ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

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# Clinical Characteristics and Risk Factors of COVID-19 Pneumonia Patients Hospitalized in a Tertiary Intensive Care Unit: A Retrospective Descriptive Study

## Üçüncü Basamak Yoğun Bakım Ünitesinde Yatan COVID-19 Pnömoni Hastalarının Klinik Özellikleri ve Risk Faktörleri: Retrospektif Tanımlayıcı Çalışma

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**ABSTRACT Objective:** A new viral disease was identified in December 2019, and named COVID-19 by WHO in February 2020. In this article, demographic data, risk factors of the disease, intensive care scores, and the relationship between all these and mortality of patients with COVID-19 severe pneumonia followed in our intensive care unit (ICU) were examined. **Material and Methods:** The data of 865 COVID–19 severe pneumonia patients hospitalized in our ICU between 01-03-2020 and 31-03-2021 were analyzed. Demographic data, comorbidities, SOFA and APACHEII scores of the patients, and correlation of these parameters with mortality were evaluated. **Results:** The mean age of the patients was 67.28±14.9. The mean age of the patients in the non-survivor and surviving groups was found to be statistically different (72.41±12.7 vs. 62.08±15.1 respectively). For APACHEII score on first day, the cut-off value was 10.5, which was statistically significant. The effect of SOFA scoring on mortality was analyzed separately for the 1st, 7th, 14th and 28th days. It was found that chronic kidney failure (CKF), heart failure (HF), coronary artery disease (CAD), and neurologic pathology had significant effects on mortality. Mortality was 1.782 times higher for those without CKF, 1.714 times for those without HF, 1.605 times for those without CAD, and 1.331 times for those without Neurological Pathology. **Conclusion:** Risk factors in patients with COVID-19 severe pneumonia were revealed in detail. While treating the disease, it should be considered that age, presence of additional disease and intensive care scores are important in the management of the disease.

**Keywords:** COVID-19 pneumonia; risk factors; SOFA score; APACHE II score

**ÖZET Amaç:** İlk olarak Aralık 2019'da Wuhan'da yeni birviral enfeksiyon tanımlandı ve dünyada hızlı yayılım gösteren bu hastalık DSÖ tarafından Şubat 2020'de COVID-19 olarak adlandırıldı. Bu makalede COVID-19 ağır pnömonili, yoğun bakımımızda izlenen hastaların demografik verileri, risk faktörleri, yoğun bakım skorlamaları ile mortalite ilişkisi incelenmiştir. **Gereç ve Yöntemler:** 01 Mart 2020 - 31 Mart 2021 tarihleri arasında anesteziyoloji yoğun bakımlarında yatan 865 COVID-19 ağır pnömonisi tanılı hastanın verileri incelendi. Hastaların demografik verileri, ek hastalıkları, SOFA ve APACHE II skorları ile bu parametrelerin mortalite ile korelasyonu değerlendirildi. **Bulgular:** Hastaların yaş ortalaması 67.28±14.9 idi. Ölen ve hayatta kalan gruplardaki hastaların yaş ortalamaları istatistiksel olarak farklı bulundu (sırasıyla 72.41±12.7, 62.08±15.1). APACHE II 1.gün skorları için %70,3 duyarlık ve % 66 özgüllük ile cut-off değeri 10,5 olup anlamlı bulundu.SOFA skorlamasının mortalite üzerine etkisi 1,7,14 ve 28. günler için ayrı ayrı incelendi ve tüm zamanlar için bu skorlamanın mortalite üzerinde etkisi olduğu görüldü. Hastaların ek hastalıkları incelendiğinde kronik böbrek yetmezliği (KBY), kalp yetmezliği (KY), koroner arter hastalığı (KAH) ve nörolojik patolojinin mortalite üzerinde anlamlı etkileri bulunmuştur. Mortalite için KBY varlığı 1,782 kat, KY varlığı 1,714 kat, KAH varlığı 1,605 kat ve nörolojik patoloji varlığı ise olmayanlara göre 1,331 kat daha fazla idi. **Sonuç:** Sonuç olarak bu çalışma ile COVID-19 ağır pnömoli hastalarda risk faktörleri ayrıntılı olarak ortaya konulmuştur. Hastalığı tedavi ederken yaş, ek hastalık varlığı ve yoğun bakım skorlamalarının hastalığın yönetiminde önemli olduğunun dikkate alınması gerekmektedir.

