Higher rate of covid-19 mortality in patients with type 1 than type 2 diabetes: a nationwide study

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Abstract

Purpose

COVID-19 disease has a worse prognosis in patients with diabetes, but the comparative data about the course of COVID-19 in patients with type 1 (T1DM) and type 2 diabetes (T2DM) are lacking. The purpose of this study was to find out the relative clinical severity and mortality of COVID-19 patients with T1DM and T2DM.

Methods

A nationwide retrospective cohort of patients with confirmed (PCR positive) COVID-19 infection (n=149,671) was investigated. After exclusion of individuals with unspecified diabetes status, the adverse outcomes between patients with T1DM (n=163), T2DM (n=33,478) and the non-diabetics (n=115,108) were compared by using the propensity score matching method. The outcomes were hospitalization, the composite of intensive care unit (ICU) admission and/or mechanical ventilation and mortality.

Results

The patients with T1DM had higher mortality than the age and gender matched patients with T2DM (n=489) and the non-diabetics (n=489) ($p<0.001$). After further adjustment for the A1c, microvascular and macrovascular complications, the odds of mortality (OR:3.35, 95% CI:1.41–7.96, p=0.006) and ICU admission and/or mechanical ventilation (OR: 2.95, 95% CI:1.28–6.77, p=0.011) were significantly higher in patients with T1DM compared to those with T2DM. Older age (OR:1.06, 95% CI:1.01–1.12, p=0.028) and lymphopenia (OR:5.13, 95% CI:1.04–25.5, p=0.045) were independently associated with mortality in patients with T1DM.

Conclusion

According to the results, patients with T1DM had poorer COVID-19 prognosis than those with T2DM or the non-diabetics. These patients should be cared diligently until more data will be available about the causes of increased COVID-19 mortality in T1DM.

1. Introduction

Patients with Type-1 diabetes mellitus (T1DM) and Type-2 diabetes mellitus (T2DM) are at increased risk of lower respiratory tract, urinary tract, and skin and mucous membrane infections [1]. These patients are also at increased risk of complicated Influenza A (H1N1) infections, with no difference in adverse outcomes between the two types of diabetes [2]. As with other infectious etiologies, certain populations, such as men, the elderly, or those with comorbid diseases including diabetes mellitus, are more vulnerable to an unfavorable outcomes of new coronavirus disease 2019 (COVID-19) [3–7]. The frequency of T2DM among confirmed COVID-19 patients varies between 10.1% and 68.3% in different studies [8–10], and the mortality rate range between 8% and 60% [11–14].

Little is known about the course of COVID-19 infection in patients with T1DM rather than T2DM [15–17]. So far, only a few studies reported the prevalence of T1DM in patients with COVID-19 infection between 0.6% and 2.1%, and the mortality rates range from 3–9%. However, these studies were too small to identify the characteristics of this vulnerable population [16, 18–20]. Moreover, potential causes of severe outcomes of COVID-19 have not been sufficiently elucidated in different settings [18–20].

This study aimed to investigate the rates of mortality, hospitalization, and admission to intensive care unit (ICU) due to COVID-19 in patients with T1DM in comparison to those with T2DM and non-diabetic patients. Moreover, we addressed the potential factors associated with poor outcomes in T1DM.

2. Materials And Methods

2.1. Study design and participants

This multi-center retrospective cohort study was carried out using the National Electronic Database of the Turkish Ministry of Health. We identified 149,671 adult patients with a confirmed diagnosis of COVID-19 (PCR positive) between 11 March through 30 May 2020 in the database. After exclusion of individuals with unspecified diabetes status (n=922), we classified the remaining sample as T1DM (n=163), T2DM (n=33478) and non-diabetics (n=115108). To explore the relative risk of adverse outcomes in the T1DM group (see below), age and gender-matched comparator groups were formed using the propensity score matching (PSM) method in the T2DM and non-diabetic patient datasets. To increase the precision and performance of the PSM procedure, we repeated the matching by propensity scores 3 times in the T2DM and non-diabetic patients (Figure 1). After the initial analyses, the PSM groups were pooled, totaling a final sample of 1141 subjects.

The design and procedures in the study are in accordance with the declaration of Helsinki and the study protocol was approved by the Ministry of Health Ethical Board (95741342-020/27112019).

2.2. Data collection

Sociodemographic data including age, gender, education, smoking, and body mass index (BMI), comorbid diseases, and medications were recorded. Laboratory parameters obtained from the national database were blood glucose, HbA1c (for patients with diabetes), low-density lipoprotein cholesterol (LDL-C), creatinine, aspartate transaminase (AST), alanine transaminase (ALT), C-reactive protein (CRP), lymphocyte count, lactate dehydrogenase (LDH) and ferritin. The tests were performed in hospital laboratories certificated by the Turkish Ministry of Health. Chest computerized tomography (CT) reports were available in the national database as positive or negative for COVID-19.

