Original Article

HEALTH SCIENCES MEDICINE

DOI: 10.32322/jhsm.1062633

J Health Sci Med 2022; 5(2): 607-613

The effect of the COVID-19 pandemic on the increase of hyperlipidemia and metabolic syndrome in the Turkish population: a retrospective study

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Cite this article as: Karabulut A, Şahin M. The effect of the COVID-19 pandemic on the increase of hyperlipidemia and metabolic syndrome in the Turkish population: A retrospective study. J Health Sci Med 2022; 5(2): 607-613.

ABSTRACT

Aim: With the Coronavirus Disease 2019 (COVID-19) pandemic starting in late 2019 and continuing into 2020, permanent or periodic quarantine processes and curfews have been implemented. The objective of the study was to investigate the impact of extended quarantine processes during the pandemic on the development of metabolic syndrome (MET-S) due to physical inactivity.

Material and Method: This retrospective study consists of two groups. The first group consists of patients who applied to our hospital in the 12 months preceding the pandemic. The second group consists of the same patients who applied to the same hospital within 12 months of the onset of the pandemic. A total of 44,024 participants who had lab data prior to and during the pandemic were included in the study. Fasting plasma glucose (FPG), Triglyceride (TRIG), Total Cholesterol (T-Chol), High Density Lipoprotein-Cholesterol (HDL-C), Low Density Lipoprotein-Cholesterol (LDL-C) levels and demographic characteristics of the patients were recorded. The test averages were compared between the two groups and their effects on the development of MET-S were subjected to statistical analysis.

Results: When we compared our patients' HDL-C, FPG and TRIG levels measured during the pandemic and the pre-pandemic period, we found a statistically significant increase ($p<0.001$ for all three). We examined whether the COVID-19 pandemic affected the diagnosis criteria for MET-S (TRIG, HDL-C, FPG). The proportion of patients with FPG>100 mg/dL and TRIG>150 mg/dL during the pandemic was statistically significantly higher than during the pre-pandemic period (51.7% vs 45.8%, $p<0.001$; 45.7% vs 42.7%, $p<0.001$).We found that the proportion of patients with HDL-C<50 mg/dL in women and HDL-C<40 mg/dL in men during the pandemic was statistically significantly lower than during the pre-pandemic period (43.7% vs 46.9%, $p<0.001$; 32.4% vs 36.7 $p<0.001$, respectively).

Conclusions: The influence of sedentary living on the development of MET-S, insulin resistance, diabetes mellitus and cardiovascular diseases is known. The levels of FPG, TRIG and HDL-C constitute three of the five diagnostic criteria of MET-S, and abnormal changes in these tests are effective in the formation of MET-S. We have detected a significant increase in FPG and TRIG levels in patients due to the COVID-19 pandemic. Thus, we have established that patients became more susceptible to MET-S on the pandemic due to quarantine. On the other hand, there is a need for further research, including waist circumference and blood pressure data, which are included in the diagnostic criteria for MET-S.

Keywords: Hyperlipidemia, metabolic syndrome, pandemic, COVID-19

INTRODUCTION

The SARS-CoV-2 outbreak was referred to as Coronavirus Disease 2019 (COVID-19) by the World Health Organization (WHO). COVID-19 has spread rapidly across many countries and has been officially declared a pandemic by the WHO since March 11, 2020, with thousands of deaths (1). To prevent the spread of this virus, states have chosen quarantine or taken measures that make it mandatory for all citizens to stay at home. As a result, all sports and fitness events were suspended or cancelled. Hyperventilation during physical activities, particularly in group activities, increases the risk of infection, even if the recommended rules of social distance of 1.5 meters are respected. Because it has been reported that droplets of any size can reach up to 7-8 meters in various environmental and

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Received: 25.01.2022 **Accepted:** 16.02.2022

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disease conditions (2). Home quarantine was applied to protect human health and to reduce the spread rate and speed of the disease, but sedentary behaviours such as staying at home for a long time, sitting, lying, playing games, watching TV, using mobile devices were observed to increase, regular physical activity decreased, therefore less energy was spent (3). During the quarantine period, physical inactivity has reached high levels in our society that is not used to exercise (4).

