JOURNAL OF COMMUNITY HOSPITAL INTERNAL MEDICINE PERSPECTIVES
2021, VOL. 11, NO. 5, 590–596
https://doi.org/10.1080/20009666.2021.1957555

Diabetes-associated nephropathy and obesity influence COVID-19 outcome in type 2 diabetes patients

Martin Schiller[a], Kim Solger[a], Stefanie Leipold[a], Hans Ulrich Kerl[b] and Wolfgang Kick[a]

[a]Internal Medicine, HochFranken Hospitals, Munchberg, Germany; [b]Department of Radiology, HochFranken Hospitals, Munchberg, Germany

ABSTRACT

Coronavirus disease 2019 has rapidly spread around the globe and various comorbidities, such as diabetes have been recognized as risk factors for an unfavorable outcome. We analyzed a cohort of COVID-19 patients (n = 75) treated at a German community hospital. With a focus on diabetes mellitus, we evaluated the impact of distinct comorbidities on the COVID-19 disease course. The duration of hospital stay was prolonged if diabetes was present. An older age was associated with a poor outcome. The percentage of non-survivors increased in the presence of congestive heart failure or chronic kidney disease. In the group of diabetes patients, mortality was increased if any organ complication was present and diabetic nephropathy or the combination of obesity plus diabetes were by far the most important risk factors. Taken together, an older age, congestive heart failure, and chronic kidney disease significantly influenced COVID-19 disease course and survival. Diabetic nephropathy or the combination of obesity plus diabetes had the strongest impact on patients' outcome.

ARTICLE HISTORY
Received 14 April 2021
Accepted 15 July 2021

KEYWORDS
COVID-19; diabetes mellitus; diabetic nephropathy; metabolic syndrome; obesity; SARS-COV-2

Introduction

Coronavirus disease 2019 (COVID-19) is a novel disease caused by the SARS-CoV-2 virus. Since its first recognition in December 2019 (in Whuan), this virus has now spread worldwide causing a global health emergency. The disease mainly affects the respiratory tract [1]. Other manifestations and complications include cytokine release syndrome, involvement of the central nervous system, acute kidney injury, myocardial damage, and secondary infections [2,3]. Several diagnostic and prognostic markers have been described, such as sofa score (Sepsis-related organ failure assessment score), lymphocytopenia, and d-dimer levels [4–6]. Radiologic findings include ground glass opacity, posterior/peripheral involvement of the lung, or bilateral infiltration [7,8].

Various conditions have been reported as predictors of an unfavorable outcome in COVID-19 patients. Thus, most severe cases seem to occur in the elderly or in patients with distinct comorbidities including cardiovascular disease or diabetes [9–11].

Diabetes is also a risk factor in patients infected with viruses other than SARS-CoV-2. An increased mortality has been discussed in influenza, respiratory syncytial virus, SARS-coronavirus, and MERS-coronavirus infected patients [12–14]. We investigated the outcome of COVID-19 patients treated at a German community hospital with the focus on diabetes mellitus as a relevant comorbidity. Our patient cohort is representative for elderly patients who are typically treated by primary health care providers. Diabetes patients required a significantly prolonged in-hospital treatment, when compared to the non-diabetes group. The percentage of diabetes patients who did not survive COVID-19 infection was elevated if any diabetes-associated organ complication was present. Most importantly, patients with an established diabetic nephropathy or obese diabetes patients had the worst outcome, with more than 70% of non-survivors.

Material and methods

This work was conducted at the Kliniken Hochfranken Munchberg, a German community hospital. Laboratory and radiologic findings from 75 hospitalized COVID-19 patients, as well as their respective comorbidities were analyzed. COVID-19 was diagnosed by a positive PCR-result (Real Star SARS-CoV-2 PCR Kit, Altona Diagnostics GmbH, Hamburg, Germany) and/or typical radiologic findings. All patients showed COVID-19 symptoms, such as fever, cough, and shortness of breath. . Samples for PCR were obtained from throat swabs or qualified sputum. COVID-19 patients were treated in our hospital from March 2020 to August 2020. Mean values and graphs were calculated using Microsoft Excel software. Statistical analysis was performed using

CONTACT Martin Schiller marvin-1@gmx.net Internal Medicine, HochFranken Hospitals, Hofer Straße 40, Münchberg 95213, Germany

students t-test for parametric data (Table 2 and 3(a)). Proportions for categorical variables were compared using the chi square test (Table 1). The Fisher exact test was used when data size was limited (Table 3(b)).