2.3. Definitions

Patients with T1DM were first identified by ICD-10 codes. Each diagnosis of T1DM was further verified within the health insurance database through trace records of the patients. T2DM was defined as previously described [7] using the ICD-10 codes or having any HbA1c ≥6.5%, or monthly refill of

antidiabetic medications following the diagnosis of T2DM. Undetermined records of diabetes type were considered “unclassified” therefore, these patients were excluded from the study.

Smoking was defined as currently smoking at the time of the COVID-19 diagnosis. Higher education described as the attained level of education for more than eight years. BMI was calculated as the ratio of weight to the square of heights (kg/m^2). Hypertension, dyslipidemia, chronic obstructive pulmonary disease (COPD), asthma, heart failure, coronary artery disease, peripheral artery disease, and cerebrovascular disease were identified using the ICD-10 codes. The composite of coronary artery disease, peripheral artery disease, and cerebrovascular disease was recorded as cardiovascular disease (CVD). Obesity was defined as BMI ≥30 kg/m^2. Chronic kidney disease was specified as estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 using the CKD-EPI equation [21]. Renin-angiotensin system (RAS) medication use was composed of receiving any angiotensin-converting enzyme inhibitors or angiotensin receptor blockers with/without their combination forms.

2.4. Outcomes

The primary outcome was mortality due to Covid-19 in patients with T1DM, compared with patients with T2DM and non-diabetic patients. The secondary outcomes were the hospitalization and the composite of ICU admission and/or mechanical ventilation.

2.5. Statistical analyses

Numerical data were expressed as median (interquartile range-IQR) and categorical variables as counts (n) and percentage (%). Normality of distribution was assessed using the Kolmogorov-Smirnov test. Differences between groups were assessed using the Chi-square test for categorical variables and the student’s t-test or the Mann-Whitney U test, as appropriate.

Confirmed T1DM patients (n=163) in the full dataset were matched using the propensity score on a scale of 1:1 by age and gender to individuals in a COVID-19 (+) control group of patients with T2DM and non-diabetic patients. Univariate analyses were performed to evaluate the potential variables associated with mortality, hospitalization, and ICU admission/mechanical ventilation in patients with T1DM and presented by odds ratio (OR) and its 95% confidence interval (CI). Multivariable logistic regression analysis was used to study the independent predictors of the three outcomes. Variables with significant univariate association with the outcomes and variables which could be potential predictors despite the lack of significant univariate association were included in a multivariate model. Hosmer and Lemeshow test and likelihood ratio test were used to assess final model fitting. Statistical significance was defined as 2-sided p values ≤0.05. Kaplan-Meier survival curves were plotted to visualize the difference between 30-day mortality rates of T1DM and PSM control groups. All data were analyzed using SPSS Statistics for Windows version 25.0 (SPSS Inc. 111 Chicago, IL).

3. Results

3.1. Basic Characteristics

Demographic and clinical variables in the overall, unmatched sample are shown in Table 1. Of the total sample of 149,671 patients with confirmed COVID-19 disease, 0.1% (n=163) had T1DM, 22.4% had T2DM (n=33478) and %76.9 were non-diabetic (n=115,108). The median (IQR) age of patients with T1DM was lower than patients with T2DM but higher than non-diabetic patients ($p<0.05$ for all). There was male predominance among patients with T1DM (63.2%) and non-diabetics (55.3%), whereas fewer patients were male among patients with T2DM (42.4%) (Figure 1 and Table 1). The group with T1DM had more chronic kidney disease and coronary heart disease compared to both T2DM and non-diabetic groups; a higher rate of micro-and macro-vascular complications than patients with T2DM; and a higher rate of hypertension, dyslipidemia, asthma/COPD than non-diabetic groups ($p<0.05$ for all) (Table 1). On-admission blood glucose level, the proportion of above normal LDH and ferritin, and the proportion of lymphopenia were also higher in the group with T1DM compared to T2DM and non-diabetic groups ($p<0.05$) (Table 1). The proportion of patients using antihyperglycemic drugs was similar in the groups with T1DM and T2DM groups except for insulin therapy. The use of RAS blockers, statins and acetyl salicylic acid was higher in both diabetes groups than the group of non-diabetic patients.

After matching the T1DM group (n=163) with three different patient groups of T2DM and the non-diabetic patients, the final sample consisted of 1141 individuals, of which 14.2% had T1DM, 42.9% had T2DM (n=489, 163 subjects in each of 3 PSM groups), and %42.9 were non-diabetic (n=489, 163 subjects in each of 3 PSM groups). The median (IQR) age of the sample was 41 (36) years, and 63.2% of patients were male (Figure 1 and Table 2). The comparison of demographic and clinical variables after matching is shown in Table 2. The prevalence of hypertension, heart failure, chronic kidney disease, and coronary artery disease was higher when compared to patients with T2DM and the non-diabetic patients ($p<0.05$ for all). The micro- and macro-vascular complications were more common in patients with T1DM when compared to those with T2DM, and the rate of dyslipidemia and asthma/COPD were more common than in the non-diabetic group ($p<0.001$ for all). Increases blood glucose level on admission and lymphopenia were also more prevalent in the group with T1DM when compared to patients with T2DM and non-diabetic patients ($p<0.05$) (Table 2). Similar to the crude comparisons, the proportion of patients taking antihyperglycemic medications except of insulin therapy was similar in the groups with T1DM and T2DM after matching., The use of RAS blockers, statins and acetyl salicylic acid use was higher in both diabetes groups compared with the group of non-diabetics in matched analysis.

