/mL	<26.2	9.35(3.58–32.03)	9.2(3.38–31.88)	9.55(3.75–37.4)	0.646
Increased	_	22(16.7)	9(11.8)	13(23,2)	0.242
Infection-related biomarkers					
Serum ferritin, ng/mL	21–274.7	566.78(363.76–945.4)	538.95(356.64–926.37)	642.16(371.31–1082.91)	0.567
Increased	–	87(65.9)	52(68.4)	35(62.5)	0.748
Interleukin-6, pg/mL	<7	9.97(7.4–13.07)	8.64(6.74–12.25)	10.77(8.05–15.5)	0.032
Increased	–	71(53.8)	34(44.7)	37(66.1)	0.006
Procalcitonin, ng/mL	<0.5	0.05(0.05–0.11)	0.05(0.05–0.13)	0.05(0.05–0.09)	0.940

Table 2 – (continued)

	Normal range	All patients (n = 132)	Group 1 (n = 76)	Group 2 (n = 56)	p value
Erythrocyte sedimentation rate, mm/h	<15	53.63 ± 27.53	49.28 ± 27.59	61.61 ± 25.93	0.025
Increased	–	98(74.2)	63(82.9)	35(62.5)	0.655
C-reactive protein, mg/L	<8	47.45(13.23–108.8)	33.29(5.35–97.75)	66.59(27.5–128.8)	0.008
Increased	–	94(71.2)	50(65.8)	44(78.6)	0.004
Serum amyloid protein A, mg/L	<10	176.5(60.68–245.76)	170.7(41.45–248.35)	185(75.2–240.7)	0.713
Increased	–	85(64.4)	48(63.2)	39(69.6)	0.695

Data are expressed as n (%) or mean (SD) or median (IQR). The *p* values reflect comparisons between group 1 and group 2.

count, albumin, LDH, myoglobin, high-sensitivity troponin I and procalcitonin were also associated with odds of in-hospital complications.

Considering the relatively small number of in-hospital deaths (n = 15) and complications (n = 31) in our study and to avoid overfitting of the model, we have chosen age, hypertension, total CT score of the pulmonary involvement, lymphocyte count and six laboratory indices as indicators for the relative different organ functions in the final multivariable analysis using a stepwise algorithm model. Those six laboratory indices included FBG, d-dimer, ALT, LDH, creatinine and CRP. In the multivariable analysis, compared with admission glucose of ≤11 mmol/l, patients with a blood glucose of >11 mmol/l had an increased risk of death (OR: 7.629, 95%CI: 1.391–37.984) and in-hospital complications (OR: 3.232, 95%CI: 1.393–7.498). D-dimer ≥1.5 μg/mL (OR: 6.645, 95%CI: 1.212–36.444) and total CT score ≥10 (OR: 7.792, 95%CI: 2.195–28.958) were also associated with increased odds of death and in-hospital complications, respectively (Fig. 2).

4. Discussion

The median age of COVID-19 patients with diabetes were (65 [IQR: 57–71] years) in our study, higher than previous publications on patients without diabetes (53 [IQR: 40–63] years) [19] and the overall COVID-19 population (47 [IQR: 35–58] years) [20]. Fever and cough were the most common symptom, which were consistent with previous reports [1,3]. A recent multi-centered study showed that patients with FBG > 10 mmol/L had multiple organ injury and a higher mortality rate than individuals with FBG levels from 3.9 to 10 mmol/L [19]. Similarly, in our study, patients with poorly-controlled FBG (>11 mmol/L) had a greater incidence of acute cardiac injury, ARDS, and ICU entry, and a higher death rate than those with FBG ≤ 11 mmol/L.

