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Weight loss in subjects with type 2 diabetes before and after SARS-CoV2 infection - A retrospective observational study

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ABSTRACT

Objectives. As weight modification during the COVID-19 pandemic was reported in several circumstances, we aimed to assess the body composition changes using bio impedance in patients with type 2 diabetes mellitus (T2DM) during this period. *Materials and Methods*. We conducted an observational, retrospective study, from January 2021- June 2021, in two outpatient clinics, enrolling all patients with T2DM and SARS-CoV2 infection that presented for evaluation after the infection. Blood tests (serum creatinine, urea, blood glucose, lipid profile, transaminases, HbA1c) were available before the onset of infection as well as at an interval of 1-3 months post-infection. *Results*. From a total of 118 patients, 101 subjects were eligible, 50.5% males. 68.6% had a mild form of SARS-CoV2 infection. There is a significant decrease in mean weight (91.9 ± 26.00 kg before and 90.00 ± 23.00 kg after infection vs. control, $p<0.05$), body mass index (31.80 ± 8.89 kg/m2 before and 30.47 ± 8.48 after infection vs. control, $p<0.05$), and visceral fat (15.00 ± 8.00% vs.14.5 ± 7.25 %) after infection. Median HbA1c increased in patients that were infected (6.5 ± 1.5 before vs 7.1 ± 1.5 after infection, non-significant) and significantly decreased in the control group (7.0 ± 2.3 % vs. 6.4 ± 1.00 %). We did not find any significant correlation between weight decrease and clinical or biological parameters in the SARS-CoV2 group. *Conclusions*. Weight, body mass index, and visceral fat decreased at 3-month follow-up in T2DM subjects with SARS-CoV2 infection vs controls.

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Introduction

The virulence of SARS-CoV2 infection in subjects with high blood pressure, diabetes mellitus (DM), or obesity in combination with age and sex significantly increases the mortality rate [1,2]. These chronic diseases are often associated with protein-energy malnutrition [3] induced by low-grade inflammation and other coexisting conditions [4]. This malnutrition is further highlighted in acute infections [5,6]. In severe cases with prolonged hospital admission, malnutrition is higher [7,8], but unintentional weight loss was described also in mild and moderate infections [6]. The decrease in appetite, dysgeusia, and anosmia are frequent symptoms that decrease food intake [9]. This secondary malnutrition, denutrition, or sarcopenia is difficult to evaluate, and given the gravity of some infections [10], was among the last on the list of therapeutic priorities. The diagnostic challenge is even greater for sarcopenic obesity where the adipose tissue masks the loss of muscle mass.

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From one point of view, the basal metabolic rate increases during infection [11], activating catabolism. The immune cells do not have a nutrient reserve and rely on the immediate glucose or amino acid supply, which is lower in malnourished subjects [11,12]. Hypoalbuminemia increased mortality significantly with an Odds Ratio of 6.26 (95% Confidence Interval 3.26-12.04) in previous meta-analysis [13]. Also, there is a reduction of the T cells response in malnutrition which could be explained by the atrophy of lymphoid organs or by an abnormal hormonal regulatory response involving leptin [14].

From another point of view, white adipose tissue has an excessive immunologic activity in obesity characterized by low-grade inflammation [4,15] and the preactivation of specific cytokines [12,16]. This proinflammatory status decreases antigen response and impairs the function of Natural Killer (NK) cells or macrophages [17]. Consecutively, the obese host's immune response to infections is altered [17] with incoordination between innate and adaptive pathways [18]. This unbalanced inflammation is a favorable factor for "cytokine storm" or overreaction to viral spread [12,18].

The obesity-sarcopenia interconnection was described in a prospective observational study including 67% patients with body mass index (BMI) above 25 kg/m2 admitted to the hospital for SARS-CoV2 infection. 35% were malnourished at admission defined according to weight loss: >5% in 1 week and/or >10% in 1 month and/or >10% lower than their regular body weight, or if BMI was <18.5 kg/m2. The risk of sarcopenia assessed by SARC-F questionnaire was 73%. Although patients had nutritional complaints, the median duration of nutritional therapy after discharge was 2 weeks [19]. The authors of this study applied the recommendations of the European Society for Clinical Nutrition and Metabolism (ESPEN) for nutritional intervention in COVID-19 which includes: (a) evaluation of malnutrition; (b) optimization of nutritional status by diet counseling; (c) supplementation with vitamins and minerals; (d) regular physical activity with safety precautions; (e) oral nutrition supplements when needed; (f) enteral nutrition if oral nutrition is not indicated or insufficient; (g) parenteral nutrition if enteral nutrition is not indicated or insufficient [20].