3.2. Outcome analysis

Comparison of study outcomes between unmatched groups showed a significantly higher rate of mortality, hospitalization, and the composite of ICU admission and/or mechanical ventilation in patients with T1DM compared to non-diabetics ($p<0.001$ for all) (Table 1). The rate of mortality and ICU admission and/or mechanical ventilation were also higher than the T2DM group ($p<0.05$).

The risk of mortality was also higher in patients with T1DM than the pooled PSM groups of T2DM ($p<0.001$). There was no significant difference between the groups with T1DM and T2DM regarding

hospitalization or ICU admission and/or mechanical ventilation. On the other hand, the risk of mortality, hospitalization, and ICU admission and/or mechanical ventilation in the group with T1DM were higher in comparison to the non-diabetic group when the three non-diabetic PSM groups were pooled ($p<0.01$ for all) (Table 2). The comparison of outcomes across each PSM group is given in Supplementary Table 1.

After further adjustment for the A1c, microvascular and macrovascular complications, the odds of mortality (OR: 3.35, 95% CI: 1.41 – 7.96, p = 0.006) and ICU admission and/or mechanical ventilation (OR: 2.95, 95% CI: 1.28 – 6.77, p = 0.011) were significantly higher in patients with T1DM compared to the group with T2DM (Figure 2). The odds of mortality (OR: 6.44, 95% CI: 3.27 – 12.67, $p<0.001$), hospitalization (OR: 1.74, 95% CI: 1.21 – 2.50, p=0.003), and ICU admission and/or mechanical ventilation (OR: 3.78, 95% CI: 2.08 – 6.84, $p<0.001$) were also significantly higher in patients with T1DM compared to the non-diabetic group.

3.3. Predictors of Outcomes

Multivariate logistic regression analyses showed that older age (OR: 1.06, 95% CI: 1.01 –1.12, p = 0.028) and lymphopenia (OR: 5.13, 95% CI: 1.04 – 25.5, p = 0.045) were independently associated with mortality in patients with T1DM. CT findings of COVID-19 (OR: 4.41, 95% CI: 1.12 – 17.3, p = 0.033) was associated with an increased risk of hospitalization, while older age (OR: 1.05, 95% CI: 1.01 – 1.10, p = 0.016) was associated with a higher risk ICU admission (Supplementary Table 2).

3.4. The survival curves

The Kaplan Meier curves showing the cumulative survival rates of 30-day mortality are displayed for the crude analysis in Figure 3a and matched analysis in Figure 3b. Both analyses yielded lower survival rates for patients with T1DM (Log rank test $p<0.001$).

4. Discussion

The results of this nationwide retrospective observational cohort study showed a significantly higher risk of hospitalization, ICU admission/intubation, and mortality in patients with T1DM than in non-diabetic patients. Also, the results revealed that patients with T1DM have an approximately 3-fold higher risk of ICU admission/mechanical ventilation and mortality when compared to patients with T2DM. The risk remained higher even after the results were adjusted for age, gender, micro-vascular and macro-vascular complications. To our knowledge, this is one of the most comprehensive studies conducted so far, on COVID-19 in patients with T1DM.

There are a number of studies in the literature showing the relationship between COVID-19 disease and T2DM. Most of these studies reported that COVID-19 disease is quite common among T2DM patients, and generally, with a more complicated course [5–7]. Very few studies have been published on COVID-19 in patients with T1DM, however, similar findings to T2DM have been reported [15–17, 19, 22]. The low prevalence of T1DM in the general population, the relatively younger age of T1DM patients compared to

T2DM patients, and the fact that COVID-19 infection affects older patients rather than younger ones are among the proposed reasons for the scarcity of data on T1DM [23, 24].

We observed a 16% overall risk of mortality rate in COVID-19 patients with T1DM. Compared to the 1.8% mortality in the non-diabetic population in the same dataset, such an increased risk deserves special attention as it seems the highest number reported so far. The rate of mortality in the CORONADO study was 5.4% [22], while one multicenter and another small-scale study from the United States reported 9% and 3% death rates in COVID-19 patients with T1DM, respectively [17, 18]. Also, a more recent whole-population study from England reported a 3.5% death rate among T1DM patients [16, 20]. Higher mortality of patients with T1DM in our study may be explained by the increased burden of comorbidities. In a national registry from England [20] patients with T1DM who died due to COVID-19 had markedly higher rates of comorbidities including cardiovascular or renal comorbidities by 62.3%, heart failure by 23.9%, and stroke by 11.0%. T1DM patients in our study had even a more severe comorbidity burden, such as coronary artery disease, chronic kidney disease, and heart failure by 39.9%, 54.4%, and 23.3%, respectively. Almost half of these patients had at least one microvascular complication.