Additionally, a previous study reported that the plasma glucose level was an independent predictor for morbidity and mortality in SARS [8]. The present study showed that FBG of >11 mmol/l was associated with an increased risk of death and complications in COVID-19 patients with diabetes. Similarly, a large cohort study by Kornum et al. [21] found that the admission FBG of >11 mmol/L was a predictor for mortality in type 2 diabetic patients with community-acquired pneumonia (CAP). It was proposed that hyperglycemia may impair the normal endothelial function, hinder phagocytosis, delay the chemotaxis and reduce the microbiocidal capacity [22–24]. These abnormalities are prone to progress when the glucose level is greater than 11 mmol/L and can be improved by better glycemic control [22–24]. A recent publication on COVID-19 patients showed that although glucose level was higher on admission, it subsequently decreased, while it continued to increase in deceased patients [25]. Therefore, timely blood glucose testing and better glycemic control play a key role in COVID-19 patients' prognosis.

As described in recent studies [1,26–28], coagulation abnormalities were common in severe COVID-19 patients, and were marked by elevated d-dimer concentrations. In our study, d-dimer of ≥1.5 μg/mL was associated with higher odds of death, similar to a previous report in 191 COVID-19 patients

Table 3 – The initial HRCT score and features of COVID-19 patients with diabetes.

HRCT score	All patients (n = 132)	Group 1 (n = 76)	Group 2 (n = 56)	*p* value
Left upper lobe	2(1–3)	2(1–3)	3(1–4)	0.020
Left lower lobe	3(1–4)	2(1–4)	3(2–5)	0.238
Right upper lobe	2(1–4)	2(1–3)	3(1–4)	0.017
Right middle lobe	2(3–1)	1(0–3)	2(1–4)	0.063
Right lower lobe	3(2–5)	3(1–5)	3(2–5)	0.040
Total CT score of the pulmonary involvement	11.5(6–18)	9.5(5–17)	14.5(9–20)	0.010
HRCT characteristics				
Lung involvement				
Unilateral	13(9.8)	8(10.5)	5(8.9)	0.761
Bilateral	119(90.2)	68(89.5)	51(91.1)	–
Location				
Central	7(5.3)	5(6.6)	2(3.6)	0.698
Peripheral	55(41.7)	32(42.1)	23(41.1)	0.905
Both central and peripheral	70(53)	39(51.3)	31(55.4)	0.646
Predominant distribution				
Septal/subpleural	62(47)	34(44.7)	28(50)	0.549
Peribronchovascular	15(11.4)	10(13.2)	5(8.9)	0.449
Both	2(1.5)	1(1.3)	1(1.8)	1.000
Random	52(39.4)	31(40.8)	21(37.5)	0.702
Bilateral lower lobe	1(0.8)	0(0)	1(1.8)	0.424
Extent of lesion involvement				
Focal	7(5.3)	4(5.3)	3(5.4)	0.981
Multifocal	38(28.8)	27(35.5)	11(19.6)	0.046
Diffuse	87(65.9)	45(59.2)	42(75)	0.059
Predominant CT pattern				
Ground glass opacity	80(60.6)	48(63.2)	32(57.1)	0.485
Consolidation	29(22.0)	15(19.7)	14(25.0)	0.470
Reticular pattern	5(3.8)	2(2.6)	3(5.4)	0.650
Mixed pattern	18(13.6)	11(14.5)	7(12.5)	0.744
Air bronchogram	95(72)	50(65.8)	45(80.4)	0.066
Interlobular septal thickening	84(63.9)	48(63.2)	36(64.3)	0.894
Crazy paving	39(29.5)	23(30.3)	16(28.6)	0.833
Bronchiolar dilatation	21(15.9)	14(18.4)	7(12.5)	0.358
Round cystic changes	11(8.3)	4(5.3)	7(12.5)	0.243
Tree-in-bud	0(0)	0(0)	0(0)	–
Cavitation	0(0)	0(0)	0(0)	–
Pleural effusion	23(17.4)	14(18.4)	9(16.1)	0.770
Unilateral	11(8.3)	9(11.8)	2(3.6)	0.167
Bilateral	12(9.1)	5(6.6)	7(12.5)	0.242
Pericardial effusion	13(9.8)	8(10.5)	5(8.9)	0.761
Lymphadenopathy	2(1.5)	1(1.3)	1(1.3)	1.000

Data are expressed as n (%) or mean (SD) or median (IQR). The *p* values reflect comparisons between group 1 and group 2.