The main objective of this study was to describe the changes in body composition after the SARS-CoV-2 infection in patients with type 2 DM (T2DM). As secondary objectives, we evaluated the modifications of glycemic control, lipid profile, and renal function in infected patients versus control group.

Materials and Methods

We designed an observational, retrospective study, lasting 6 months (January 2021- June 2021) enrolling all patients with T2DM and SARS-CoV2 infection that presented on an outpatient basis at the National Institute of Diabetes, Nutrition and Metabolic Diseases (NIDNMD) N.C. Paulescu and individual medical practice Dr. Stoica Roxana Adriana. This study was approved by the Ethical Committee of NIDNMD (protocol number 2/23.06.2020) and follows the recommendations of the Helsinki Declaration. Informed consent was not required as the study is an observational one.

For the diagnosis of T2DM, we used American Diabetes Association guidelines [20]. We followed retrospectively all patients who had SARS-CoV2 infection (confirmed using a real-time reverse transcription polymerase chain reaction test) by analyzing the medical records to collect demographic information and blood tests results collected before the onset of infection and at an interval of 1-3 months post-infection.

The glomerular filtration rate (eGFR) was calculated taking into consideration the gender, race, age, and serum creatinine of the patient with CKD-EPI formula [21,22]. Regarding the results of body composition measurements, we used the Tanita SC240MA® professional device. This is a non-invasive bioimpedance (BIA) procedure that uses four electrodes that send a low, safe electrical signal through the feet to the legs and abdomen. The electrical signal passes rapidly through the water that is present in hydrated muscle tissue but meets resistance when it faces fat tissue. This resistance (impedance) is measured and input into scientifically validated TANITA equations to calculate body composition measurements [23].

The database and final analysis were performed using SPSS® version 20 (IBM®). For normally distributed variables we used parametric tests, the results being expressed as a mean and standard deviation. Most variables did not have a normal distribution, so they were analyzed by non-parametric tests, and the values are written as a median and interquartile range (IQR). Wilcoxon signed-rank test or paired samples t-test (SPSS® version 20) were used for testing the differences. The correlation analysis was performed using the Spearman coefficient. The level of statistical significance was set at $p < 0.05$.

Results

From a total of 118 patients, we included 101 patients who met the inclusion criteria in the study (50.5% males), 51 subjects in Group A had a documented SARS-CoV2 infections and 50 subjects were considered a control group or Group B (not infected). Most of patients in Group A (86.3%) were from an urban setting and 45.1% were employed. All subjects had a mean age of 59.44 ± 11.17 years and a median duration of DM of 6.00 ± 7.00 years. The characteristics of the population (weight, BMI, cholesterol, triglycerides, creatinine, blood urea nitrogen, uric acid, etc.), at the first and second visit are presented in Table 1.

Table 1. General characteristics of the type 2 diabetes mellitus population

Variable	First visit (n=101)	Second visit (n=101)	p-value
Weight (kg)	88.00 ± 24.45	86.80 ± 23.35	<0.001
BMI (kg/m2)	31.00 ± 7.93	30.30 ± 7.93	<0.001
FM (kg)	30.55 ± 17.47	28.70 ± 16.00	0.097
FFM (kg)	57.00 ± 21.94	54.00 ± 22.00	0.583
TBW (kg)	38.69 ± 11.05	39.70 ± 11.59	0.818
VF (%)	13.00 ± 9.00	12.5 ± 8.00	<0.001
HbA1c (%)	7.38 ± 1.59	6.87 ± 1.06	0.006
Total cholesterol (mg/dl)	180.50 ± 72.12	172.00 ± 63.25	0.071
HDL cholesterol (mg/dl)	42.90 ± 18.40	43.00 ± 15.32	0.05
Triglycerides (mg/dl)	144.00 ± 93.3	148.00 ± 79.5	0.909
Serum Creatinine (mg/dl)	0.81 ± 0.3	0.90 ± 0.29	0.344
Blood urea nitrogen (mg/dl)	33.50 ± 17.35	36.00 ± 16.00	0.041
Uric acid (mg/dl)	5.53 ± 2.41	5.9 ± 2.4	0.405
eGFR (ml/min/1.73m2)	95.00 ± 22.00	93.00 ± 31.5	0.068
UACR (mg/g)	10.00 ± 24.6	10.00 ± 19.28	0.490