MET-S is a primary and growing public health issue due to global urbanization, excess energy intake, increased obesity and sedentary lifestyles (5). MET-S is a combination of interdependent risk factors associated with cardiovascular disease and diabetes. These factors include dysglycemia, hypertension, low High Density Lipoprotein-Cholesterol (HDL-C) levels and obesity (6). International Diabetes Federation (IDF) has proposed a number of conditions for the diagnosis of metabolic syndrome. These conditions include increased waist circumference (102 cm in men, 88 cm in women), high Triglycerides (TRIG) (≥150 mg/dL), low HDL-C (<40 mg/dL in men, <50 mg/dL in women), high blood pressure (systolic blood pressure ≥130 mm Hg and/or diastolic blood pressure ≥85 mm Hg), increased fasting plasma glucose (FPG) (≥100 mg/dL) and are among the diagnostic criteria of MET-S (7).

Both genetic and acquired factors play a role in each of these conditions. Clinical and epidemiological research shows that obesity is highly associated with cardiovascular risk factors. Fatty tissue is recognized as a source of many potentially pathogenic molecules which are highly unesterified fatty acids, cytokines (tumor necrosis factor-α), resistin, adiponectin, Leptin and Plasminogen Activator Inhibitor (PAI-1). Visceral fatty tissue can be particularly active in the production of most of these factors. However, the mechanisms underlying the association between abdominal lipoidosis (in particular visceral adiposity) and MET-S are not fully understood (8). Exercise is an important element in treating metabolic syndrome. Not only does exercise improve the plasma lipid profile (increased TRIG and decreased HDL-C ratios), it also has positive effects on other risk factors (9). Physical exercise has been shown to reduce skeletal muscle lipid levels and insulin resistance, regardless of Body Mass Index (BMI) (10, 11). Regular exercise has been shown to increase insulin sensitivity, lower plasma TRIG levels and reduce cardiovascular morbidity and mortality (12). Studies on the endocrinological and metabolic effects of exercise have shown that physical exercise increases the use of blood sugar and free fatty acids in the muscles and reduces blood sugar levels in well-controlled diabetic patients. Sustained, light and regular jogging increases the effect of insulin on carbohydrate and lipid metabolism without affecting BMI or maximum oxygen use (13-15).

Since our current data do not include information on waist circumference and arterial blood pressure, we wanted to demonstrate statistically the effect of changes in FPG, HDL-C and TRIG values on the development of MET-S.

In this study, we explained the effect of long quarantine processes on the lipid profile of a particular society in the pandemic and its contribution to the development of MET-S.

MATERIAL AND METHOD

This retrospective study received ethics committee approval of Hitit Univesity Faculty of Medicine Clinical Studies Ethics Committee (Date: 28/04/2021, Decision No: 2021-53). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The hospital data used in this study covers the 12-months period before and after the COVID-19 pandemic was declared by the WHO. Demographic information, lipid profil and fasting plasma glucose values of 214.112 patients admitted to our hospital on an outpatient basis before (2019-12 months) and during the pandemic (2020-12 months) were recorded. Patients over the age of 18 who had been admitted to the outpatient clinic were included in the study. In our study, to reduce the effect of errors in analytical, fasting blood glucose >50 mg/dl, total cholesterol (T-Chol)>30 mg/dl, Triglycerides>20 mg/dl, LDL cholesterol (LDL-C)>20 mg/dl and HDL cholesterol>10 mg/dl were included in the study. Patients admitted to the outpatient clinic of obesity, endocrinology, oncology, diabetes, pediatrics and pediatrics surgery were excluded from the study. Of these patients; 44024 of whom, had laboratory data both before and during pandemic period were included in the study. The study was designed to have two groups. The first group includes outpatients who were admitted to our hospital within 12 months before the pandemic. The second group includes the same patients who were admitted to our hospital on an outpatient basis within a 12-month period after the pandemic began. The Metabolic syndrome diagnostic criteria determined by IDF were based on the study (7).

Laboratory Analysis

The FPG, T-Chol, LDL-C and HDL-C tests used in the present study were performed in the Beckman Coulter AU5800 (Beckman Coulter, Inc, CA, USA) clinical chemistry autoanalyzer in the medical biochemistry laboratory.