[28]. The state of hypoxia in severe pneumonia can lead to a hypercoagulable state of the blood by activating the exogenous coagulation pathway, and can also stimulate thrombus formation by increasing the blood viscosity [29]. In addition, chronic hyperglycemia can cause vascular injury, oxidative stress and inflammation, which can lead to the formation of atherosclerosis and thrombus [30]. Therefore, severe SARS-CoV-2 infection with diabetes is more likely to cause coagulopathy and resultant poor outcome.

The present study found that the HRCT score of ≥10 was associated with increased odds of in-hospital complications. CT was an important inspection tool for COVID-19 and the score of the lesions involvement of the lung was correlated with histopathology [31]. In our study, patients with FBG of >11 mmol/L had a significantly higher CT score than those with FBG of ≤11 mmol/L. This might be explained by the previous finding that patients with diabetes and hyperglycemia have restrictive ventilatory dysfunction, as well as small airway obstruction and diffuse dysfunction [32]. It was suggested that the CT score may be used as one of the indicators for poor prognosis in COVID-19 patients with diabetes, but large-scale multicenter studies are needed to further confirm this finding. Additionally, in our study, a considerable proportion of patients had pleural effusion (17.4%), higher than previously reported (2.5% & 5.0%) [16,17]. Some previous studies have shown that pleural effusion is an independent predictor for mortality in patients with CAP and MERS [33,34]. Thus, the early appearance of pleural effusion in COVID-19 patients with diabetes should be paid more clinical attention.