In addition to the mortality outcome, the risk of hospitalization in the present study seems to be the highest among similar publications in the literature. Overall, six out of ten patients with T1DM in our study were hospitalized following COVID-19 diagnosis. Previous studies from different countries reported the hospitalization rates in patients with T1DM between 21.9% and 51%. Also, almost one-third of our patients were admitted to the ICU, which was recorded by 5–23% in other studies from different countries [17, 24, 25]. In the CORONADO study, 19.6% of patients with T1DM required mechanical ventilation [22]. Not surprisingly, the risk of a more severe COVID-19 course was higher in the T1DM population with a higher burden of significant comorbidities.

The present study compared T1DM and T2DM patients in terms of mortality and other prognostic factors using three different PSM models. In all models, the mortality rate was significantly higher in patients with T1DM, while there was no significant difference in the hospitalization, ICU admission, and intubation rates. Few studies so far have compared patients with T1DM and T2DM in terms of COVID-19 severity and mortality. One study reported fewer deaths in patients with T1DM compared to patients with T2DM (5.4% vs 10.6%), although the analysis was limited to 56 patients with T1DM [22]. In addition, there were significant differences in age and gender between the T1DM and T2DM groups. Another study from the UK reported that the odds of mortality from COVID-19 was 3.5 times higher in patients with T1DM and 2.0 times higher in those with T2DM relative to non-diabetic patients [16]. In our three PSM models, T1DM and T2DM groups were matched for age and gender, and the median age in both groups was 41 years. Albeit the data on the duration of diabetes duration was not available in our study, it is well-known that is typically longer in individuals with T1DM than those with T2DM of the same age because the onset of diabetes is much earlier in T1DM. Thus, one major reason for the increased mortality in patients with TIDM might be the longer duration of diabetes. Also, the median HbA1c level in patients with T1DM in the present study was significantly higher than the patients with T2DM. The risk of mortality from COVID-19 was reported higher at markedly increased HbA1c levels in both T1DM and T2DM in a recent study from

England [20]. Therefore, poor glycemic control may also be involved in the mechanism of increased mortality in our study. For this reason, we conducted a further comparison of age, gender, HbA1c levels, and microvascular and macrovascular complications between the matched groups of T1DM and T2DM. The results showed that patients with T1DM had higher mortality rate independent of HbA1c levels and complications. These findings suggest that T1DM and T2DM are completely different diseases and different immune dysfunctions in patients with T1DM may induce higher mortality rates in these patient groups.

Numerous studies have repeatedly identified older age as a significant factor in the course of COVID-19, not only in T2DM [26–28] but also in T1DM [16, 20, 24]. Our findings are consistent with the earlier findings that in COVID-19 patients with T1DM, age is a strong predictor of mortality and poor prognosis as well. Likewise, we identified lymphopenia as a predictor of worse prognosis in the T1DM group, which is in line with the previous reports from others [7, 29, 30]. In this regard, T1DM patients with older age and lymphopenia should be treated more carefully during COVID-19.

Several limitations of the present study should be acknowledged. First, its observational design precludes establishing a causal relationship between the type of diabetes and outcomes. Second, all patients included in the study had confirmed diagnosis of COVID-19 (PCR Positive). The lack of symptomatic but unconfirmed COVID-19 cases or patients with false-negative COVID-19 PCR results may reduce the generalizability of our findings. Third, some data were unavailable in the dataset, such as duration of diabetes and insulin doses, which could be important factors to predict prognosis. And finally, the low number of patients with Type 1 diabetes can be considered as a limitation. One major strength of this study is its population-based, nationwide design. Also, to our knowledge, this study is the most comprehensive report of COVID-19 outcomes in adult patients with T1DM.

In conclusion, COVID-19 patients with T1DM have higher mortality rate than non-diabetic patients and those with T2DM. This increased mortality rates in patients with T1DM appear to be independent of age, gender, glycemic control, and complications; suggesting that T1DM and T2DM have different pathophysiological mechanisms. Therefore, patients with T1DM seem to be particularly disadvantaged during the COVID-19 pandemic, suggesting some prioritization needs for prevention and care.

Declarations

5.1. Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

5.2. Conflict of Interest

The authors declare that they have no conflict of interest.

5.3. Availability of Data and Material

The datasets generated during the current study is secured in a network and not open to public share. The outputs can be copied following analysis but not the core patient registry. Practically, if requested in the future for any reason, additional information can be retrieved from the registry by contacting the corresponding author on reasonable request.

5.4. Author contributions

Ibrahim Demirci, Alper Sonmez, Ilhan Satman and Ilker Tascı were involved in the conceptualization and methodology of the study. Naim Ata, Osman Celik, Murat Caglayan and Suayip Birinci were responsible for the data download and verification. Ibrahim Demirci, Cem Haymana and Ilker Tasci performed the formal analysis and investigation. Ilker Tasci, Alper Sonmez, Aysegul Atmaca, Rifat Emral and Ilhan Satman critically reviewed and edited the first draft. All the authors were involved in the writing of the manuscript.