Results and discussion

The mean age of hospitalized COVID-19 patients was 74.2 years (22–99 years), with 35 female and 40 male patients. In total, 23 of the patients did not survive (30.7%) and the death rate in male patients was higher than in female ones (37.5% vs. 22.9%; $p = 0.315$). Eleven patients (out of which 10 required mechanical ventilation) were treated at our intensive care unit. The average age of patients who survived was 71 years, while non-survivors were significantly older (81.6 years; $p < 0.0005$; for details see Table 1).

summarized in Table 1. We observed an increased mortality in patients suffering from congestive heart failure ($p = 0.0406$) and chronic kidney disease ($p = 0.0182$).

The group of diabetes patients also showed an increased death rate (46.2% vs. 30.7%; $p = 0.1317$). However, this was only statistically significant if any diabetes-associated organ complication was present (57.9% vs. 30.7%; $p = 0.0406$). Importantly, diabetic nephropathy was by far the most substantial risk factor for an unfavourable outcome (73.3% non-survivors in this group; $p = 0.0082$).

Type 2 diabetes is often associated with metabolic syndrome, and an increased death rate in respiratory infections has been described for obese patients [15,16]. Thus, we were interested, whether obesity (BMI > 30 kg/m^2) alone or in combination with diabetes has an impact on survival in our cohort.

Table 1. Demographics and comorbidities of COVID-19 patients.

	Total $n = 75$	Survivor $n = 52$ (69.3%)	Non-survivors $n = 23$ (30.7%)	p-value
Demographics:				
Age, years	74.2 (22–99)	71.0 (22–96)	81.6 (61–99)	**0.0005**
Sex				0.5283
- male	40	25	15	
- female	35	27	8	
Comorbidities:				
- Diabetes	26 (34.7%)	14 (53.8%)	12 (46.2%)	0.1317
- Obesity	20 (26.7%)	9 (45%)	11 (55%)	0.0563
- Hypertension	50 (66.7%)	33 (66%)	17 (34%)	0.5135
- Atrial Fibrillation	21 (28%)	11 (52.4%)	10 (47.6%)	0.1626
- Coronary heart disease	16 (21.3%)	8 (50%)	8 (50%)	0.1895
- Congestive heart failure	19 (25.3%)	8 (42.1%)	11 (57.9%)	**0.0406**
- Obstructive lung disease	20 (26.7%)	9 (45%)	11 (55%)	0.0563
- History of stroke	15 (20%)	7 (46.7%)	8 (53.3%)	0.1433
- Chronic kidney disease	25 (33.3%)	11 (44%)	14 (56%)	**0.0182**
- Malignancy	9 (12%)	4 (44.4%)	5 (45.6%)	0.0230
- **Diabetes + any complication**	19 (25.3%)	8 (42.1%)	11 (57.9%)	**0.0406**
- **Diabetic nephropathy**	15 (20%)	4 (26.7%)	11 (73.3%)	**0.0082**
- **Diabetes + Obesity**	14 (18.7%)	4 (28.6%)	10 (71.4%)	**0.0155**
COVID-19 diagnosis:				
PCR positive		67 (89.3%)		
- Throat swab		– 62 (82.7%)		
- Qualified sputum		– 5 (6.6%)		
Characteristic CT-scan and PCR negative		8 (10.7%)		

COVID-19 patients with an established diagnosis of type 2 diabetes (according to the criteria of the German diabetes society) were compared to non-diabetes patients. As expected, diabetes patients had higher blood glucose and HbA1c levels. Further, diabetes patients showed an impaired renal function and higher CRP levels, when compared to the non-diabetes group (Figure 1). No significant differences were found for troponin, d-dimer levels, white blood cells counts, or lactate dehydrogenase (LDH).

Analyzing the comorbidities of COVID-19 patients, the most common diagnoses were arterial hypertension (66.7%) and diabetes mellitus (34.7%). All diabetes patients in this cohort had been diagnosed with type 2 diabetes. Comorbidities are

While obesity itself caused only a non-significant increase in the percentage of non-survivors (55%; $p = 0.0563$), we observed a substantial increase in mortality, if obesity was present together with type 2 diabetes (71.4%; $p = 0.0155$, see Table 1).