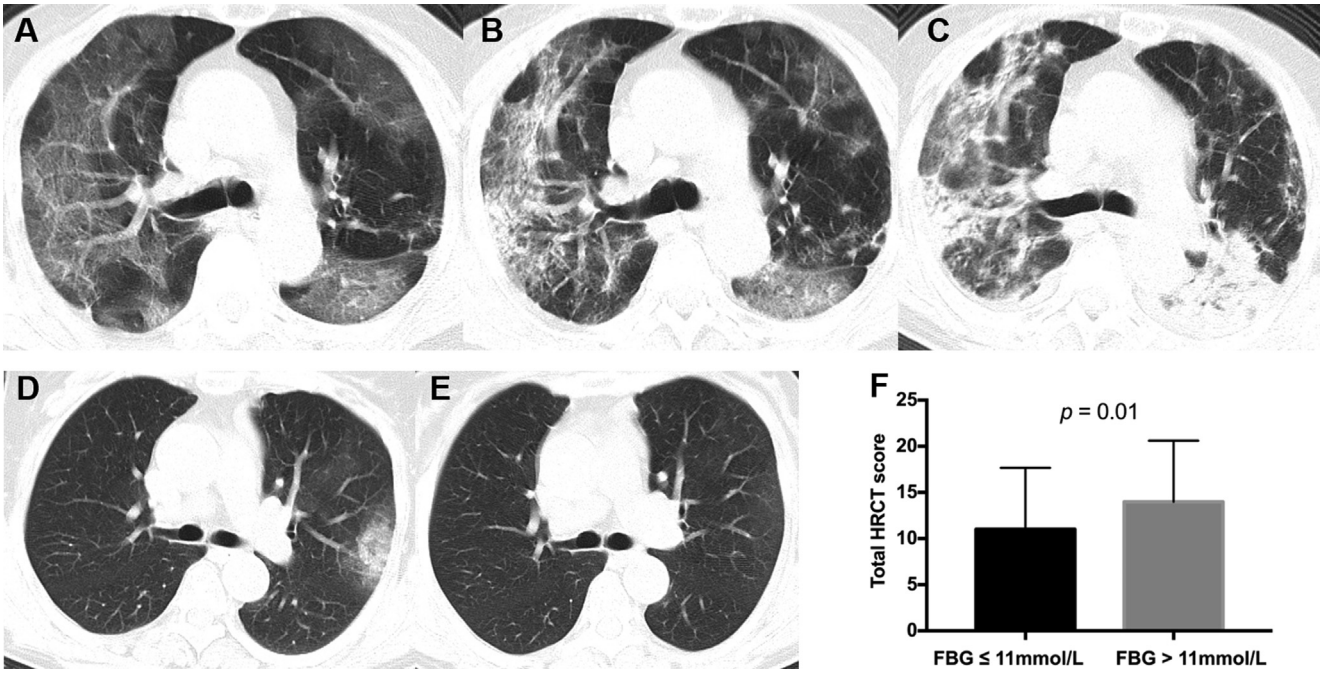

Fig. 1 – The initial HRCT score and features. (A–C) Transverse CT scans in a 59-year-old female with type 2 diabetes for 10 years. FBG was 20.7 mmol/L on admission. (A) Scan obtained on the 7th day from onset of symptoms shows extensive ground-glass opacities in both lungs. (B, C) Scan obtained on the 13th and 20th day shows progressive expansion of the bilateral pulmonary lesions and development of consolidations. The patient died 13 days after the final scan. (D, E) Transverse CT scans in a 68-year-old female with type 2 diabetes for 3 years. FBG was 8.8 mmol/L on admission. (D) Scan obtained on the 6th day from onset of symptoms shows focal patchy ground glass opacities in the left upper lobe posteriorly. (E) Scan obtained on the 12th day shows that the previous ground-glass opacities were nearly resolved. The patient was discharged from hospital 3 days after the final scan. (F) Comparison of the total HRCT score in two groups with different fasting blood glucose (FBG) levels.

The present study has several limitations. First, this was a retrospective study, and the findings might be limited by the small sample size. Second, some laboratory results were missing in the electronic medical records, which may have led to a selection bias when identifying the risk factors for adverse outcomes. Third, this study did not assess the non-diabetic patients, since there have been numerous descriptive studies on the clinical and imaging characteristics of the general population.

In conclusion, our study suggested that COVID-19 patients with poorly-controlled FBG (>11 mmol/L) had worse outcomes. Admission FBG of >11 mmol/L was a risk factor for death and complications in COVID-19 patients with diabetes. Elevated d-dimer and HRCT score also contributed to the adverse outcomes. Our findings may provide useful information for the management of this special population and guide the strategies for more targeted intervention to improve the prognosis.

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6. Authors' contributions

Conception and drafting the article: Yumin Li, Xiaoyu Han, Heshui shi, Yanqing Fan and Lixia Wang. Data collection, analysis, and interpretation: Yumin Li, Xiaoyu Han, Heshui shi, Yanqing Fan and Lixia Wang. Data collection and analysis: Osamah Alwalid, Yue Cui, Yukun Cao, Jia Liu and Jin Gu. Final approval of the manuscript to be published: all authors. Accountable for all aspects of the work: All authors.