**Anahtar Kelimeler:** COVID-19 pnömonisi; risk faktörler; SOFA skoru; APACHE II skoru

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A new virus that causes pneumonia was first identified in December 2019 in Wuhan, named as severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) by World Health Organization in February 2020. While patients may have clinically flu-like symptoms at the onset of the disease, this clinical spectrum can suddenly turn into severe respiratory failure.[1] There are many clinical and laboratory parameters associated with morbidity and mortality in patients with coronavirus disease-2019 (COVID-19) severe pneumonia hospitalized in the intensive care unit (ICU). Some studies have examined the epidemiological, demographic and clinical characteristics of severe COVID-19 patients. Among these, factors such as advanced age, hypertension, lymphopenia, elevated neutrophil count, lactate dehydrogenase, C-reactive protein (CRP), and symptoms such as dyspnea, fatigue, anorexia and lethargy were found to be important in critically ill patients.[2] Among of comorbid factors especially older age, cardiovascular disease, diabetes, chronic respiratory disease, hypertension, and cancer were all associated with an increased risk of death.[3-5]

In this study, it is aimed to investigate the demographic data, comorbid diseases, Sequential Organ Failure Assessment (SOFA) and The Acute Physiology and Chronic Health Evaluation II (APACHE II) scores and the effects of all these on mortality in COVID-19 patients with severe pneumonia who were treated in the 2nd and 3rd stage ICU between March 2020 and May 2021.

## MATERIAL AND METHODS

### DATA SOURCE

We conducted a retrospective study after approval of the Ethics Committee of Ankara Training and Research Hospital (approval date: 11.02.2021/ number: 537) focusing on patients who hospitalized between 01 March 2020 and 31 March 2021 at Ankara Training and Research Hospital. The study was planned in accordance with the principles of the Declaration of Helsinki. The criteria for hospitalization were increased respiratory distress and worsening of the general condition in other clinics where the patients were hospitalized or in the emergency department. Polymerase chain reaction tests and computed tomography scanning of the patients were done in the clinics they came from. The patients were followed in a total of three ICUs, level 2 and 3, affiliated to the Ankara Training and Research Hospital. During this period, data of 865 patients were examined.

### DATA COLLECTION

We collected data on ages, gender, body mass index (BMI), APACHE II and SOFA scores, comorbid diseases of 865 patients. Age, gender, BMI, APACHE II score on the 1st day of admission to the ICU were recorded. Using the SOFA score system for organ failure scoring, the SOFA scores of the patients on the 1st, 7th, 14th and 28th days in the ICU were noted. Comorbid diseases of all patients, those with no disease, only one additional disease and more than one disease were also recorded. The effects of age, gender, presence of additional diseases, APACHE II and SOFA scoring on mortality of the patients were examined.

All data were analyzed using the SPSS 15 program. For analyzing, chi-squared test, Friedman test, logistic regression analysis, Cox regression analysis were applied.

## RESULTS

### PATIENTS' CHARACTERISTICS

In this study, 865 patients were included who were between the ages of 20 and 95. The mean age of the patients was 67.28+/-14.9 years. The results showed that the median age of the non-surviving group was higher than that of the surviving group (72.41+/-12.7 vs. 62.08+/-15.1 respectively). Cox regression analysis applied, and we find that age was an independent risk factor for mortality ($p<0.001$). Of the patients, 491 (56.8%) were male, and 374 (43.2%) were female, and statistically, the male gender was significantly different ($p=0.0002$). However, no relationship was found between the gender of the patients and their mortality. The demographic data of the patients are given in Table 1 and Table 2.

The mean BMI of the patients was 27.07+/-3.7 kg/m$^2$. The percentage of patients with a BMI>30 was 13%. No statistically significant relationship was found

**TABLE 1:** Demographic data.

| | n | % |
|---|---|---|
| Gender | | |
| Male | 491 | 56.8 |
| Female | 374 | 43.2 |
| | **Mean±SD** | **Minimum-Maximum** |
| Age | 67.23±14.9 | 20-95 |
| Non-survivor | 72.41±12.7 | 26-95 |
| Survivor | 62.08±15.1 | 20-92 |
| BMI | 27.07±3.7 | 15-45 |

SD: Standard deviation; BMI: Body mass index.

between obesity and mortality (Chi-squared test, p=0.187).