5.5. Ethics Approval

The design and procedures in the study are in accordance with the declaration of Helsinki and the study protocol was approved by the Ministry of Health Ethical Board (95741342-020/27112019).

5.6. Consent to Participate: Not applicable.

5.7. Consent for Publication: Not applicable

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Tables

Table 1. Basic characteristics and Comparison of clinical and demographic parameters of COVID-19 patients with T1DM, T2DM, and non-diabetic patients (Crude analysis, before PSM)

	T1DM n=163	T2DM n=33478	Non-diabetic n=115108	p1	p2
Age, years, median (IQR)	41 (36)	54 (81)	38 (21)	**<0.001**	**<0.001**
Gender, Male, n (%)	103 (63.2)	14209 (42.4)	63703 (55.3)	**<0.001**	**0.044**
Smoking (current smoker - n,%)	29 (25.7)	3612 (16.2)	18914 (22.3)	**0.006**	0.397
Follow-up center, n (%)					
Public hospitals	118 (72.4)	25216 (75.3)	92361 (80.3)	0.431	**0.010**
University hospitals	17 (10.4)	2596 (7.8)	6386 (5.5)		
Private centers	28 (17.2)	5664 (16.9)	16342 (14.2)		
Education (9 years and over - n,%)	10 (43.5)	1309 (27.9)	6642 (39.4)	0.098	0.690
Comorbid conditions					
Hypertension, n (%)	110 (67.5)	22897 (68.4)	28497 (24.8)	0.803	**<0.001**
Dyslipidemia, n (%)	80 (49.1)	14923 (44.6)	8371 (7.3)	0.248	**<0.001**
Obesity, n (%)	5 (18.5)	2112 (49.5)	2136 (21.0)	**0.001**	0.755
Asthma/COPD, n (%)	57 (35.0	11112 (33.2)	18222 (15.8)	0.631	**<0.001**
Chronic kidney disease, n (%)	43 (54.4)	2187 (18.8)	1605 (7.7)	**<0.001**	**<0.001**
Coronary artery disease (CAD), n (%)	65 (39.9)	10778 (32.2)	9488 (8.2)	**0.036**	**<0.001**
Cancer, n (%)	8 (4.9)	2402 (7.2)	2954 (2.6)	0.263	0.059
Microvascular complications, n (%)	77 (47.2)	6120 (18.3)	NA	**<0.001**	NA
Macrovascular complications, n (%)	73 (44.8)	11864 (35.4)	NA	**0.013**	NA
Laboratory values					
CT findings of COVID-19	60 (39.0)	10900 (34.5)	22281 (21.1)	0.251	**<0.001**
Glucose, mg/dL, median (IQR)	188 (124)	127 (78)	103 (188)	**<0.001**	**<0.001**
HbA1c, %, median (IQR)	8.5 (3.1)	7 (2.4)	NA	**<0.001**	NA

HbA1c, mmol/mol, median (IQR)	69.4 (33.6)	53 (26.2)	NA	**<0.001**	NA
LDL-cholesterol, mg/dL, median (IQR)	117 (71)	116 (53)	112 (52)	0.566	0.871
eGFR, ml/min/1.73 m^2, median (IQR)	58 (94)	96.4 (46)	108 (43)	**<0.001**	**<0.001**
AST, >ULN, n (%)	8 (20)	1061 (21.1)	1685 (17.0)	0.866	0.611
ALT, >ULN, n (%)	2 (4.5)	1048 (20.6)	1947 (19.6)	**0.009**	**0.012**
CRP, >ULN, n (%)	52 (76.5)	6460 (70.0)	10638 (56.9)	0.244	**0.001**
Lactate dehydrogenase, >ULN, n (%)	20 (62.5)	2348 (44.2)	3019 (33.4)	**0.038**	**0.001**
Ferritin, >100 ng/mL, n (%)	36 (85.7)	3016 (60.7)	3798 (49.6)	**0.001**	**<0.001**
Lymphopenia, Lym# <1000, n (%)	31 (32.0)	3810 (19.9)	8704 (15.7)	**0.003**	**<0.001**
Treatments					
RAS blocker, n (%)	78 (47.9)	15746 (47.0)	13889 (12.1)	0.834	**<0.001**
Insulin, n (%)	163 (100)	7705 (23.0)	0	**<0.001**	NA
Statin, n (%)	51 (31.3)	8648 (25.8)	3047 (2.6)	0.112	**<0.001**
Acetylsalicylic acid, n (%)	58 (35.6)	10219 (30.5)	8721 (7.6)	0.162	**<0.001**
Outcomes					
Hospitalization, n (%)	99 (60.7)	18621 (55.6)	44648 (38.8)	0.190	**<0.001**
ICU admission & Intubation, n (%)	31 (31.6)	3832 (20.6)	4371 (9.8)	**0.007**	**<0.001**
Mortality, n (%)	26 (16.0)	2565 (7.7)	2095 (1.8)	**<0.001**	**<0.001**