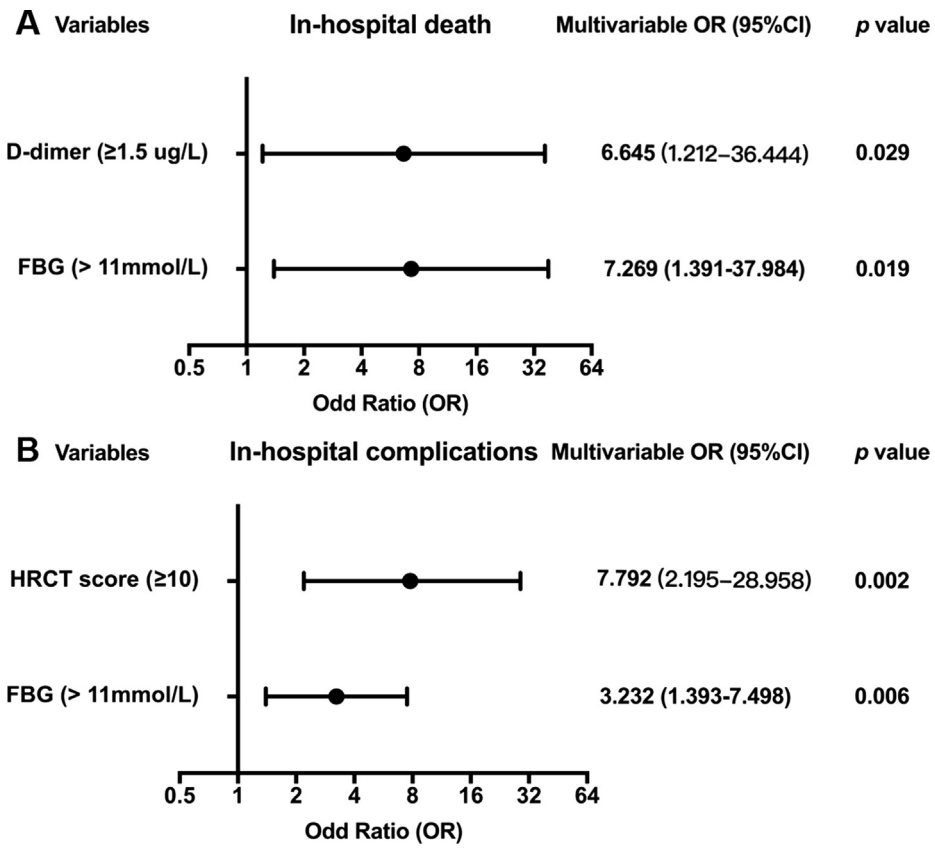

Fig. 2 – The risk factors associated with in-hospital death (A) and complications (B) on multivariable logistic regression analysis.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2020.108299.

REFERENCES

[1] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The Lancet. 2020;395(10223):507–13.

[2] Coronavirus disease 2019 (COVID-19) situation report e 119. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200518-covid-19-sitrep-119.pdf?sfvrsn=4bd9de25_4.

[3] Wang D, Hu Bo, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, Zhao Y, Li Y, Wang X, Peng Z. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. JAMA 2020;323(11):1061. https://doi.org/10.1001/jama.2020.1585.

[4] Yang X, Yu Y, Xu J, Shu H, Ja X, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. The Lancet. Respir Med 2020;8(5):475–81.

[5] International Diabetes Federation. IDF diabetes atlas. 9th ed. Brussels: IDF, 2019. https://www.diabetesatlas.org/en/sections/worldwide-toll-of-diabetes.html.

[6] Koziel H, Koziel MJ. Pulmonary complications of diabetes mellitus. Infect Dis Clin North Am 1995;9(1):65–96.

[7] Kornum JB, Thomsen RW, Riis A, Lervang HH, Schonheyder HC, Sorensen HT. Diabetes, glycemic control, and risk of hospitalization with pneumonia: a population-based case-control study. Diabetes Care 2008;31(8):1541–5.

[8] Yang JK, Feng Y, Yuan MY, Yuan SY, Fu HJ, Wu BY, et al. Plasma glucose levels and diabetes are independent predictors for mortality and morbidity in patients with SARS. Diabet Med 2006;23(6):623–8.

[9] Allard R, Leclerc P, Tremblay C, Tannenbaum TN. Diabetes and the severity of pandemic influenza A (H1N1) infection. Diabetes Care 2010;33(7):1491–3.

[10] Kulcsar KA, Coleman CM, Beck SE, Frieman MB. Comorbid diabetes results in immune dysregulation and enhanced