The mean APACHE II score of the patients at 1st day was 12.62+/-7.4. For the APACHE II scores evaluated at the 1st day, the cut-off value was 10.5 with a sensitivity of 70.3% and a specificity of 66%, and it was found to be statistically significant (p<0.001; Table 3).

The SOFA scores of the patients were evaluated four times (Figure 1 and Table 4). At the 1st, 7th, 14th and the 28th day. SOFA score averages are given in Figure 1. The highest level occurred between day 7 and day 14 (p=0.001). SOFA 1st day scores were found to be statistically significant with 64.8% sensitivity and 74.9% specificity and a cut-off value of 3.5 (p<0.001; Figure 2). The effect of all times of SOFA scoring on mortality was examined separately and it was seen that this scoring had an effect on mortality for all times separately (logistic regression analysis; p<0.001). The change in SOFA scoring on the 1st day explained 26.42% of the mortality, the change on the 7th day was 39.5%, the change at the 14th day was 25.8%, and the change at the 28th day was 25.5% (Figure 1, Table 4; logistic regression analysis and Friedman test).

Comorbid diseases of the patients were examined under 14 headings (Table 5). These diseases are given in Table 5 in order of frequency. Accordingly, the first 3 ranks are hypertension, diabetes and coronary artery diseases. The effects of these diseases on mortality were examined by Cox regression analysis. According to the Cox regression analysis, statistically significant effects of chronic renal failure (CRF), heart failure (HF), coronary artery disease and neurological pathology were found on mortality. Mortality is 1.782 times higher for those without CRF, 1.714 times for those without HF, 1.605 times for those without coronary disease, and 1.331 times for those without neurological pathology, all of which are statistically significant (Table 5).

The patients were analyzed as groups with one comorbidity, more than one comorbidity, and no comorbid disease. With the Cox regression analysis, we found that, those with more than one disease have a

**TABLE 2:** Relationship between gender of patients and mortality.

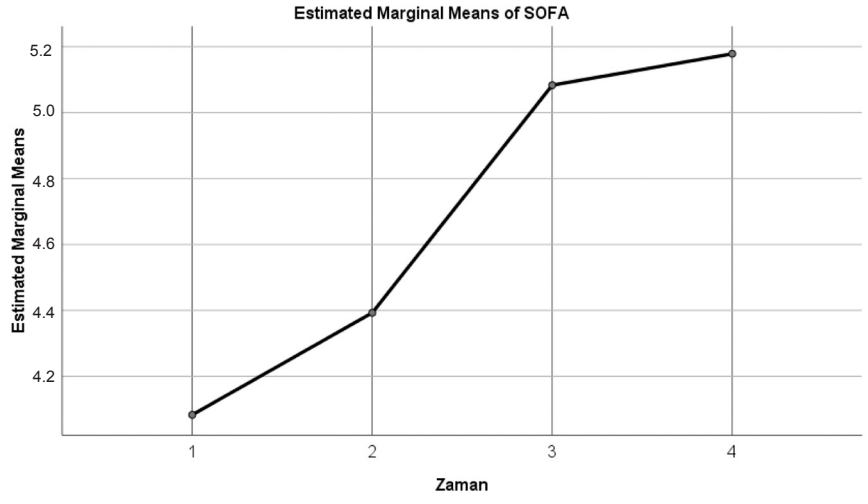
| | | | Mortality | | | |
|---|---|---|---|---|---|---|
| | | | **Survivor** | **Non-survivor** | **Total** | **$\chi^2$; p value** |
| Gender | Male | n | 250 | 241 | 491 | 0.179; 0.672 |
| | | % | 50.9 | 49.1 | 100.0 | |
| | Female | n | 185 | 189 | 374 | |
| | | % | 49.5 | 50.5 | 100.0 | |
| | Total | n | 435 | 430 | 865 | |
| | | % | 50.3 | 49.7 | 100.0 | |

There is no statistically significant relationship between gender and mortality (Chi-squared test; p>0.05).

