In COVID-19 Era, STEMI Decreasing May Predicted with Google-Trend Data by Time-Series Model

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ABSTRACT

Introduction: The explanation for the decrease of ST elevation myocardial infarction (STEMI) due to Coronavirus Disease (COVID-19) is poorly described. Our goal is to identify whether there is a temporal association between COVID pandemics and STEMI admissions and investigate the decreased number of STEMI could be associated to the search volume of Covid, Death and chest pain, measured by Google-Trend (GT).

Patients and Methods: We collected our hospital admission of STEMI data and search of covid, death and chest pain in GT search data between March 01, 2020 and May 21, 2020, also we compared to STEMI count same time-limit in the previous year. We used vector-autoregressive model (VAR) to combine the number of daily new cases STEMI and search index to relative association daily covid, and death term search in using GT.

Results: During this time-frame, we collected a total of 302 STEMI admitted to our hospital when compared previous year we found a 34% reduction. Spearman's correlation-coefficient between covid, stemi, and death trend with STEMI, results [(-0.560) p< 0.001, (-0.631) p< 0.001, respectively]; model-1 and model-2 VAR bivariate analysis results in coefficient (-0.532, -2.694), also we found Granger-causality for covid and death to STEMI. Impulse response functions (IRF) depicted the STEMI decreased a relatively large amount by death and covid trend.

Conclusion: In the COVID-19 period, our study showed that the uses of Google-Trend data have predict decreasing STEMI cases. Also, plausible Granger causality relationships between covid, death GT data and daily counts of STEMI. GT about Covid and Death might provide to developing appropriate behaviour of patients with the STEMI for healthcare supporter.

Key Words: STEMI; Google-Trend; COVID-19.

COVID-19 Döneminde, STEMI Azalması Zaman Serisi Modeline Göre Google-Trend Verileri ile Tahmin Edilebilir

ÖZ

Giriş: Koronavirüs hastalığı (COVID-19)'na bağlı ST yükselmeli miyokart enfarktüsü (STEMI) düşüşü gösterilmiş, ancak nedenleri yeterince araştırılmamıştır. Amacımız, COVID pandemisi ile STEMI başvurusu arasında bir ilişki olup olmadığını belirlemek ve Google-Trend (GT) ile ölçülen Covid, Ölüm terimi arama hacmiyle ilişkilendirilebilecek STEMI sayısındaki azalmayı araştırmaktır.

Hastalar ve Yöntem: Hastanemize başvuran STEMI verileri ile 01 Mart 2020-21 Mayıs 2020 tarihleri arasında GT arama verilerinde covid ve ölüm araması toplandı, ayrıca STEMI sayımı bir önceki yıl aynı zaman limitiyle karşılaştırıldı. Günlük yeni STEMI olgu sayısı ve GT arama indeksinin kullanımında günlük covid ve ölüm terimiyle göreceli ilişki ile birleştirmek için vektör otoregresif model (VAR) kullanıldı.

Bulgular: Bu zaman çerçevesinde hastanemize kabul edilen toplam 302 STEMI toplanmış, bir önceki yıla göre %34 azalma bulunmuştur. Spearman'ın STEMI ile "covid, stemi ve ölüm" trendi arasındaki korelasyon katsayısı, sonuçlar [(-0.560) p< 0.001, (-0.631) p< 0.001, sırasıyla]; model-1 ve model-2 VAR iki değişkenli analiz sonuç katsayısı (sırasıyla -0.532, -2.694); ayrıca COVID ve STEMI'ye ölüm için Granger nedenselliği bulunmuştur. Etki tepki fonksiyonu (IRF), STEMI'nin ölüm ve covid eğilimiyle nispeten büyük bir miktarda azaldığını göstermiştir.