p1 : T1DM vs. T2DM**; p2** : T1DM vs. non-DM

Abbreviations: T1DM, Type 1 Diabetes Mellitus,; T2DM, Type 2 Diabetes Mellitus; COPD, Chronic obstructive pulmonary disease; CT, Computerized tomography; HbA1c, Glycated hemoglobin; LDL-Cholesterol, Low-Density Lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; AST, Aspartate aminotransferase; ALT, Alanine aminotransferase; CRP, C-reactive protein; ULN, upper limit of normal; RAS, renin-angiotensin-aldosterone system; ICU, Intensive-care unit.

Table 2. Comparison of demographic and clinical parameters among COVID-19 patients with T1DM, T2DM, and non-diabetic patients.

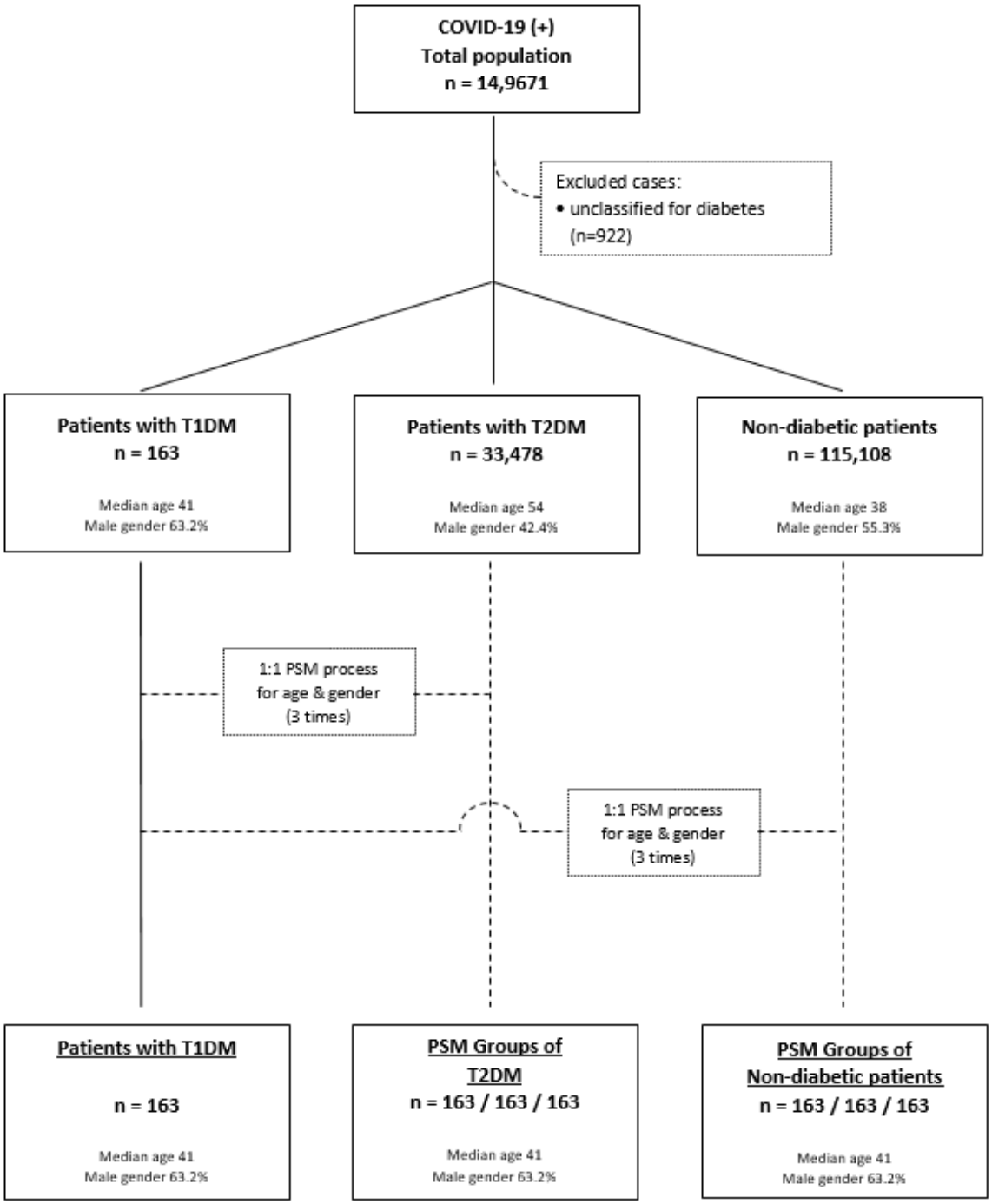
	T1DM n=163	T2DM n=489 (Pooled PSM)	Non-diabetic n=489 (Pooled PSM)	p1	p2
Age, years, median (IQR)	41 (36)	41 (36)	41 (36)	1.000	1.000
Gender, Male, n (%)	103 (63.2)	309 (63.2)	309 (63.2)	1.000	1.000
Smoking (current smoker - n,%)	29 (25.7)	71 (20.1)	76 (21.5)	0.236	0.363
Follow-up center, n (%)					
Public hospitals	118 (72.4)	367 (75.1)	406 (83.0)		
University hospitals	17 (10.4)	33 (6.7)	21 (4.3)	0.309	**0.003**
Private centers	28 (17.2)	89 (18.2)	62 (12.7)		
Education (9 years and over - n,%)	10 (43.5)	24 (31.2)	12 (20.7)	0.199	**0.038**
Comorbid conditions					
Hypertension, n (%)	110 (67.5)	286 (58.5)	170 (34.8)	**0.025**	**<0.001**
Dyslipidemia, n (%)	80 (49.1)	222 (45.4)	52 (10.6)	0.234	**<0.001**
Obesity, n (%)	5 (18.5)	31 (43.7)	11 (30.6)	**0.017**	0.383
Asthma/COPD, n (%)	57 (35.0)	140 (28.6)	88 (18)	0.140	**<0.001**
Hearth Failure, n (%)	38 (23.3)	46 (9.4)	16 (3.3)	**<0.001**	**<0.001**
Chronic kidney disease, n (%)	43 (54.4)	40 (22.0)	14 (13.1)	**<0.001**	**<0.001**
Coronary artery disease (CAD), n (%)	65 (39.9)	135 (27.6)	79 (16.2)	**0.003**	**<0.001**
Microvascular complications, n (%)	77 (47.2)	90 (18.4)	NA	**<0.001**	NA
Macrovascular complications, n (%)	73 (44.8)	151 (30.9)	NA	**0.001**	NA
Cancer, n (%)	8 (4.9)	31 (6.3)	16 (3.3)	0.505	0.337
Laboratory values					
CT findings of COVID-19	60 (39.0)	153 (33.5)	110 (24.2)	0.217	**<0.001**
Glucose, mg/dL, median (IQR)	188.5 (124)	139 (62)	107 (26)	**0.001**	**<0.001**
HbA1c, %, median (IQR)	8.5 (3.1)	6.6 (2.5)	NA	**<0.001**	NA
HbA1c, mmol/mol, median (IQR)	69.4	48.2 (27.3)	NA	**<0.001**	NA