Statistical Analysis

Statistical analysis was performed using the SPSS software package (SPSS for Windows-Version 20.0; IBM Corporation, Armonk, NY, USA). Results were taken as mean ± standard deviation for variables with normal distribution. McNemar test was used to determine the differences between two related groups (year). Paired t-test was used to compare mean values between two related samples. $p<0.05$ values were considered statistically significant.

RESULTS

The number of patients whose lipid profile and FPG values were measured both in the 12-month period before the pandemic (2019) and in the first 12 months (2020) from the onset of the pandemic on March 11, 2020, their distribution by gender and average age are shown in **Table 1**. The measured FPG and lipid profile values of the patients who applied to our hospital both in the 12-month period before the pandemic (2019) and in the first 12 months (2020) from the onset of the pandemic on March 11, 2020 were compared (**Table 2**). A statistically significant increase was detected in patients' HDL-C, FPG and TRIG levels measured during the pandemic and the pre-pandemic period (12 months before), ($p<0.001$ for all three). In this study, we have also examined whether the COVID-19 pandemic affected the diagnosis criteria for metabolic syndrome (TRIG, HDL-C, FPG) (**Table 3**). The rate of patients with a TRIG >150 mg/dL, one of the diagnostic parameters of metabolic syndrome, was 45.7% during the pandemic period compared to 42.7% in the pre-pandemic period. This rate was increased statistically significantly during the pandemic period ($p<0.001$)(**Figure 1**). The rate of patients with a FPG >100 mg/dL, one of the diagnostic parameters of metabolic syndrome, was 51.7% during the pandemic period compared to 45.8% in the pre-pandemic period. This rate was increased statistically significantly during the pandemic period ($p<0.001$) (**Figure 2**). The rate of patients with a HDL-C<50 mg/dL, one of the diagnostic parameters of metabolic syndrome, was 43.7% during the pandemic period compared to 46.9% in the pre-pandemic period. This rate was statistically decreased during the pandemic ($p<0.001$) (**Figure 3**). The rate of patients with a HDL-C<40 mg/dL, one of the diagnostic parameters of metabolic syndrome, was 32.4% during the pandemic period compared to 36.7% in the pre-pandemic period. This rate was statistically decreased during the pandemic ($p<0.001$) (**Figure 4**).

Table 1. Demographic characteristics of the patients and number of the measured tests

	Number of female	Number of male	Mean age of women	Mean age of men	Overall mean age	P valuea
FPG	26595	17429	53.30 16.19	59.48±15.61	55.35±16.71	<0.001*
TRIG	13136	9912	55.08±15.28	58.51±15.19	56.55±15.33	<0.001*
T-Chol	13215	9987	55.01±15.30	58.48±15.18	56.51±15.34	<0.001*
HDL-C	12790	9738	55.34±15.12	58.71±14.99	56.8±15.15	<0.001*
LDL-C	20315	14270	55.34±16.04	58.52±16.18	56.65±16.17	<0.001*

[a]Independent t test, *Significance for 0.05, Abbreviations: FPG: Fasting Plasma Glucose, TRIG: Triglyseride, T-Chol: Total Cholesterol, HDL-C: High Density Lipoprotein Cholesterol, LDL-C: Low Density Lipoprotein Cholesterol

Table 2. Comparison of lipid profile and FPG values of patients admitted to the hospital both in the 12-month period before and in the first 12 months the pandemic

	Pre-pandemic Period (Mean±SD)	Pandemic period (Mean±SD)	[b]P value
HDL-C (n=22468)	47.86±11.37	48.96±11.87	<0.001*
Female (n=12730)	51.29±11.46	52.51±12.00	<0.001*
Male (n=9738)	43.38±9.57	44.31±9.93	<0.001*
LDL-C (n=34585)	122.4±39.03	122.48±57.70	0.716
Female (n=20315)	126.44±39.50	121.07±56.41	<0.001*
Male (n=14270)	116.52±37.59	124.50±59.41	<0.001*
FPG (n=44024)	115.46±53.46	119.45±54.70	<0.001*
Female (n=26595)	112.75±50.98	116.72±52.95	<0.001*
Male (n=17429)	119.61±56.80	123.61±57.01	<0.001*
TRIG (n=23048)	165.06±127.69	171.38±131.39	<0.001*
Female (n=13136)	159.68±118.41	165.98±138.71	<0.001*
Male (n=9912)	172.22±138.71	178.93±137.00	<0.001*
T-Chol (n=23202)	201.60±51.15	199.63±50.82	<0.001*
Female (n=13215)	209.35±51.84	208.16±49.57	0.012*
Male (n=9987)	191.33±48.35	188.36±50.27	0.001*