Sonuç: COVID-19 döneminde, çalışmamız GT verilerinin kullanımının STEMI olgularının azalmasını öngörebildiğini göstermiştir. Ayrıca, covid ve ölüm GT verileri ve günlük STEMI sayıları arasındaki makul Granger nedensellik ilişkileri mevcuttur. Covid ve Ölüm ile ilgili GT, STEMI hastalarının azalmasını önlemek için sağlık bakımı sunanlar için uygun davranışların geliştirilmesine yön verebilir.

Anahtar Kelimeler: STEMI; Google-Trend; COVID-19.

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INTRODUCTION

On March 11, 2020, the World Health Organization (WHO) declared Coronavirus Disease-2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as an epidemic due to the ever-increasing number of cases globally[1]. Circulating cytokines released during infection increase the risk of plaque rupture and thrombus formation, resulting in either an ST-elevation MI (STEMI) or non-ST-elevation MI (NSTEMI)[2]. On the contrary, recent data demonstrated that the admission rate for ACS during the pandemic is much lower than the expected[3].

Google search data is a source of information that contains useful information to predict outbreaks[4]. Google-Trend (GT) was developed to help researchers analyze temporary and geographic trends in online search terms or topics through Google search engines. Previously, Google search data was applied to monitor new diagnoses of sexually transmitted diseases[5]. Infodemiology measurements of GT may allow monitoring of symptoms or disease in the general population[6]. STEMI is an important health problem, if left untreated, it can cause life-threatening complications such as cardiogenic shock, heart failure, arrhythmias, and even death. Mortality may increase up to 40% among untreated STEMI. In this regard, starting reperfusion therapy; either thrombolytic application or percutaneous coronary intervention is very important for STEMI patients[7,8].

According to our current observations, STEMI admission decreased during the outbreak of COVID-19 in our region. We used GT to investigate online searching trends regarding "death", "covid" to monitor their relationship with STEMI admissions during coronavirus pandemic in Turkey. The purpose of this infodemiological study is to apply digital epidemiology to determine the effect of a COVID-19 pandemic on STEMI hospital admission rates in the relevant time frame. In this context, we aimed to determine whether there is a statistically significant temporal relationship between COVID pandemics and STEMI applications and to investigate whether the reduced number of STEMI can be predicted with the search volume of Covid and Death measured by GT.

PATIENTS and METHODS

Data Sources

Daily new STEMI cases were conducted retrospectively for large volume tertiary referral from March 01, 2020 to May 21, 2020 (Kosuyolu High Specialization Training and Research Hospital, Istanbul). Our hospital is a heart hospital, and only those who have cardiovascular diseases complain to the admission to our emergency department. Therefore we assume that given data is safe in terms of diagnosis of STEMI.

Search Query Databases

Google-Trend is a public, open-access search tool (trends.google.com/trends), and getting started is some of Google's web portals or freely available software[8]. The "search volume" data were obtained from the website of "Google Trend" which provides data on the relative search volumes of inquiries and topics over time and across geographical areas. Values are not real call counts, total geography (Turkey) and in the period (March 01, 2020-May 21, 2020) are based on a percentage of total calls. The numbers obtained are then scaled from 0 to 100. This normalization has the effect of controlling the total volume of internet use over time. The authors used this normalized search as the search value. The online data in this study are anonymous and available publicly.

March 01, 2020, was defined as the beginning of the period when Turkish media attracted attention to the coronavirus. Countries reported the first COVID-19 incident on March 11 by the Turkish authorities. Therefore, we evaluated the GT for searches on relevant keywords, beginning from the March 01, 2020 (ie. 10 days before the incidental cases reported in Turkey).

Although it is not known exactly when COVID-19 started in the world and our country, the first confirmed case was declared on the 10th of March in Turkey. We assume that the concern about COVID-19 arose in Turkey before the first case confirmed, therefore we have determined the 1st of March as the appropriate date to start our assessment.

Keyword Selection

Google Trends searched "Covid", "Death" between March 01, 2020, and May 21, 2020. COVID, which is the abbreviated form of Coronavirus Disease-2019 was used as a search term.