At the time of admission, all COVID-19 patients (diabetes and non-diabetes) showed a relative lymphocytopenia (lymphocytes: 14.49% normal range: 20.5–51.1%), elevated CRP (82,36 mg/L; normal range: < 5 mg/L), troponin (42.9 pg/mL; normal range: < 14 pg/mL), LDH (351.82 U/L; normal range < 250 U/L), and d-dimer levels (1146.86 ng/mL; normal range: < 250 ng/mL). The elevation of CRP levels was pronounced in patients who did not survive, and

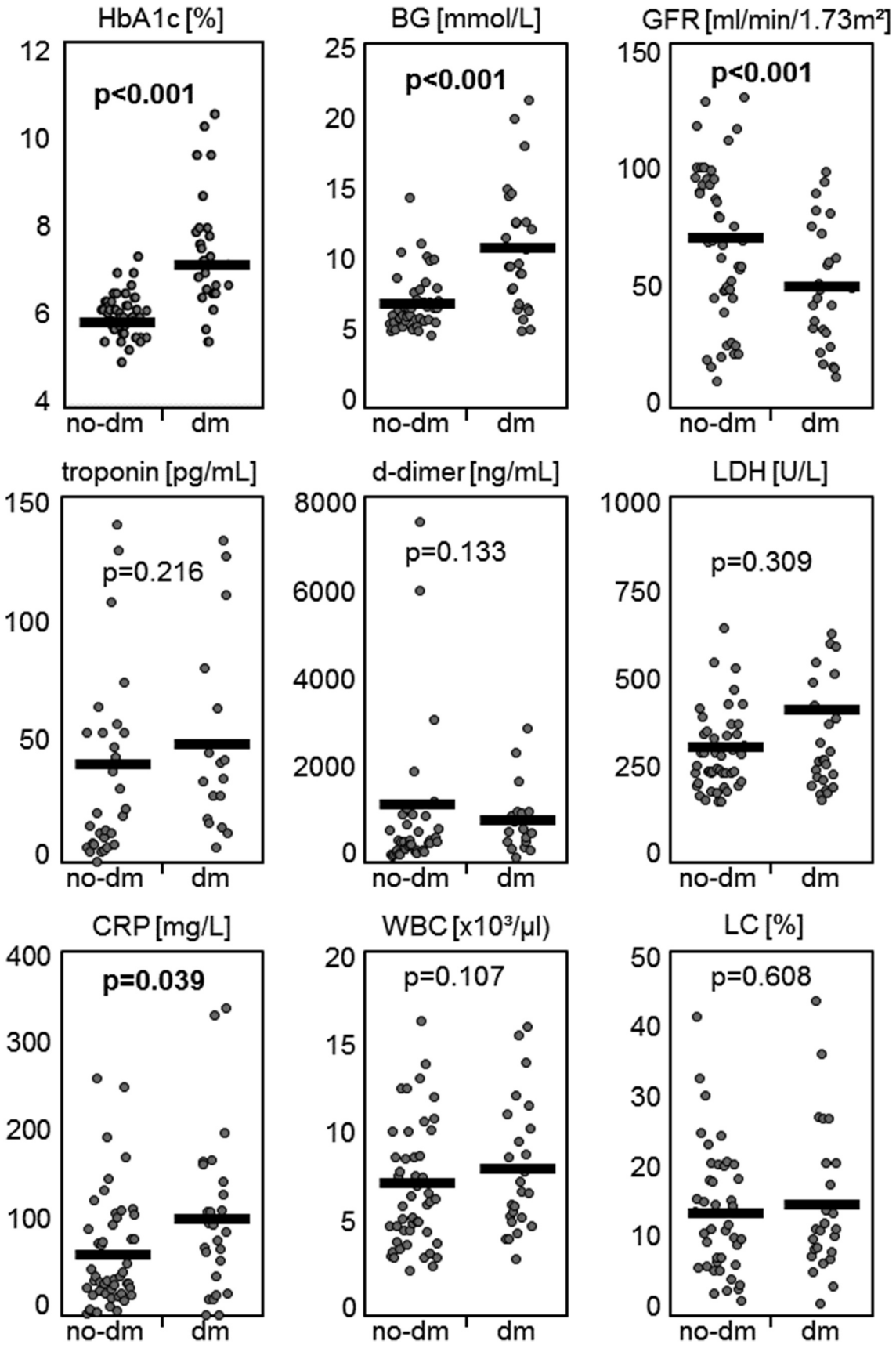

Figure 1. Laboratory results obtained from COVID-19 infected diabetes and non-diabetes patients.