disease severity following MERS-CoV infection. JCI Insight 2019;4(20).
[11] Yang JK, Lin SS, Ji XJ, Guo LM. Binding of SARS coronavirus to its receptor damages islets and causes acute diabetes. Acta Diabetol 2010;47(3):193–9.
[12] Wrapp D, Wang N, Corbett KS, Goldsmith JA, Hsieh CL, Abiona O, et al. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. Science 2020;367(6483):1260–3.
[13] WHO. Clinical management of severe acute respiratory infection when Novel coronavirus (nCoV) infection is suspected: interim guidance. Jan 11, 2020. https://www.who.int/internalpublicationsdetail/clinicalmanagementofsevereacuterespiratoryinfectionwhennovelcoronavirus(ncov)infectionissuspected (accessed Jan 20, 2020)
[14] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395(10223):497–506.
[15] Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. Nephron Clin Pract 2012;120(4):c179–84.
[16] Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. Lancet Infect Dis 2020;20(4):425–34.
[17] Zhou SC, Wang YJ, Zhu TT, Xia LM. CT Features of Coronavirus Disease 2019 (COVID-19) Pneumonia in 62 Patients in Wuhan, China. AJR Am J Roentgenol 2020;214(6):1287–94.
[18] Chang YC, Yu CJ, Chang SC, Galvin JR, Liu HM, Hsiao CH, et al. Pulmonary sequelae in convalescent patients after severe acute respiratory syndrome- evaluation with thin-section CT. Radiology 2005;236(3):1067–75.
[19] Zhu L, She ZG, Cheng X, Qin JJ, Zhang XJ, Cai J, et al. Association of blood glucose control and outcomes in patients with COVID-19 and pre-existing type 2 diabetes. Cell Metab 2020.
[20] Guan WJ, Ni ZY, Hu Y, Liang WH, Qu CQ, He JX, et al. Clinical characteristics of 2019 novel coronavirus infection in China. N Engl J Med. 2020;382(18):1708–20.
[21] Kornum JB, Thomsen RW, Riis A, Lervang HH, Schonheyder HC, Sorensen HT. Type 2 diabetes and pneumonia outcomes: a population-based cohort study. Diabetes Care 2007;30(9):2251–7.
[22] Vague P, Raccah D, Juhan-Vague I. Hemobiology, vascular disease, and diabetes with special reference to impaired fibrinolysis. Metabolism. 1992;41(5 Suppl 1):2–6.
[23] Williams SB, Goldfine AB, Timimi FK, Ting HH, Roddy MA, Simonson DC, et al. Acute hyperglycemia attenuates endothelium-dependent vasodilation in humans in vivo. Circulation 1998;97(17):1695–701.
[24] MacRury SM, Gemmell CG, Paterson KR, MacCuish AC. Changes in phagocytic function with glycaemic control in diabetic patients. J Clin Pathol. 1989;42(11):1143–7.
[25] Yang JK, Jin JM, Liu S, Bai P, He W, Wu F, et al. Blood glucose is a representative of the clustered indicators of multi-organ injury for predicting mortality of COVID-19 in Wuhan, China. MedRxiv 2020. https://doi.org/10.1101/2020.04.08.20058040.
[26] Yin S, Huang M, Li D, Tang N. Difference of coagulation features between severe pneumonia induced by SARS-CoV2 and non-SARS-CoV2. J Thromb Thrombolysis 2020. http://doi:10.1007/s11239-020-02105-8. [Epub ahead of print].
[27] Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost 2020;18(5):844–7.
[28] Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The Lancet. 2020;395(10229):1054–62.
[29] Gupta N, Zhao YY, Evans CE. The stimulation of thrombosis by hypoxia. Thromb Res 2019;181:77–83.
[30] Domingueti CP, Dusse LM, Carvalho M, de Sousa LP, Gomes KB, Fernandes AP. Diabetes mellitus: The linkage between oxidative stress, inflammation, hypercoagulability and vascular complications. J Diabetes Complications 2016;30(4):738–45.
[31] Kazerooni EA, Martinez FJ, Flint A, Jamadar DA, Gross BH, Spizarny DL, et al. Thin-section CT obtained at 10-mm increments versus limited three-level thin-section CT for idiopathic pulmonary fibrosis: correlation with pathologic scoring. Am J Roentgenol 1997;169(4):977–83.
[32] Primhak RA, Whincup G, Tsanakas JN. Reduced vital capacity in insulin dependent diabetes. Diabetes 1987;36(3):324–6.
[33] Hasley PB, Albaum MN, Li YH, Fuhrman CR, Britton CA, Marrie TJ, et al. Do pulmonary radiographic findings at presentation predict mortality in patients with community-acquired pneumonia?. Arch Intern Med 1996;156(19):2206–12.
[34] Das KM, Lee EY, Enani MA, AlJawder SE, Singh R, Bashir S, et al. CT correlation with outcomes in 15 patients with acute Middle East respiratory syndrome coronavirus. AJR Am J Roentgenol 2015;204(4):736–42.