Since multiple iterations of a word may be used to search for the same symptom (chest pain and angina), GT groups a cluster of search terms as a topic or disease[6]. After receiving the search term "Covid", we searched for "Covid" related issues using the "gtrendsR" package[9]. The most common term except related covid was found to be the term "death".

As a result, we collected our STEMI hospital admission data between March 01, 2020, and May 21, 2020, and "Covid", "Death" in the GT search data between March 01 and May 21, 2020. We compared the number of STEMI, in the same timeframe as the previous year.

Analysis Testing Stationary

We tested the normality of all variables (STEMI count and covid trend, death trend in GT). The Kolmogorov-Smirnov test was used to assess the normality of the distribution, we used log-transformation for all parameters to achieve normality. We tested the stationary of all variables (STEMI-count and Covid-trend, death-trend in GT). The augmented Dickey-Fuller

(ADF) t-statistic value was used to check the stationarity. If the variables were not stationary, then the logarithm of the series was taken. If still the stationary was not achieved, we differenced the time series and applied ADF test once again on the differenced and logged value. We use log-transformed data for STEMI, death, however for covid term also first difference and log-transformed used to make stationary. Also, we performed Johansen test to assess cointegration.

Selecting Lag Length and Building a Bivariate VAR Model

Using the VAR model, the future potential behaviour of a selected variable can be predicted by taking other variables into account. Analyzes are made by considering the effect of all variables included in the model. If the series is stationary and no cointegrated, we predict them by adjusting a VAR to the data directly (classified as a "VAR in levels"). The Vector Autoregressive (VAR) model is a model for this type of data, in which each variable is predicted at previous time points by a linear function of all variables. A central hypothesis of this model is that its' parameters over time are constant (or stationary). VAR models represent the conditional mean of a stochastic process given past observations. Hence, they are natural tools for prediction for medicine also forecasting for econometric analysis. Predicting a set of similar variables where no clear interpretation is required; examining whether one predictor is useful for predicting another variable (based on Granger causality tests). Also, VAR model useful for impulse response function, in which one variable is evaluated in reaction to a sudden yet temporary alteration in another variable. The two models used were used to estimate the number of STEMI cases admitted to the emergency department. The models' predictivity was also evaluated by the impact of model fitting by R2. The equations were be solved using ordinary squares estimation. The general structure of the VAR model is a model that can be summarized as follows[10].

$$Y_t = \delta + \theta Y_{t-1} + E_t$$

Y_t: Variables vector, δ: Constant vector, θ: Coefficients matrix, E_t: Error matrix.

We combined the columns of the two existing variables (model-1; STEMI-covid, model-2; STEMI-death) to create a two-variable model for time-series model. Since it can be difficult to interpret and explain with more than two variables in the VAR model, two different two-variable time series models are used with a simpler expression. Thereafter, we used information criteria to decide upon the number of lags to include The selection lag length was important for the inferring in VARs, the selection of the lag length was performed with the following two estimators; Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC). If different values were presented by these two tests, we chose to use BIC. As a result, the information criteria suggest using 1 delay, which indicates that lag is set to 1 in terms of VAR estimation for model-1, model-2.

Testing the Residual Autocorrelation and Evaluating the Stability of the VAR Model

We had performed some diagnostic tests on the residual of the model to assess whether the model matches the observed data. For the serial correlation test, we applied a Portmanteau test applied as follows; a p value of greater than 5% to interpret these statistics usually indicates that there is no serial correlation. We did a multivariate ARCH Lagrange-Multiplier test, as well as doing a heteroscedasticity test on the residuals. Once again, the p value above 5% indicates that there is no heterodactility.

Granger Causality, Impulse Response Function and Variance Decomposition

We tested Granger causality to determine if the one-time series was useful in predicting another. Granger causality is based on the notion of linear predictability, the null hypothesis was evaluated with the Granger causality test. In context, the definition of "Granger cause" under these circumstances based on the predictability of series (Xt), where if another series (Yt) contains information in past terms that can be used to aid in predicting Xt, then Yt is said to "cause" Xt, according to Granger.