The quantitative laboratory values are shown on the respective x-axes. HbA1c, blood glucose (BG), glomerular filtration rate (GFR), troponin, d-dimer, lactate dehydrogenase (LDH), C-reactive protein (CRP), white blood cell counts (WBS), and percentage of lymphocytes (LC) are depicted. Non-diabetes patients (no-dm) are compared to diabetes patients (dm). Statistical significance was calculated using the students t-test.

these patients showed a significant increase in procalcitonin levels (0.65 ng/mL vs. 0.98 ng/mL; p = 0.1374) and neutrophil counts (73.59% vs. 81.92%; p = 0.0065). Moreover, mortality was associated with a pronounced lymphocytopenia (p = 0.0031) and an impaired renal function (p < 0.001). Laboratory results at the time of admission are shown in Table 2.

Table 2. Laboratory findings in COVID-19 patients.

	Total *n* = 75	Survivor *n* = 52 (69.3%)	Non-survivors *n* = 23 (30.7%)	*p*-value
Laboratory findings:				
- HbA1c [%]	6.35	6.34	6.36	0.7760
- Blood glucose [mg/dl]	8.42	8.01	9.34	0.2935
- creatinine [µmol/L]	125.33	99.50	183.72	**<0.001**
- eGFR [ml/min/1.73 m^2]	63.08	70.79	45.65	**<0.001**
- C-reactive protein [mg/L]	82.36	68.11	114.44	0.0713
- Creatine Kinase [U/L]	241.57	249.57	268.17	0.5044
- Lactate Dehydrogenase [U/L]	351.82	299.66	476.48	0.1378
- Troponin [pg/mL]	42.9	34.7	66.23	0.0013
- D-dimer [ng/mL]	1146.86	916.15	1596.75	0.0963
- Procalcitonine [ng/mL]	0.75	0.65	0.98	0.1374
- Platelets [/nl]	231.77	228.14	239.83	0.7373
- Lymphocytes [%]	14.49	16.84	9.58	**0.0031**
- Neutrophiles [%]	76.26	73.59	81.92	**0.0065**

Interestingly, while blood glucose was elevated in the diabetes group (p < 0.001), we found no differences in blood glucose levels when we compared the group of diabetic non-survivors to surviving diabetes patients (Figure 2). Renal function was impaired in the diabetes group (p < 0.001; compared to non-diabetes patients) and a further significant impairment of glomerular filtration rate was observed in diabetes patients who did not survive (Figure 2). Lymphocytopenia was highly pronounced in the group of diabetic non-survivors (p = 0.046).

Diabetes patients who survived COVID-19 required a significantly prolonged hospital treatment (22.3 days vs. 11 days; p = 0.0096), when compared to non-diabetes patients. Diabetes-specific medication had no significant effects on patients‘ outcome (see Table 3).

As an impact of blood glucose levels on radiologic findings in COVID-19 has been discussed previously [17], we analyzed and compared chest computed tomography (CT) images obtained from our patients. We did not observe any striking differences comparing diabetes patients to the non-diabetes group. Figure 3 shows representative chest CT images of diabetes and non-diabetes patients diagnosed with COVID-19 pneumonia.

Conclusion

Diabetic nephropathy or the combination of obesity plus diabetes were associated with a substantial increase in COVID-19 mortality. These comorbidities were the strongest risk factors with a death rate of more than 70%. Prominent laboratory findings were an impaired kidney function and lymphocytopenia, which were significantly pronounced in the group of diabetes patients with a poor outcome.

Disclosure statement

No potential conflict of interest was reported by the author(s).