**TABLE 3:** Average APACHE II score values of the patients and APACHE II score cut-off value for day 1.

| | n | Minimum | Maximum | Mean | SD |
|---|---|---|---|---|---|
| APACHE II day 1 | 854 | 0 | 40 | 12.62 | 7.4 |
| | **AUC (%)** | **Cut-off** | **p value** | **Sensitivity (%)** | **Specificity (%)** |
| APACHE II day 1 | 0.731 (0.698;0.765) | 10.5 | <0.001 | 70.3 | 66.0 |

**SD:** Standard deviation; **AUC:** Area under the curve.



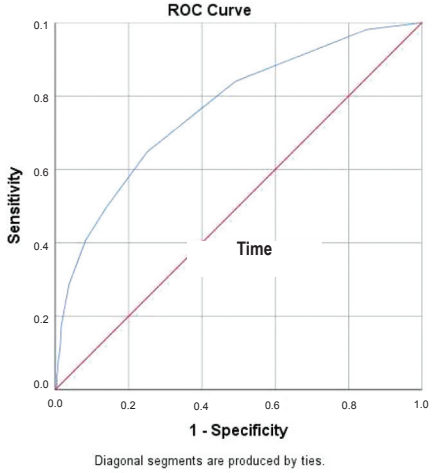

SOFA increase is statistically significant. (Friedman test; p<0.001) The most dramatic increase was between day 7 and day 14.

| | n | Mean | SD | Mean rank | $\chi^2$ | p value |
|---|---|---|---|---|---|---|
| SOFA day 1 | 84 | 4.08 | 2.5 | 2.21 | 22.221 | <0.001** |
| SOFA day 7 | 84 | 4.39 | 2.7 | 2.33 | | |
| SOFA day 14 | 84 | 5.08 | 3.3 | 2.77 | | |
| SOFA day 28 | 84 | 5.18 | 3.6 | 2.68 | | |

Friedman test; p<0.001; SOFA: Sequential Organ Failure Assessment; SD: Standard deviation.

**FIGURE 1:** SOFA increase and its statistically significance (1st day, 7th day, 14th day, 28th day).

| | AUC (%) | Cut-off | p value | Sensitivity (%) | Specificity (%) |
|---|---|---|---|---|---|
| SOFA day 1 | 0.765 (0.734; 0.797) | 3.5 | <0.001 | 64.8% | 74.9% |




Diagonal segments are produced by ties.

**FIGURE 2:** The cut-off value of SOFA score and ROC curve for SOFA scores spesifity.

ROC: Receiver operating characteristic; AUC: Area under the curve; SOFA: Sequential Organ Failure Assessment.

SOFA 1st day scores are 64.8% sensitivity and 74.9% specificity, and the cut-off value is 3.5, which is statistically significant. (p<0,001)

**TABLE 4:** SOFA scores at 1st, 7th, 14th and 28th days. With their effects on mortality.

| | $\chi^2$ | p (Model) | -2 Log likelihood | $R^2$ | p (SOFA) | Exp (B) |
|---|---|---|---|---|---|---|
| SOFA day 1 | 188.81 | <0.001** | 999.2 | 0.264 | <0.001** | 1.579 |
| SOFA day 7 | 188.179 | <0.001** | 554.9 | 0.395 | <0.001** | 1.772 |
| SOFA day 14 | 50.959 | <0.001** | 276.1 | 0.258 | <0.001** | 1.445 |
| SOFA day 28 | 17.785 | <0.001** | 98.5 | 0.255 | <0.001** | 1.37 |

**p<0.01; the effect of all times of SOFA scoring on mortality was examined separately and it was seen that this scoring had an effect on mortality for all times separately (logistic regression analysis; p<0.001); SOFA: Sequential Organ Failure Assessment

1.776 times higher risk of mortality compared to those without any, and those with just one disease have a mortality risk 1.612 times higher than those without any disease, and it was found to be statistically significant. There is no statistically difference on mortality between just one disease or more than one disease (Table 6).