Also, we aimed to generate impulse response functions of "Covid" and "Death" GT search terms of describing the response of STEMI. For statistical analysis, R 4.02 software (Vienna, Austria) "vars", "fpp2", "MASS" "kfilter" "gtrendR" package were used.

RESULTS

As shown in Figure 1, the daily count of STEMI was demonstrated to be sharply downwards in the beginning, however by the time it tends to have a slightly upward trend compared the previous year (Figure 1a-b). On the other hand,

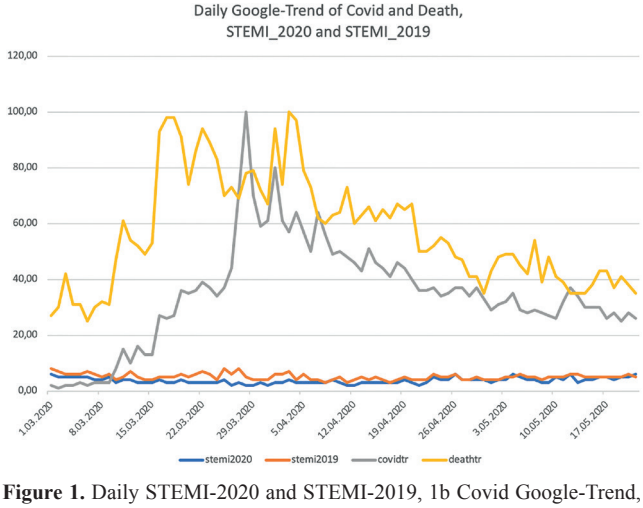

Figure 1. Daily STEMI-2020 and STEMI-2019, 1b Covid Google-Trend, Death Google-Trend, and Chest-pain-Trend.