References

[1] Lescure FX, Bouadma L, Nguyen D, et al. Clinical and virological data of the first cases of COVID-19 in

Table 3. Duration of hospitalization and medication of diabetes and non-diabetes patients

A) Duration of hospitalization	Hospital stay [days]	*p*-value	
All patients (***n*** = 75)	**12.8 (1–35)**		
No diabetes (*n* = 49)	11.1 (3–34)	0.3051	
Diabetes patients (*n* = 26)	15.8 (1–35)		
Survivor, no diabetes (*n* = 38)	11 (2–34)	**0.0096**	
Survivor, diabetes (*n* = 14)	22.3 (4–35)		
Dead, no diabetes (*n* = 11)	11.5 (5–22)	0.2755	
Dead, diabetes (n = 12)	8.3 (1–21)		
B) Medication of diabetes patients			
	Survivors [abs. (%)]	**Non-survivor** [abs. (%)]	**p-value**
Diabetes patients (*n* = 26):	14 (53.8%)	12 (46.2%)	
- Metformin (*n* = 11)	9 (81.9%)	2 (18.2%)	0.1578
- Insulin (*n* = 7)	5 (71.4%)	2 (28.6%)	0.6893
- Sitagliptin (*n* = 6)	5 (83.3%)	1 (16.7%)	0.3954
- Empagliflozin (*n* = 2)	2	0	n.d.
- Dapagliflozin (*n* = 1)	1	0	n.d.
- no medication (*n* = 7)	1 (14.3%)	6 (85.7%)	0.2701