BMI= Body Mass Index, FM= Fat Mass, FFM= Fat Free Mass, TBW= Total Body Water, VF= Visceral Fat, HDL= high density lipoprotein, eGFR= glomerular filtration rate, UACR= Urinary Albumin Creatinine Ratio

There was a significant decrease in weight, BMI, and visceral fat postinfection with similar fat-free mass in Group A (see Table 2), but there were no significant modifications of the body composition in Group B. The weight, BMI and VF differences (Δ visit 2 – visit 1) were also significant between groups (p<0.001) with a median weight loss of 3.2 kg in Group A as presented in Table 3.

The data available for biological tests of this study are presented in Table 2. HbA1c decreased significantly in Group B at the second visit (7.0 ± 2.3 vs. 6.4 ± 1.00 %) and increased in Group A but did not reach significance. Also, Blood urea nitrogen increased in Group A (significant) with an increased serum creatinine and UACR (non-significant).

Table 2. Body composition and biological variables before (V1) and after (V2) SARS-CoV2 infection

Variable	Group A (n=51) V1	Group B (n=50) V1	Group A (n=51) V2	Group B (n= 50) V2
Weight (kg)	91.9 ± 26.00	82.60 ± 17.73	90.00 ± 23.00*	82.30 ± 18.28
BMI (kg/m2)	31.80 ± 8.89	30.80 ± 7.4	30.47 ± 8.48*	30.15 ± 7.07
FM (kg)	31.39 ± 9.82	29.0 ± 14.85	28.90 ± 15.55	28.45 ± 16.67
FFM (kg)	57.96 ± 18.8	54.55 ± 17.27	51.20 ± 26.2	54.35 ± 21.0
TBW (kg)	34.90 ± 19.15	38.50 ± 14.3	37.40 ± 18.6	38.10 ± 16.25
VF (%)	15.00 ± 8.00	11.0 ± 7.00	14.5 ± 7.25*	11.00 ± 6.00
HbA1c (%)	6.5 ± 1.5	7.0 ± 2.3	7.1 ± 1.5	6.4 ± 1.00*
Total cholesterol (mg/dl)	195.0 ± 61.1	158.0 ± 73.0	183.5 ± 66.08	152.0 ± 53.25
HDL cholesterol (mg/dl)	42.00 ± 7.00	43.0 ± 23.0	41.50 ± 14.0	45.0 ± 18.0
Triglycerides (mg/dl)	151.0 ± 76.0	123.0 ± 98.0	147.0 ± 77.95	152.0 ± 78.0
Serum Creatinine (mg/dl)	0.76 ± 0.21	0.90 ± 0.29	0.83 ± 0.27	0.99 ± 0.2
Blood urea nitrogen (mg/dl)	30.0 ± 15.0	39.0 ± 18.5	38.20 ± 15.08*	32.00 ± 15.5
Uric acid (mg/dl)	5.36 ± 2.30	6.0 ± 2.8	5.95 ± 2.16	5.50 ± 2.45
eGFR (ml/ min/1.73m2)	92.7 ± 19.0	96.50 ± 43	92.2 ± 25	93.50 ± 35.75
UACR (mg/g)	6.18 ± 14.7	25.49 ± 34.15	10.0 ± 8.88	23.0 ± 36.5

* p<0.05

Table 3. Differences in weight between Group A and B

Variable	Group A (n=51)	Group B (n=50)	p-value
Δ Weight (kg)	-3.2 ± 4.8	-0.6 ± 3.1	<0.001
ΔBMI (kg/m2)	1.2 ± 1.63	0.20 ± 1.15	0.001
ΔVF (%)	1.0 ± 2.0	0.00 ± 0.02	0.001
Δ HbA1c (%)	-0.2 ± 1.3	0.75 ± 2.0	0.018

Results are presented as median and IQR. Δ represents the difference between values at second evaluation vs first evaluation.

Regarding DM complications, in group A 2.0% had retinopathy and 23.5% were diagnosed with polyneuropathy. Cardiovascular (CV) disease was also assessed: 7.8% had a history of myocardial infarction, 7.8% had a stroke, and 9.8% had peripheral artery disease.