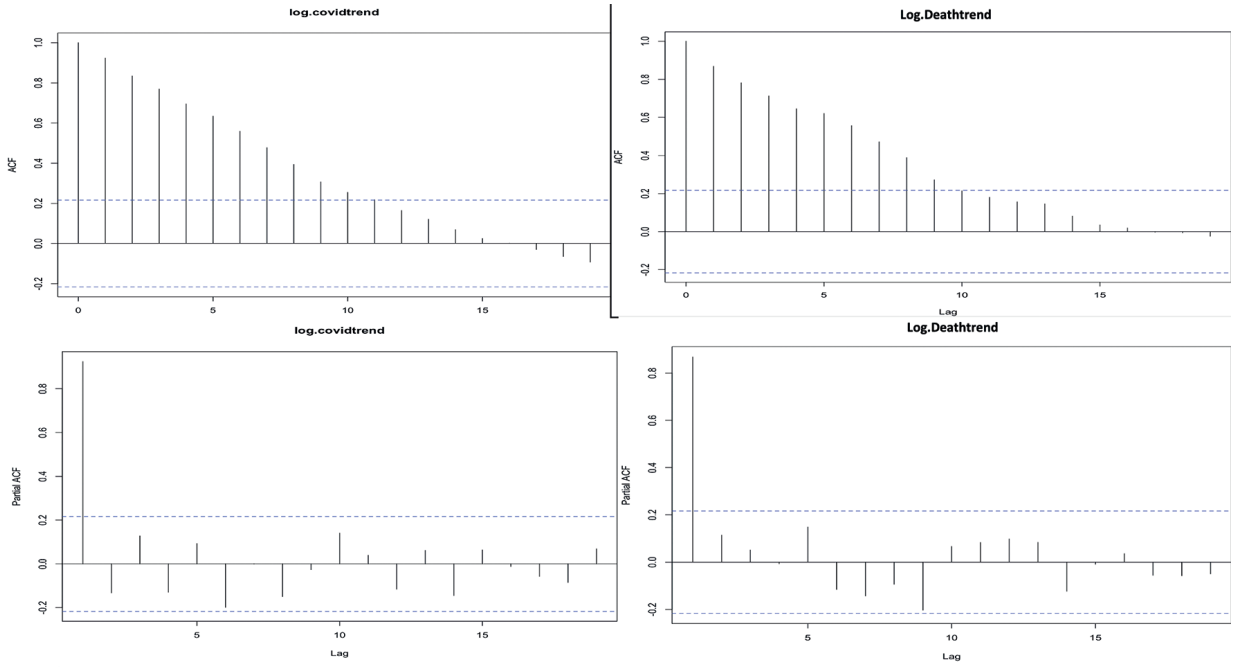

Figure 2. Autocorelation and partial autocorelation of Covid Google-Trend, Death Google-Trend, and Chest-pain-Trend.

"covid" and "death" searches have an upward trend in the beginning and by the time they tend to have a downward trend (Figure 2). The number of STEMI cases in the same timeframe as compared with the previous year and by 34% reduction was shown. The Spearman rank correlation coefficient between the Covid trend and STEMI, the death trend and STEMI showed negative correlations [(-0.560) p< 0.001, (-0.631) p< 0.001].

Result of Testing Stationary and Cointegration

The augmented Dickey-Fuller (ADF) t-statistic value is described in Table 1. Where we note that we can reject the null hypothesis of the unit root when using the augmented Dickey-Fuller test. Johansen Eigen test procedure, we are able to reject covid bivariate the null of there being no cointegrating vectors as the calculated test statistic is 39.18 is greater than critical values of 13.75, 15.67 and 20.20 and the 10%, 5% and 1% levels. This would imply that no cointegration, other data presented in Table 1. Also, autocorrelation and partial autocorrelation results were presented in Figure 2.

Bivariate VAR Models and Granger Causality Result

Covid and STEMI were taken as model-1. As a result of the AIC and BIC proposal, one lag was proposed to the VAR

Table 1. Augmented Dickey-Fuller statisonary test result and Johansen cointegration test result

Augmented Dickey-Fuller Test					
Regression variable	**ADF test statistic**	**Critical values**			**Result**
		1%	**5%**	**10%**	
Stemi2020 log.1	-3.480	-4.04	-3.45	-3.15	stationary
Covid-trend log.1 and df.1	-5.04	-4.04	-3.45	-3.15	stationary
Death-Trend log.1	-6.093	-4.04	-3.45	-3.15	stationary
Johansen cointegration test					
Covid.log.1and df.1	Test statistics	10pct	5pct	1pct	
r ≤ 1	9.91	7.52	9.24	12.97	
r = 0	39.18	13.75	15.67	20.20	
Death.log.1					
r ≤ 1	24.52	7.52	9.24	12.97	
r = 0	46.66	13.75	15.67	20.20	

ADF: Augmented Dickey-Fuller, df1: First-order differential variables. log.1: Log-transformed variables.

Table 2. VAR model result, Portmanteau test, ARCH multivariate test

VAR Model-1 Covid trend STEMI response				VAR Model-2 Death trend STEMI response			
Regression variable	**Coefficient**	**Standart error**	**Adj. R2**	**Regression variable**	**Coefficient**	**Standart error**	**Adj. R2**
Stemi.l1	0.41	0.10	0.31	Stemi.l1	0.27	0.11	0.36
Covid.l1	-0.53	0.25		Death.l1	-2.69	0.74	
const	2.88	0.67		const	7.31	1.56	
Portmanteau test Chi-squared		**p value**		**Portmanteau test** Chi-squared		**p value**	
45.5		0.41		43.6		0.48	
ARCH multivariate test Chi-squared		**p value**		**ARCH multivariate test** Chi-squared		**p value**	
138.25		0.06		122.24		0.16	

l.1: lag.1.