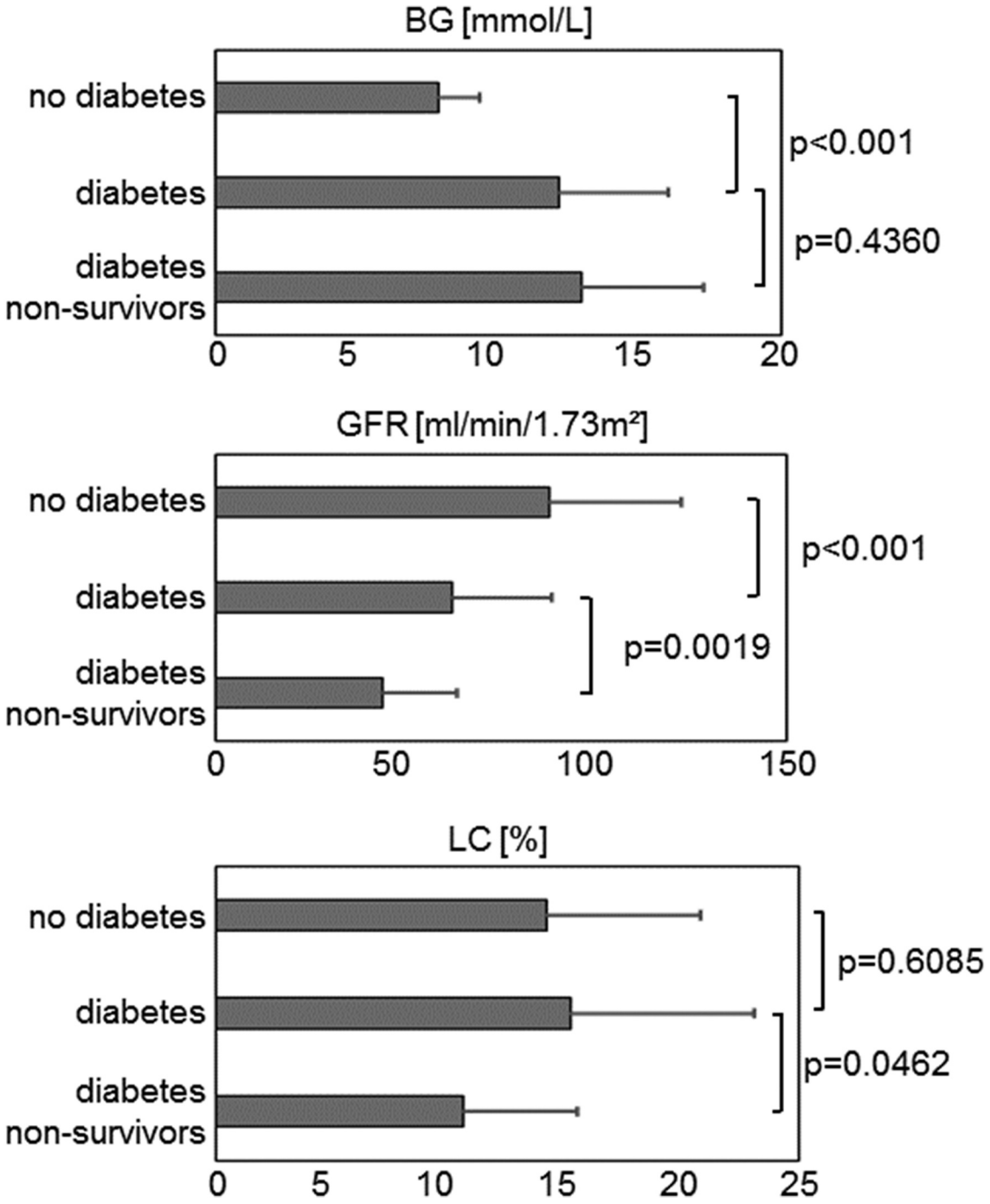

Figure 2. Lymphocyte counts and glomerular filtration rate are impaired in diabetic COVID-19 non-survivors.

Blood glucose levels (BG), glomerular filtration rate (GFR) and percentage of lymphocytes (LC) are shown. Diabetes patients showed elevated BG levels, however no difference was observed comparing survivors and non-survivors. GFR was diminished in diabetes, with a further decrease in the population of non-survivors. Lymphocytopenia was mostly pronounced in diabetic non-survivors. Statistical significance was calculated using the students t-test.

Europe: a case series. Lancet Infect Dis. 2020;20 (6):697–706.

[2] Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020;323(11):1061–1069.

[3] Karagiannidis C, Mostert C, Hentschker C, et al. Case characteristics, resource use, and outcomes of 10 021 patients with COVID-19 admitted to 920 German hospitals: an observational study. Lancet Respir Med. 2020;8(9):853–862.

[4] Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229):1054–1062.

[5] Schiller M, Fisahn J, Huebner U, et al. Coronavirus disease (COVID-19): observations and lessons from primary medical care at a German community hospital. J Community Hosp Intern Med Perspect. 2020;10(2):81–87.

[6] Wang L, He W, Yu X, et al. Coronavirus disease 2019 in elderly patients: characteristics and prognostic