Other frequent associated diseases were chronic kidney disease with 19.6% prevalence and heart failure in 11.8% of subjects. We also analyzed the treatment before and after SARS-CoV2 infection. We observed an increase in the number of patients treated with insulin postinfection (Figures 1 and 2). Regarding the associated treatment, for 15 of 51 subjects corticotherapy was used.

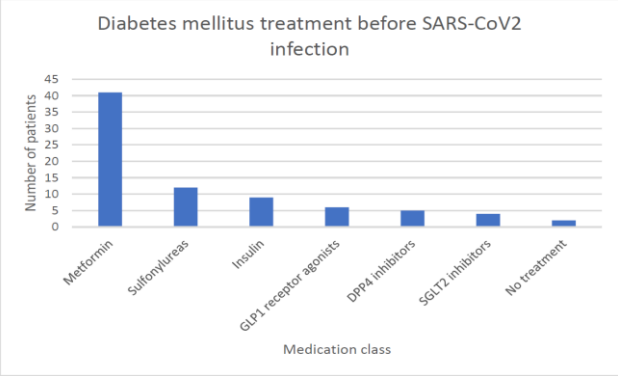

Figure 1. Diabetes mellitus treatment before SARS-CoV2 infection. GLP1- Glucagon-Like Peptid 1. DPP-4 - Dipeptidyl peptidase-4. SGLT2 - sodium glucose co-transporter-2

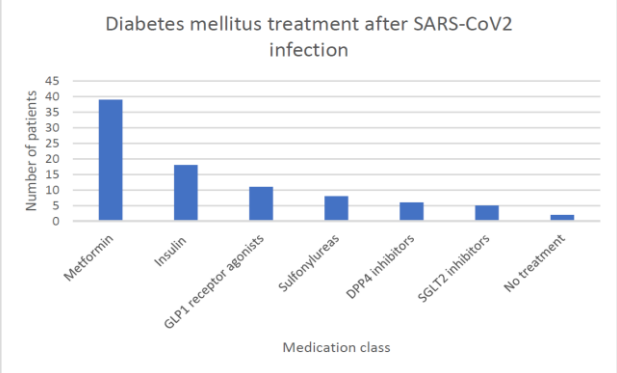

Figure 2. Diabetes mellitus treatment after SARS-CoV2 infection. GLP1- Glucagon-Like Peptid 1. DPP-4 - Dipeptidyl peptidase-4. SGLT2 - sodium glucose co-transporter-2

During the infection, 74.5% presented symptoms, including fever, anosmia, dysgeusia, myalgia, headache, and diarrhea. In total, 45 patients had a mild or moderate infection, and only 6 had a severe infection. 14 of them were hospitalized.

Discussions

The main focus of this study was to evaluate the body composition and glycemic control before and after the infection with SARS-CoV2 virus. We observed that there was a decrease in the mean weight (91.9 ± 26.00 kg before and 90.00 ± 23.00 kg after infection vs. control, $p<0.05$), BMI (31.80 ± 8.89 kg/m2 before and 30.47 ± 8.48 after infection vs. control, $p<0.05$), and visceral fat (15.00 ± 8.00% vs.14.5 ± 7.25 %) after SARS-CoV2 infection. Regarding glycemic control, our study showed an increase in HbA1c, from a median of 6.5% before to 7.1% after COVID-19 and a significant decrease in the control group from 7.0% to 6.4%.