Table 3. Granger causality test

	F test	**p value**
Model-1	3.93	***0.049***
Model-2	13.18	***< 0.001***

Model-1: Covid Granger cause to STEMI, Model-2: Death Granger cause to STEMI, Model-3: Chest-pain Granger cause to STEMI.

model. In the subsequent VAR model; the coefficient was -0.532. Portmanteau test's X^2 value was 45.5 and, the p value was 0.41. ARCH multivariate test's X^2 value was 138.2 and p value was 0.06. Granger causality test was performed, F-test value was 3.93 and the p value was 0.049 for covid trend. This indicates the increased GT of covid is predicted with the decrease of STEMI (Table 2,3).

Death and STEMI were taken as model-2. As a result of the AIC and BIC proposal, one lag was proposed to the VAR model. In the subsequent VAR model; the coefficient was -2.69. Portmanteau test's X^2 value was 43.6 and, the p-value was 0.48. ARCH multivariate test's X^2 value was 122.24 and p value was 0.16. Granger causality test was performed, F-test value was 13.18 and p value was < 0.001 for death trend. This indicates the increased GT of death is predicted with the decrease of STEMI (Table 2,3).

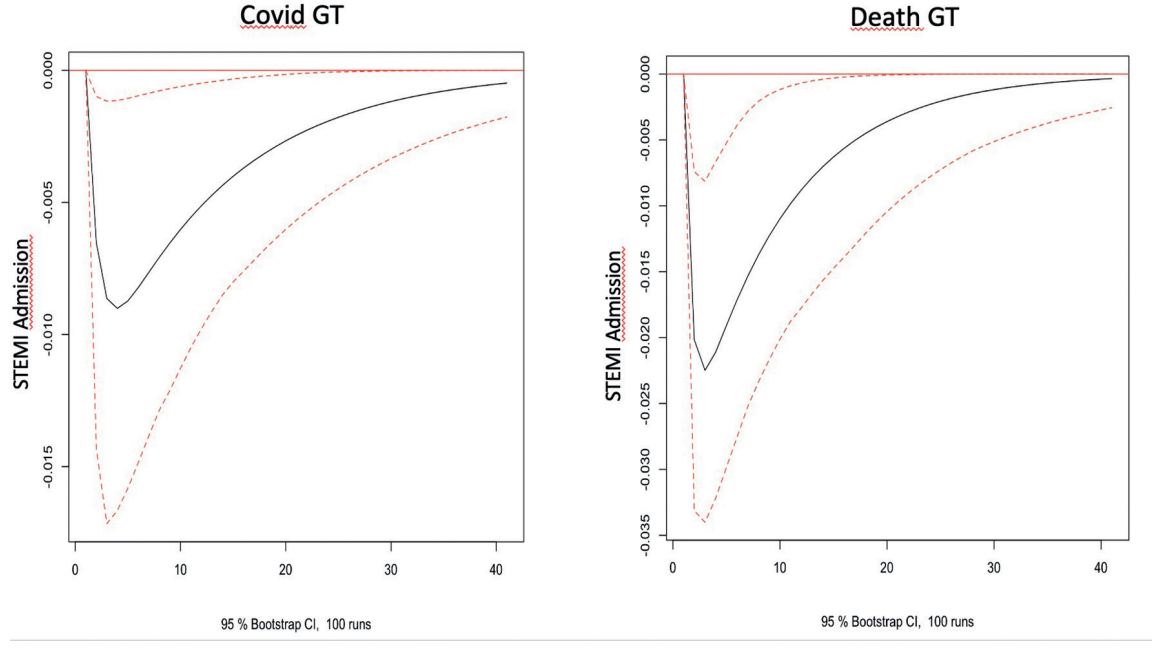

Figure 3. Impulse response function of Covid Google-Trend, Death Google-Trend (The shock of Covid and Death GT to STEMI causes significant decreases in STEMI for 30 day-period after which the effect dissipates)..

The coefficients of Covid and Death GT terms in VAR models were negative, which illustrated an overall downward trend of the number of newly diagnosed STEMI during pandemics. The R2 value of Model-2 is higher than model-1, which means model-2 is better to explain the decrease in STEMI admissions.