	(33.6)				
LDL-cholesterol, mg/dL, median (IQR)	117 (72)	109 (46)	110 (58)	0.694	0.664
eGFR, ml/min/1.73 m^2, median (IQR)	58 (94)	99 (59)	98 (49)	**<0.001**	**<0.001**
AST, >ULN, n (%)	8 (20)	15 (19.2)	8 (14.8)	0.920	0.584
ALT, >ULN, n (%)	2 (4.5)	22 (27.8)	7 (13.7)	**0.002**	0.170
CRP, >ULN, n (%)	52 (76.5)	96 (75.0)	48 (54.5)	0.820	**0.005**
Lactate dehydrogenase, >ULN, n (%)	20 (62.5)	41 (51.9)	22 (43.1)	0.309	0.086
Ferritin, >100 ng/mL, n (%)	36 (85.7)	47 (58.8)	31 (67.4)	**0.002**	0.050
Lymphopenia, Lym# <1000, n (%)	31 (32.0)	53 (20.1)	44 (16.5)	**0.018**	**0.001**
Treatments					
RAS blocker, n (%)	78 (47.9)	192 (39.3)	112 (22.9)	0.054	**<0.001**
Insulin, n (%)	163 (100)	152 (31.1)	0	**<0.001**	**NA**
Statin, n (%)	51 (31.3)	127 (26.0)	30 (6.1)	0.187	**<0.001**
Acetylsalicylic acid, n (%)	58 (35.6)	154 (31.5)	75 (15.3)	0.334	**<0.001**
Outcomes					
Hospitalization, n (%)	99 (60.7)	263 (53.8)	230 (47.0)	0.122	**0.002**
ICU admission & Intubation, n (%)	31 (31.6)	60 (22.8)	25 (10.9)	0.086	**<0.001**
Mortality, n (%)	26 (16.0)	34 (7.0)	14 (2.9)	**0.001**	**<0.001**

p1 : T1DM vs. T2DM**; p2** : T1DM vs. non-diabetics,

Abbreviations: T1DM, Type 1 Diabetes Mellitus,; T2DM, Type 2 Diabetes Mellitus; COPD, Chronic obstructive pulmonary disease; CT, Computerized tomography; HbA1c, Glycated hemoglobin; LDL-Cholesterol, Low-Density Lipoprotein cholesterol; eGFR, estimated glomerular filtration rate; AST, Aspartate aminotransferase; ALT, Alanine aminotransferase; CRP, C-reactive protein; ULN, upper limit of normal; RAS, renin-angiotensin-aldosterone system; ICU, Intensive-care unit.