[b]Paired t-test, *Significance for 0.05, ***Abbreviations:*** HDL-C: High Density Lipoprotein Cholesterol, LDL-C: Low Density Lipoprotein Cholesterol, FPG: Fasting Plasma Glucose, TRIG: Triglyseride, T-Chol: Total Cholesterol

Table 3. Effect of pandemic period on metabolic syndrome diagnostic criteria

Metabolic syndrome diagnostic criteria (IDF)	Pre-pandemic period (2019)number and percentage of patients	Pandemic period(2020) number and percentage of patients	P value [c]
FPG >100 mg/dL	20197 45.8%	22791 51.7%	0.001*
TRIG >150 mg/dL	9861 42.7%	10536 45.7%	0.001*
HDL-C <50 mg/dL (Female)	5973 46.9%	5558 43.7%	0.001*
HDL-C <40 mg/dL (Male)	3569 36.7%	3157 32.4%	0.001*

[c]Mc Nemar Test, *Significance for 0.05, ***Abbreviations:*** IDF: International Diabetes Federation, FPG: Fasting Plasma Glucose, TRIG: Triglyseride, HDL-C: High Density Lipoprotein Cholesterol.

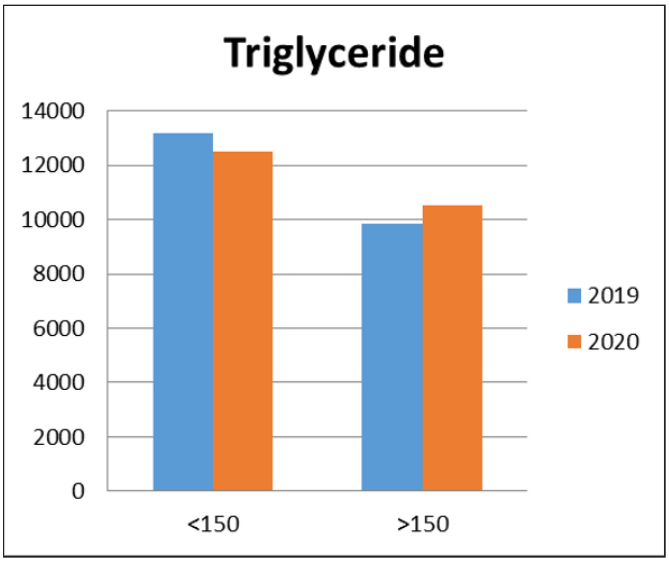

Figure 1. Contribution of pandemic on the development of metabolic syndrome based on triglyceride value

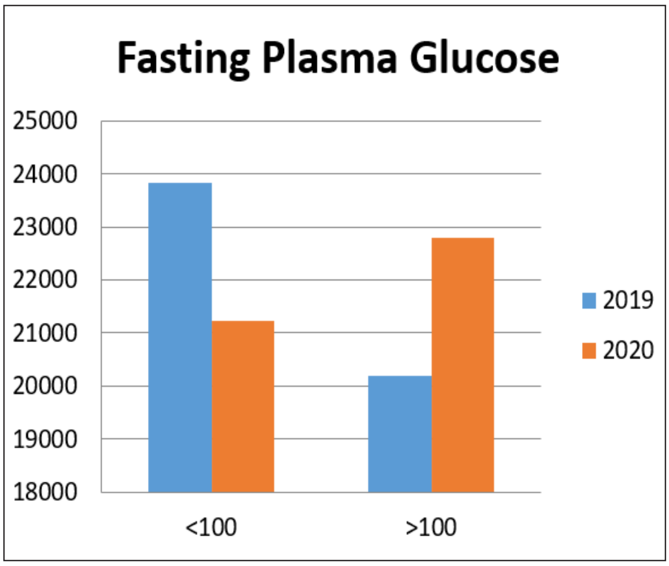

Figure 2. Contribution of pandemic on the development of metabolic syndrome based on FPG value