Impulse Response Function and Variance Decompositions Results

A one standard deviation shock of Covid and Death GT to STEMI causes significant decreases in STEMI for a 30 day-period (determined by the length of period for which the SE bands are below 0 in case of decrease) after which the effect dissipates. These are important pieces of information about the relationships between covid and Death GT on STEMI. The results in Figure 3a show that the respective impulse response function tests could capture the STEMI downward trend (Figure 3).

The study protocol has been reviewed and approved by the local Ethics Committee (12.01.2021-2021/1/426). This study was conducted in accordance with the Helsinki Declaration.

DISCUSSION

In this search, we show that the search terms "Covid" and "Death" in GT are predicted the decreasing number of daily new cases of STEMI, which demonstrates that in the COVID-era may potential feasibility of using search motors data for identification longitudinally decreasing of STEMI and public fear of contamination and death due to covid.

On the Internet, infodemiology measurements that reflect the habits of the general population follow the issues that take into account the public health and ongoing events and also provide predict them[11]. The first upward trend of "death" and "covid" searches showed that news from the media and social media affected people's alertness to the covid epidemic. According to our findings, the GT was predicted the number of STEMIs diagnosed daily. We demonstrated that; Covid GT has reached its' peak value on the 17th of March while the early peak of death due to COVID-19 infections in Turkey was seen on the 19th of April[12]. The decrease in the number of STEMI cases may be related to the misinformation that existed in the early period of the covid pandemic. In a study by Baltazar et al., it was concluded that websites providing information about COVID-19 are questionable in terms of competence and credibility[13]. Oi-Yee Li, et al., showed that the most-watched English videos on COVID-19 contain 27.5% false information[14].

As in most countries, health authorities in Turkey have decided to cancel and postpone elective interventions and operations for emergency cases to be continued yet even this decision might have led to a decline in STEMI patients apply to the hospital for emergency events. Possible causes of reduced STEMI cases during the covid pandemic were first discussed on social media, and according to surveys, there were 47.7% of respondents reported a 50.7% reduction[15]. Also, this issue was discussed by Harlan Krumhuoltz in the New York Times. In addition, analyzes were made in TCTMD and as a result, two main theories were introduced[16,17]. Decreased STEMI admissions to a hospital may be associated with fear of transmission in hospitals. The lack of verified information on media and social media resulting in the spread of misinformation among people[13,14]. Precautions for limitation in-hospital spread warnings of the public for staying away from hospital interns of preventing in-hospital spread resulted in a perception that hospitals are not safe[16,17]. From a pessimistic perspective, they speculate that people to stay at home and suffer rather than risk coming to the hospital and exposed by a COVID-19. From an optimistic view, they speculate that during the covid pandemic the lifestyle of the community has changed. Even may have removed some of the triggers for acute coronary events such as excessive drinking or eating or tend to stay indoors and live a less physically active life[16,17]. Also, several studies demonstrated that acute coronary syndromes are likely to be more frequent during respiratory tract infections which may be explained by the increased expression of genes responsible for platelet activation and subsequently increased risk of myocardial infarction[18,19].

VAR is a model for multivariate time series. Besides VAR model describing and predicting features for medical studies, causal inferences for econometric[20]. Time series analysis could bear long-term prediction opportunity to provide the health authorities and health organizations to respond in advance. This advantage is of particular significance to the surveillance of infectious diseases[4]. More specifically, VAR modelling with Granger causality test both to assess correlation and the plausibility of temporal association with univariate and multivariate relationships. VAR models represent the conditional mean of a stochastic process given past observations. Hence, they are natural tools for prediction also forecasting[4,10,20]. Our study depicted Granger causality for covid and death GT for STEMI decreasing.