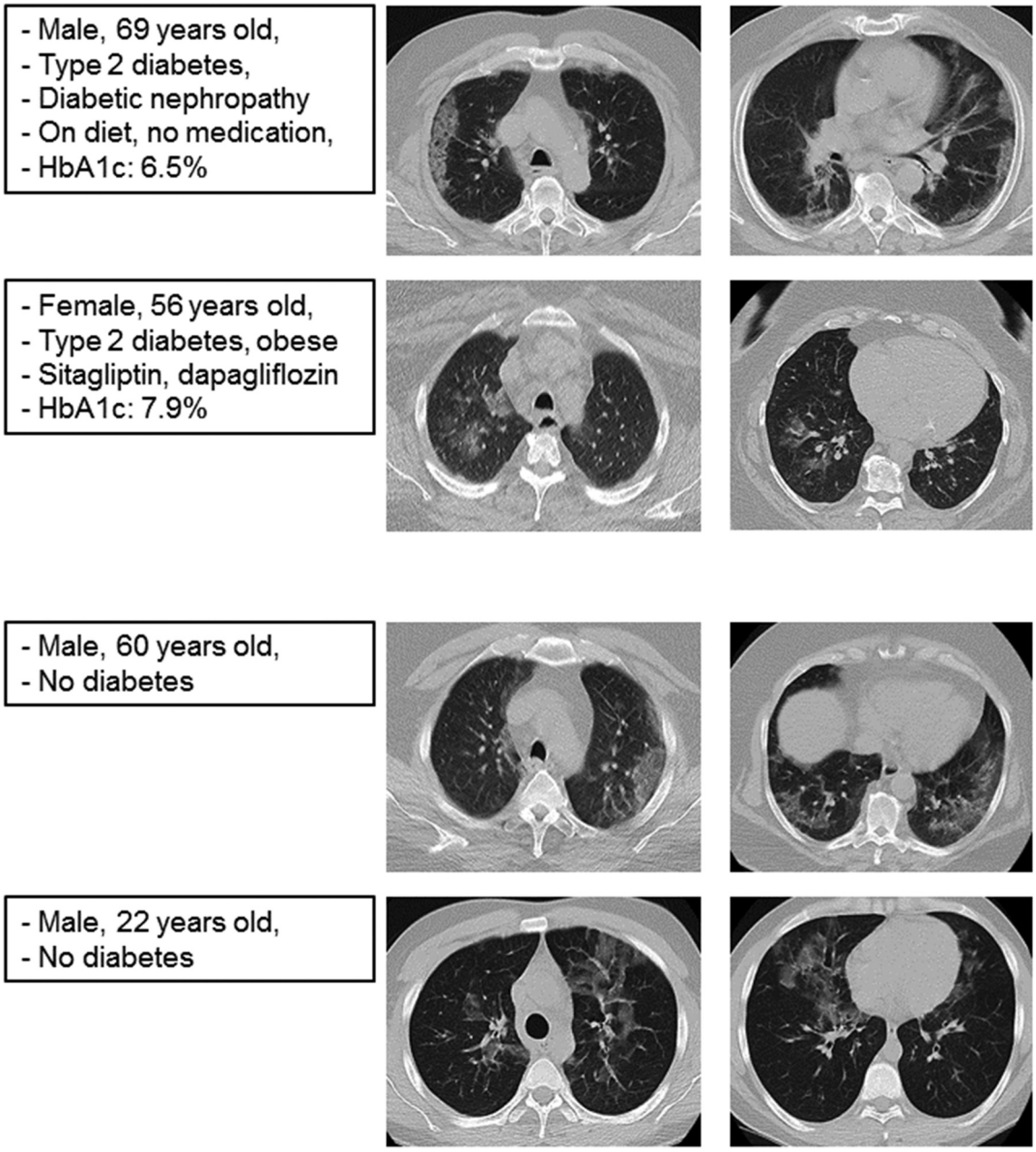

Figure 3. CT-morphologic features of COVID-19 pneumonia in diabetes and non-diabetes patients.

Representative chest CT-scans are shown for two diabetes (upper pictures) and two non-diabetes patients (lower pictures). Clinical characteristics are indicated in the figure. Chest CT-scans were performed at the time of admission. All patients showed similar ground glass opacities, characterized by bilobular and preferentially posterior/peripheral distribution.

factors based on 4-week follow-up. J Infect. 2020;80 (6):639–645.
[7] Fang Y, Zhang H, Xie J, et al. Sensitivity of chest CT for COVID-19: comparison to RT-PCR. Radiology. 2020;296(2):E115–E117.
[8] Prokop M, van Everdingen W, van Rees Vellinga T, et al. CO-RADS: a categorical CT assessment scheme for patients suspected of having COVID-19-definition and evaluation. Radiology. 2020;296(2): E97–E104.
[9] Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382(18):1708–1720.
[10] Jutzeler CR, Bourguignon L, Weis CV, et al. Comorbidities, clinical signs and symptoms, laboratory findings, imaging features, treatment strategies, and outcomes in adult and pediatric patients with COVID-19: a systematic review and meta-analysis. Travel Med Infect Dis. 2020;37:101825.
[11] Li B, Yang J, Zhao F, et al. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. Clin Res Cardiol. 2020;109(5):531–538.
[12] Banik GR, Alqahtani AS, Booy R, et al. Risk factors for severity and mortality in patients with MERS-CoV: analysis of publicly available data from Saudi Arabia. Virol Sin. 2016;31(1):81–84.
[13] Badawi A, Ryoo SG. Prevalence of comorbidities in the Middle East respiratory syndrome coronavirus (MERS-CoV): a systematic review and meta-analysis. Int J Infect Dis. 2016;49:129–133.
[14] Chuaychoo B, Ngamwongwan S, Kaewnaphan B, et al. Clinical manifestations and outcomes of respiratory

syncytial virus infection in adult hospitalized patients. J Clin Virol. 2019;117:103–108.
[15] Beumer MC, Koch RM, van Beuningen D, et al. Influenza virus and factors that are associated with ICU admission, pulmonary co-infections and ICU mortality. J Crit Care. 2019;50:59–65.
[16] Holman N, Knighton P, Kar P, et al. Risk factors for COVID-19-related mortality in people with type 1 and type 2 diabetes in England: a population-based cohort study. Lancet Diabetes Endocrinol. 2020;8(10):823–833.
[17] Iacobellis G, Penaherrera CA, Bermudez LE, et al. Admission hyperglycemia and radiological findings of SARS-CoV2 in patients with and without diabetes. Diabetes Res Clin Pract. 2020;164:108185.