Figures



Abbreviations: T1DM, Type 1 Diabetes Mellitus; T2DM, Type 2 Diabetes Mellitus; PSM, Propensity score matching.

Figure 1

Study inclusion flow chart.

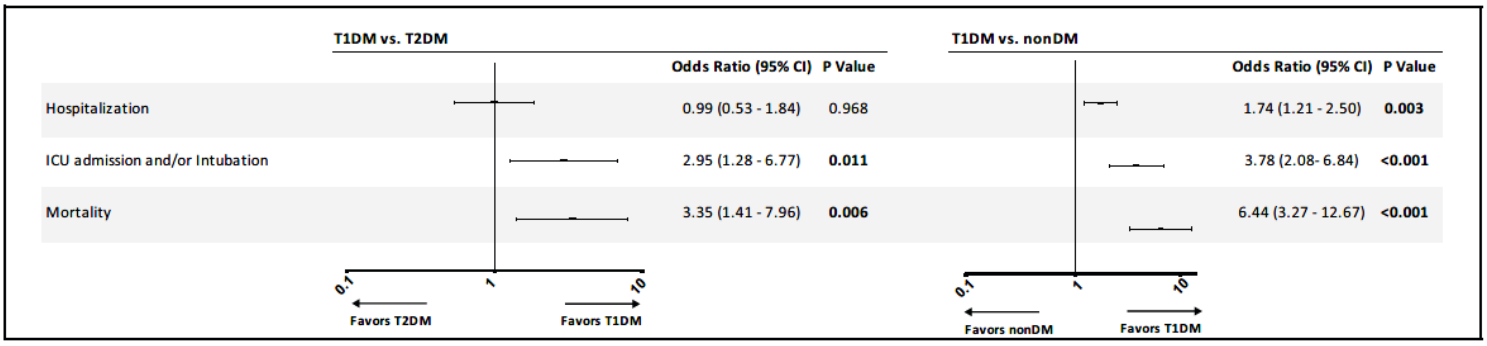


Figure 2

The risks of COVID-19 outcomes in patients with T1DM relative to the T2DM and non-diabetics.

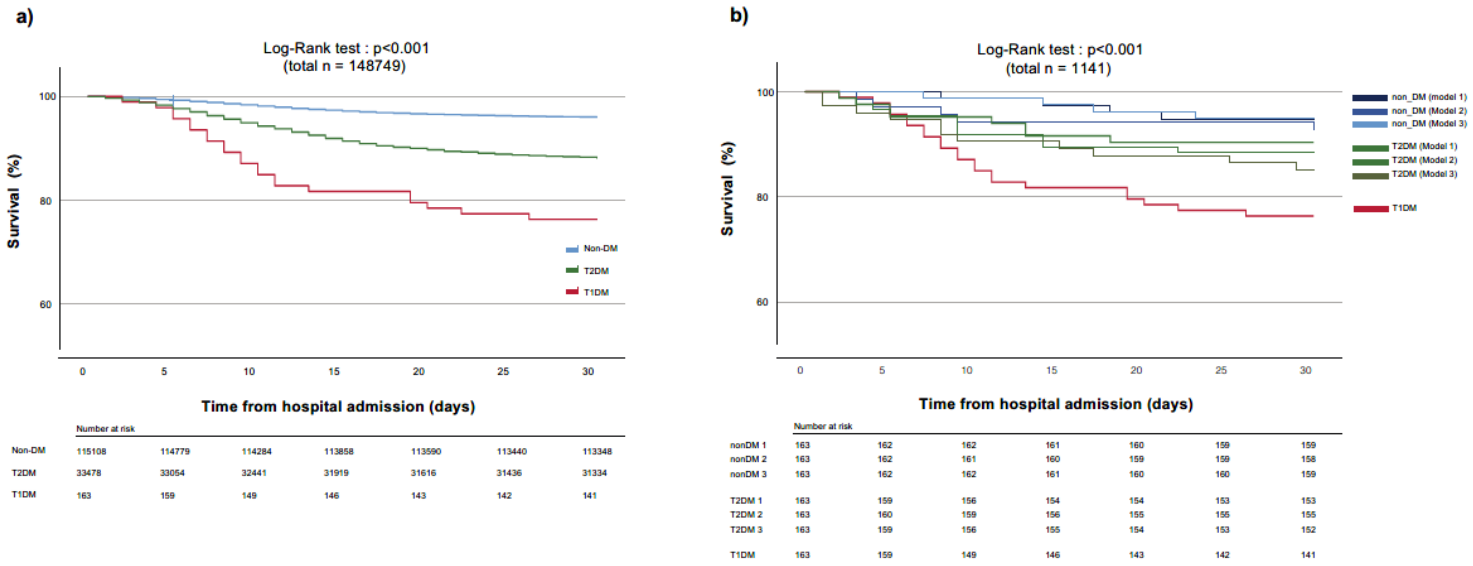


Figure 3

Kaplan Meier survival curves showing crude (a) and PSM scenarios (b)

Supplementary Files

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