In a study by Kadah et al., it is demonstrated that the numbers of cardiac procedures decreased by 48% during the corona pandemic, comparing to the former periods[21]. According to data from 73 centres in Spain, admissions with STEMI rates decreased by 40% compared to the period before the coronavirus pandemic[22]. In another study from US, the number of STEMI patients decreased by 38% compared to former periods[23]. A Survey by the European Society of Cardiology showed that 81% of respondents from Europe think that the number of STEMIs has decreased up to 41-60%[24]. In the Lombardy region, "Macro-

Hubs" was established for COVID-19 period and STEMI patients were planned to receive standard treatment without delays[25]. Nevertheless, De Rossa et al. demonstrated that STEMI rates decreased by 26.5% compared to the previous year and the STEMI mortality increased, also the risk ratio (RR) was 3.3, 95% CI 1.7-6.6 compared to 2019; p< 0.001[3]. Recent study showed that incidence of out-of-hospital cardiac arrests significantly increased compared to the previous year[26]. Our study impulse response function result shows an important association between covid and death alertness with STEMI decreasing.

The Twitter study by Kumar et al., analysis between March 17-30, 2020, the most perceived negative opinion in social media was "fear" when examining the perception on social media of COVID-19-related content[27]. Also similar tendency in our study we found, the most searched word on internet related to covid we found "death". The STEMI patients may have avoided admission to the hospital because of fear of the virus. Besides Stella et al., found STEMI decreased 21% when compared previous period, also they found chest pain admission decreased up to 54% when compared previous period[28]. Another study result supports this discrepancy, they found significant increases mortality from cardiovascular disease and other diseases during COVID-19[29]. Also, another study showed contamination obsession associated with prehospital delay[30].

To the best of our knowledge, this is the first study to associate covid and death GT to daily STEMI counts found in the time-series model. Although population health research, cohort studies, records are well-known epidemiological methods for data collection. Nevertheless, they may be inadequate to make early decisions and take measures regarding public health policies. As a result, it is very important not to postpone the necessary treatments due to fear of coronavirus pandemics, otherwise, related emergencies can lead to higher mortality rates than the virus[9,13,14]. Our study is to reduce the STEMI of the increasing search volume determined by GT. This indirectly reflects COVID-19 concern (through media search and news intensity) and perhaps is related to this inference. Healthcare providers can use GT as a viable target for prevention. We used an important tool to evaluate sequential observations using delayed variables to evaluate relationships instantly and temporarily, a time-series model to demonstrate the association between GT data and daily STEMI case numbers.

LIMITATIONS

Although STEMI data were collected in a high-volume tertiary hospital (more than 30.000 angiography procedures/per year), our study is a single large heart center study. We started enrolling STEMI patients from March 01 which was ten days before the declaration of the pandemic by WHO. We only use a single comprehensive search engine to collect the data (Google Trend). Nonetheless, GT offers a window into public discourse about fear of covid and death. We use log-transformed data for STEMI, and death however for covid term also the first difference and log-transformation was used.

CONCLUSION

In the COVID-19 period, our study showed that the uses of GT data have predicted decreasing STEMI cases. Besides, study results show plausible Granger causality relationships between covid, death GT data and daily counts of STEMI. In the COVID-19 era, our study indicated that the potential usage of GT data to evaluate the decreasing number of STEMI cases by time-series model. According to the assessment of GT about Covid and Death might provide to develop appropriate behaviour of patients with the acute coronary syndrome for healthcare supporter. Further investigations are needed to elucidate the impacts of COVID-19 pandemics on decreasing the trend of STEMI.

Ethics Committee Approval: This study was approved by the Kartal Kosuyolu High Specialization Training and Research Hospital Ethics Committee (12.01.2021-2021/1/426).

Informed Consent: Informed consent was obtained.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept/Design - AK, FO, OA, BK, BK; Analysis/Interpretation - AK, FO; Data Collection - AK, FO, HT, BK, CK, SE; Writing - AK, FO, İT, BK; Critical Revision - AK, SE, NO, CK, İT; Final Approval - All of authors; Statistical Analysis - AK, FO; Overall Responsibility - All of authors.

Conflict of Interest: The authors have no conflicts of interest to declare.

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