## DISCUSSION

In this retrospective study, the factors affecting outcomes (comorbidities and mortality) of patients hospitalized in the ICU with severe COVID-19 pneumonia were examined. According to our most important result, the mortality of these patients with severe COVID-19 pneumonia increases with age, APACHE II score on day 1 and day 1, 4, 7, 28 SOFA scores. In addition, mortality is high in patients with more than one additional disease.

The results showed that the median age in the non-surviving group was older than that in the surviving group and a majority of patients were older than 65 years in the non-surviving group. One study showed that SARS-CoV-2 infection in 99 patients with COVID-19 is more likely to affect older men with comorbidities and can lead to serious respiratory illness.[6]

Studies have reported that the elderly are more likely to develop critical illness.[7] In addition, these studies have reported that the mortality rate is higher in the elderly groups and there are more male patients than females in terms of gender.[6,7] Likewise, being old has been accepted as an independent risk factor for mortality in SARS and Middle East respiratory syndrome.[8] In a large case series study, an overall fatality of 2.3% was demonstrated in 72,314 cases. In this study, the fatality rate was reported to be 8% in patients aged between 70 and 79 years, and 14.5% in patients older than 80 years.[9]

A study of elderly patients with SARS-CoV-2 showed that 86% of patients had significant comorbid diseases such as chronic kidney disease, congestive HF,

**TABLE 5:** Frequency order of comorbid diseases and their effect on mortality individually.

| Comorbidity | n | % |
|---|---|---|
| HT | 460 | 53.2 |
| Diabetes | 283 | 32.7 |
| CAD | 183 | 21.2 |
| ORD | 156 | 18 |
| Neurological pathologies | 152 | 17.6 |
| Obesity | 118 | 13.6 |
| HF | 90 | 10.4 |
| Malignancy | 44 | 5.1 |
| CRF | 54 | 6.2 |
| Abdominal pathologies | 28 | 3.2 |
| Trauma | 11 | 1.3 |
| Immune deficiency | 5 | 0.6 |
| CLD | 4 | 0.5 |
| Hematological pathologies | 3 | 0.3 |
| | | p value |
| HT | 1.176 (0.97-1.425) | 0.1 |
| CRF | 1.782 (1.258-2.526) | <0.001** |
| HF | 1.714 (1.306-2.25) | <0.001** |
| ORD | 0.93 (0.682-1.267) | 0.645 |
| CAD | 1.605 (1.299-1.983) | <0.001** |
| CLD | 3.01 (0.747-12.135) | 0.121 |
| Malignity | 1.16 (0.763-1.763) | 0.487 |
| Diabetes | 1.155 (0.947-1.41) | 0.155 |
| Immune deficiency | 0.406 (0.057-2.891) | 0.406 |
| Neurologic pathologies | 1.331 (1.065-1.663 | <0.012* |

*p<0.05; **p<0.01; Cox regression analysis; **HT:** Hypertension; **CRF**: Chronic renal failure; **HF**: Heart failure; **ORD**: Obstructive respiratory disease; **CAD**: Coronary artery disease; **CLD**: Chronic liver diseases.

**TABLE 6:** Mortality rates in groups with no comorbidity, one additional disease, and more than one disease and their effects on mortality.

| | Survivor | | Non-survivor | | Total |
|---|---|---|---|---|---|
| | n | % | n | % | |
| No comorbidity | 138 | 70.1 | 59 | 29.9 | 197 |
| One additional disease | 107 | 48.6 | 113 | 51.4 | 220 |
| More than one disease | 190 | 42.4 | 258 | 57.6 | 448 |
| | | | | p value | |
| No comorbidity | | 1.012 (0.816-1.256) | | 0.912 | |
| One additional disease | | 1.612 (1.175-2.21) | | 0.003** | |
| More than one disease | | 1.776 (1.338-2.358) | | <0.001** | |

**p<0.01; The effect of those with more than one disease, those with only one disease, and those with no disease on mortality.

chronic obstructive pulmonary disease and diabetes.[10] Older adults with more than one comorbidity have a higher risk of death from SARS-CoV-2. Although SARS-CoV-2 infection mainly causes severe pneumonia and respiratory distress, the condition of patients can deteriorate rapidly with cardiac, renal and hepatic involvement.[11,12] For patients with comorbidities, the occurrence of these complications in the course of SARS-CoV-2 is associated with clinical worsening.[11]