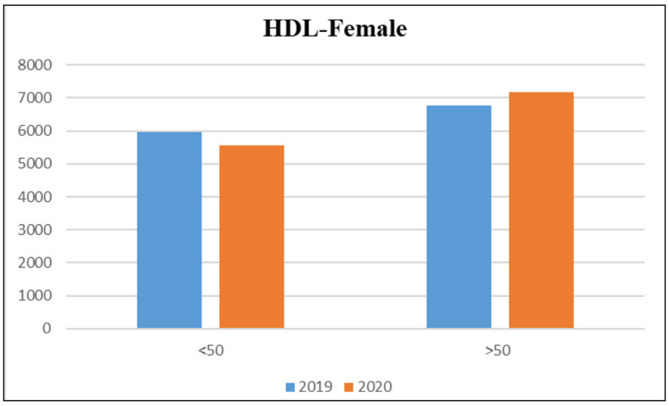

Figure 3. Contribution of pandemic on the development of metabolic syndrome based on HDL-C in female patients

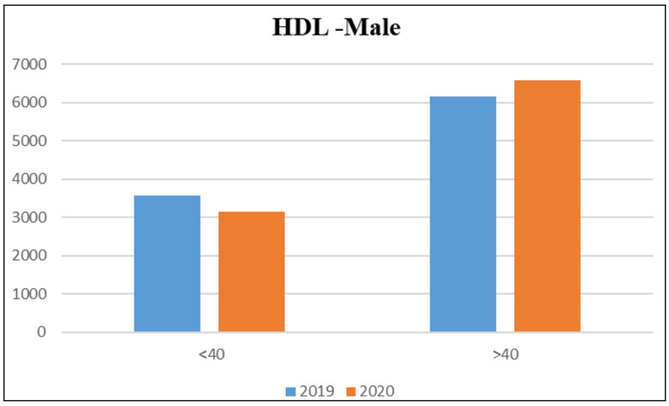

Figure 4. Contribution of pandemic on the development of metabolic syndrome based on HDL-C in men patients

DISCUSSION

During the period of social isolation adopted globally to control the spread of COVID-19, global levels of physical activity have decreased significantly. This social isolation has metabolic effects in patients with metabolic diseases or those at risk for this disease, particularly in patients with obesity and type 2 diabetes mellitus (T2DM). Although isolation measures are important for containing the virus, they may have exacerbated an ancient pandemic ('physical inactivity') (16). WHO has provided clear guidance on the minimum level of physical activity required to maintain good health and fitness. For example, recent statistics indicate that adults between the ages of 18 and 64, the age group most affected by COVID-19 (representing over 70% of all serious cases) need to have at least 150 minutes of moderate-intensity physical activity or 75 minutes of vigorous-intensity physical activity per week (17,18). Time spent while sitting seems to have harmful effects, even in those who meet current physical activity guidelines. However, health problems are less common among physically active individuals than their inactive counterparts (19-21). We anticipate increased FPG and lipid profile (LDL-C, T-Chol and TRIG) and decreased levels of HDL-C due to inactivity during the pandemic. Gennuso et al. (22) found that total sedentary time was associated with an increase in the probability of developing MET-S, and moderate and vigorous physical activity was associated with a decrease in the rate of MET-S development. Van der Berg et al. (23) stated that an additional hour of inactivity increased the likelihood of developing T2DM and MET-S by 22% and 39% respectively. The inability to take a regular walk from home as a result of a strict quarantine increases the risk of many serious diseases such as diabetes, cancer, osteoporosis and cardiovascular disease (24). Short-term bed rest studies, used as a model of sedentary behaviour, showed deteriorations in glucose metabolism and insulin sensitivity (25). In a study conducted by Olsen et al. (26), they reported that a decrease in daily steps from 6200 to 1400 increased insulin resistance among healthy people. In addition to physical inactivity, the COVID-19 pandemic has also caused excessive energy intake.