A prospective study [24] carried out on 85 patients with T2DM without SARS-CoV-2 infection showed a tendency of weight gain during lockdown (mean absolute weight gain of 1.92 kg), and an increase in mean HbA1c (8.54% before vs 9.26% after). Other observational studies [25-27] in T2DM observed a higher weight after the COVID-19 lockdown. HbA1c was either similar [25] or significantly increased [26]. As it was hypothesized that SARS-CoV2 virus may enter the pancreatic beta cells via the expression of angiotensin-converting enzyme 2 (ACE2) receptors, and it would be possible that the virus impairs the pancreatic insulin secretion, thereby either worsening the pre-existing DM control or even triggering new-onset DM. Unfortunately, newly aroused hyperglycemia is linked to unfavorable prognosis [28]. From this point of view, another important discussion would concern the associated antidiabetic medication, and as it has been shown that the duration of lockdown is directly proportional to the worsening of glycemic control and DM-related complications, the importance of proper hypoglycemiant treatment, is essential. For instance, GLP-1 receptor agonists (GLP-1 RA) use may ensure good metabolic control and, furthermore, can prevent excessive weight gain, which was associated with both short-term and long-term negative outcomes in many aspects, including SARS-CoV2 infection on one side, and CV outcomes on the other side. Furthermore, incretin-based therapies, namely DPP4 inhibitors and, particularly GLP1-RAs in particular, have been demonstrated to exert significant anti-inflammatory effects which confer additive benefits [29]. Last but not least, other concurrent anti-inflammatory and anti-thrombotic medication which could have been administered in the case of SARS-CoV2 infection (corticosteroids, nonsteroidal anti-inflammatory drugs, aspirin, and some types of biological treatment) [29] may

have influence the metabolic control as well as body composition. The explanation for the weight decreases in our study could be the loss of appetite associated with anosmia secondary to infection, in contrast with patients that are just isolated at home which tend to increase. In this direction, one post-hoc analysis observed that 29% of patients lost more than 5% of their weight after SARS-CoV2 infection. Systemic inflammation, impaired renal function, and longer disease duration were associated with greater weight loss, the latter being the only predictor in multivariate logistic regression [5].

Sarcopenia was one incriminated factor [30-32], and in our study we observed a non-significant decrease in free fat mass in Group A versus B (57.96 ± 18.8 kg before and 51.20 ± 26.2 kg after infection vs. 54.55 ± 17.27 kg and 54.35 ± 21.00 kg). Total body water increased non-significantly only in Group A and could be caused by the corticosteroid treatment associated with water retention. As corticosteroids, and especially dexamethasone in some cases, become after several multiple large-scale randomized control trials assessing glucocorticoid efficiency, one of the anti-inflammatory drugs of choice in the management of the moderate to severe SARS-CoV2 infection, meta-analyses predominantly observed associations between glucocorticoid treatment and adverse COVID-19 outcomes, implying a markedly high risk in patients with high-dose glucocorticoid therapy, especially those who associated metabolic and cardiometabolic complications. Therefore, endocrinologists suggested using the lowest effective glucocorticoid dose if the underlying disease was well controlled and for the shortest of necessary time [33,34], in order to prevent protein catabolism, and subsequent osteopenia and sarcopenia [35]. The limitations of our study are represented by the small number of patients, the absence of long-term assessment of body composition, and the unavailability of dual-energy X-ray absorptiometry (DXA). However, previous studies suggest that DXA and BIA are interchangeable [36]. This is the first study on Romanian populations investigating body composition changes after SARS-CoV2 infection.

Further studies that evaluate body composition and the possible decrease of fat free mass after SARS-CoV2 infection are needed because this could be a predictor for higher mortality rate, in addition to the presence of CV disease as was previously showed [37].

Conclusions

There is a significant decrease in weight, BMI, and VF after SARS-CoV2 infection in T2DM subjects. HbA1c tended to increase after the infection but did not reach statistical significance. The main objective of this study was to describe the changes in body composition after the SARS-CoV-2 infection in patients with T2DM.

We showed that weight, BMI, and visceral fat decreased at 3-month follow-up in T2DM subjects with SARS-CoV2 infection vs non-infected individuals and a non-significant decrease in fat free mass. Median HbA1c increased in patients that were infected (non-significant) and significantly decreased in the control group. We did not find any significant correlation between weight decrease and clinical or biological parameters in the SARS-CoV2 group.

Contributions

Conceptualization: R.A.S, F.G; Data curation A.P-S; Formal analysis: R.A.S, C.T, T.S; Investigation: R.A.S, V-A.P, D.N; Methodology: R.A.S, F.G; Project administration: R.A.S, F.G; Resources: R.A.S, D.N; Supervision: M.S.P, A.P-S; Validation: C.T, C.I.B; Visualization: R.A.S, F.G; Writing – the initial draft: R.A.S, F.G; Writing – revision and editing: R.A.S, F.G, A-V.P, T.S).

Compliance with ethical standards

Any aspect of the work covered in this manuscript has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript. Informed consent was obtained from all subjects involved in the study.

Conflict of interest disclosure

There are no known conflicts of interest in the publication of this article. The manuscript was read and approved by all authors.

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