It has been reported that both the COVID-19 case fatality rates and the prevalence of hypertension increase with age and exceed 8.0% and 50%, respectively, for the 70-79 age group.[13] The prognosis is markedly worsened in persons with hypertension who develop myocardial damage from COVID-19 infection and in the presence of additional cardiovascular disease.[14] Comorbidities in patients are important in predicting the outcome of the disease. In these cases, the treatment protocols of the disease may change. In the study of Karthic et al. comorbid conditions were detected in 40% of the patients. It was also shown that the mortality rate increased significantly with comorbidity.[15] Among these comorbidities, hypertension, diabetes, chronic heart, kidney, liver and cerebral diseases were the most common and severe disease course was reported as 77.7% in patients with comorbidities.

In our study, we found that, those with more than one disease have a 1.776 times higher risk of mortality compared to those without any, and those with just one disease have a mortality risk 1.612 times higher than those without any disease, and it was found to be statistically significant. There is no statistically significant difference on mortality between just one disease or more than one disease.

The SOFA score and its association with severity in patients with COVID-19 has been previously reported in other studies.[16,17] Another study from Spain reported a SOFA score of 2 in COVID-19 patients hospitalized in intensive care. This resulted in an area under the curve of 0.78 (0.76-0.86) in the series. It was reported as the threshold value considered differentiating septic and non-septic patients.[18] In addition, adjustments were made for other main variables such as CRP, procalcitonin, and gender in this study, and it was concluded that the SOFA score was an indicator of critical care need.[18]

In our study, SOFA score evaluation was performed on 4 different days in patients admitted to the ICU. It was determined that the changes in the scores of these days had an effect on mortality. It was concluded that the 28$^{th}$ day SOFA value increased mortality 5.5 times. Since the SOFA score system allows evaluation in terms of organ failure, it has also been used in studies to determine the need for intensive care of patients.[18] In our study, the changes in the scores at the 1$^{st}$, 4$^{th}$, 7$^{th}$ and 28$^{th}$ days of the patients treated in the ICU were examined.

The APACHE II score is the scoring system that was proposed in 1985 and is calculated within 24 hours of a patient's admission to the ICU.[19] The APACHE II score is widely used to predict the outcome of critically ill patients. In particular, the APACHE II score can also predict the likelihood of patients developing sepsis and whether patients will survive sepsis. In Karthic et al.'s

study the APACHE II score was found to be significantly lower in survivors than in patients who died.[15] In this study, values of 17 and above for APACHE II were associated with mortality. In a study from China, the average APACHE II score of patients who died was given as 23. On the other hand, a mean of 10.87 was found to be significantly lower in surviving patients.[20] In our study, the cut-off value in the APACHE II score evaluation of the patients was found to be 10.5 with a sensitivity of 70.3% and a specificity of 66%. Score values above this were found to be associated with mortality. The relatively low cut-off value compared to other studies can be explained by the difference in the patient population.

## CONCLUSION

In conclusion, there are some important risk factors in COVID-19 patients treated with severe pneumonia. Among these, the presence of at least one additional disease and high intensive care scores were particularly noteworthy in our study. Among the additional diseases, the patient's CRF, HF and coronary artery disease draw attention. The detection of APACHE II and SOFA scores at the time of admission to the ICU of high-risk patients diagnosed with COVID-19 can prevent pathophysiological abnormalities and reduce mortality.

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*During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.*

### *Conflict of Interest*

*No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.*

### *Authorship Contributions*

***Idea/Concept:*** *Ayşe Özcan;* ***Control/Supervision:*** *Murat ÜmitParpucu;* ***Data Collection and/or Processing:*** *Ceren Kaçan;* ***Analysis and/or Interpretation:*** *Mert Nakip;* ***Literature Review:*** ***H****ikmet Furkan Yalçın;* ***Writing the Article:*** *Hülya Başar;* ***Critical Review:*** *Çetin Kaymak;* ***References and Fundings:*** *Murat Kaykaç.*

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