Physical inactivity and excessive energy intake are often combined and contribute to the epidemic of obesity and type 2 diabetes (27). In a study conducted by Mikus et al. (28) in healthy young adults, they proved that reduced physical activity for three days caused an increase in insulin and C-peptide levels in the OGTT response, and also increased glycemic fluctuations. It is well known that such a sedentary lifestyle, such as desk job, watching TV, and sitting, is associated with an increase in mortality and morbidity from all causes (MET-S, cardiovascular disease, etc.) (27, 29, 30). In their study, Ekelund et al. (31) demonstrated that any intensity of physical activity and less sedentary time are associated with a reduced risk of premature death in middle-aged and older adults. Similar to the above studies, fasting blood glucose levels were also found to be elevated in our study due to the physical inactivity during the COVID-19 pandemic. This showed us that the pandemic made a statistically significant contribution to the diagnosis of metabolic syndrome by increasing FPG levels (**Table 2**). Prolonged physical inactivity also affects lipid metabolism. Indeed, inactivity leads to insulin resistance and dyslipidemia, i.e to an increase in TRIG rates associated with a decrease in HDL-C concentration. Mazzucco et al. (32) showed that inactivity following bed rest reduced the ratio of HDL-C to non-HDL-C. Being physically active is associated with a better anthropometric and metabolic health profile, whereas a sedentary life regardless of activity (Light Movers) is associated with lower HDL-C (a traditional cardiovascular risk factor) (33). Dixon et al. (34) conducted a study in which individuals had their steps reduced by less than 4,000 steps/day during a week. In this study, they compared lean and overweight people. As a result, they showed that insulin, FPG and TRIG concentrations increased in both groups, and an additional increase in CRP and ALT levels in the overweight group. There were no changes in T-Chol, LDL-C and HDL-C during the study, and no differences occurred between the groups. Bowden Davies et al. (34) found an increase in T-Chol, TRIG and LDL-C values in their study conducted in 45 healthy individuals who had their steps reduced below 1500 per day for 2 weeks. Winn et al. (36) found that there was no significant change in T-Chol, TRIG, HDL-C, LDL-C and oxidized LDL-C after 10 days of step restriction and 800 kcal diet in 10 healthy individuals. Similar to the above studies, we found a statistically significant increase in TG levels during the pandemic (sedentary period) compared to the pre-pandemic (active period) in our study ($p<0.001$) (34, 35). Contrary to the above studies HDL-C levels were higher in the pandemic period (sedentary period) than in the pre-pandemic period, (48.96±11.87 mg/dL and 47.86±11.37 mg/dL, respectively) ($p<0.001$)(32,34). While there was a significant decrease in T-Chol, we found no statistically significant differences in LDL-C levels prior to and during the pandemic (**Table 2**). We observed a statistically significant increase in FPG and TG levels, which are the MET-S criteria of the COVID-19 pandemic (both $p<0.001$). When we consider at the contribution of the pandemic to the diagnosis of MET-S through FPG, the rate of patients with FPG>100 was 51.7% during the pandemic compared to 45.8% in the pre-pandemic period. Still, when we consider at the contribution of the pandemic to the diagnosis of MET-S through TG, the rate of patients with TG>150 was increased to 45.7% during the pandemic compared to 42.7% in the pre-pandemic period. With this study, we demonstrated that the pandemic contributed to the diagnosis of MET-S by causing an increase in FPG and TRIG values. Contrary to these parameters, we found a statistically significant decrease in the ratio of female patients with HDL-C<50 and male patients with HDL-C<40 during the pandemic period (sedentary period) (**Table 3**). Once again, our study has shown that HDL-C values do not contribute to the diagnosis of MET-S during the pandemic.

Limitations: This study has some limitations despite its large sample advantage. As the present study was designed retrospectively, other metabolic syndrome diagnostic criteria such as waist circumference and systolic and diastolic blood pressure values of the patients could not be measured.

CONCLUSION

As a result, we determined that the pandemic contributed to the diagnosis of MET-S by increasing the FPG and TG levels of the patients, but could not contribute to the diagnosis of MET-S by also increasing HDL-C levels. Alternative sports activities in the long quarantine processes caused by the pandemic are of protective importance to prevent the development of obesity and metabolic syndrome. However, there is a need for further research, including waist circumference and blood pressure data, which are included in the diagnostic criteria for MET-S.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Hitit Univesity Faculty of Medicine Clinical Studies Ethics Committee (Date: 28/04/2021, Decision No: 2021-53)

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The author has no conflicts of interest to declare.

Financial Disclosure: The author declared that this study has received no financial support.

Author Contributions: The author declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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