



A Comprehensive Study of the CA-72.4 Tumor Marker Utilization and Cancer Detection: Analysis Based on Ministry of Health Data

CA-72.4 Kullanımı ve Kanser Tespitine İlişkin Kapsamlı Bir Çalışma: Sağlık Bakanlığı Verilerine Dayalı Analiz

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Abstract

Background: This study aims to explore the relevance and utilization of the CA 72.4 tumor marker in cancer diagnosis, with a particular focus on gastrointestinal tumors and ovarian cancer, based on data from the Ministry of Health.

Materials and Methods: We conducted a retrospective analysis of health records from the Ministry of Health spanning over five years. The data, consisting of various demographics, including gender, age, and clinical service requests, was statistically analyzed. The rates of reference range exceedance for the CA 72.4 tumor marker, diagnosis times, the ratio of cancer diagnosis, and the cost distribution were among the key aspects evaluated.

Results: The analysis revealed a significant increase in the request for CA 72.4 tests over the years. It was also observed that cancer detection rates slightly increased over time, with a higher percentage in patients testing positive for CA 72.4, primarily requested before diagnosis. The highest requests for the test were made by the Medical Oncology clinic. Furthermore, it was observed that gender and age groups played significant roles in the prevalence of cancer diagnoses.

Conclusions: Our study indicates that the use of CA 72.4 as a tumor marker could be valuable, especially in the detection of certain types of cancer. However, the correlation between a positive CA 72.4 test and a definitive cancer diagnosis requires further investigation, as the sensitivity and specificity of this marker are still subjects of debate. Despite certain limitations, this study offers substantial insights into the utility of CA 72.4 in the current healthcare setting.

Key Words: CA 72.4, Big Data, Tumor Marker, National Health

Öz

Amaç: Bu çalışma, Sağlık Bakanlığı'ndan alınan verilere dayanarak, özellikle gastrointestinal tümörler ve over kanserine odaklanarak CA 72.4 tümör belirtecinin kanser teşhisindeki önemini ve kullanımını araştırmayı amaçlamaktadır.

Materyal ve Metod: Sağlık Bakanlığı'nın beş yıla yayılan sağlık kayıtlarının retrospektif bir analizini yaptık. Cinsiyet, yaş, klinik hizmet talepleri gibi çeşitli demografik bilgilerden oluşan veriler istatistiksel olarak analiz edildi. CA 72.4 tümör belirtecinin referans aralığını aşma oranları, teşhis süreleri, kanser teşhisi oranı ve maliyet dağılımı değerlendirilen temel unsurlar arasındaydı.

Bulgular: Analiz, yıllar içinde CA 72.4 testleri talebinde önemli bir artış olduğunu ortaya koydu. Ayrıca, kanser tespit oranlarının zaman içinde biraz arttığı, CA 72.4 için pozitif test yapan hastalarda daha yüksek bir yüzdeyle, özellikle teşhisten önce talep edildiği gözlemlendi. Test için en yüksek talepler Tıbbi Onkoloji kliniğinden geldi. Ayrıca cinsiyet ve yaş gruplarının kanser tanılarının yaygınlığında önemli rol oynadığı görülmüştür.

Sonuç: Çalışmamız, CA 72.4'ün bir tümör belirteci olarak kullanılmasının, özellikle belirli kanser türlerinin saptanmasında değerli olabileceğini göstermektedir. Bununla birlikte, pozitif bir CA 72.4 testi ile kesin kanser teşhisi arasındaki korelasyon, bu belirtecin duyarlılığı ve özgüllüğü hala tartışma konusu olduğundan, daha fazla araştırma gerektirir. Bazı sınırlamalara rağmen, bu çalışma CA 72.4'ün mevcut sağlık hizmeti ortamındaki kullanımına ilişkin önemli bilgiler sunmaktadır.

Anahtar Kelimeler: CA 72.4, Büyük Veri, Tümör Belirteçleri, Ulusal Sağlık

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Introduction

Cancer remains a significant public health concern worldwide, with its diagnosis and treatment of paramount importance. Tumor markers play a vital role in these processes. These markers are proteins or other biological molecules produced by cancer cells or appear in response to a tumor from healthy cells. These molecules provide essential information in diagnosing the disease, determining its stage, gauging response to treatment, and assessing the patient's prognosis.

Cancer Antigen 72.4 (CA 72.4) is a molecule that particularly stands out among tumor markers. This marker is used in the diagnosis and monitoring of some types of cancer, primarily gastric, pancreatic, and ovarian cancers. However, the clinical use of a tumor marker can vary depending on sensitivity, specificity, patient population, and various other factors (1). CA 72.4 is a glycoprotein tumor marker used primarily in gastrointestinal system tumors, especially stomach cancer, and ovarian cancer. Stomach cancer is a significant health issue worldwide, and the benefits of tumor markers in diagnosis, prognosis, and follow-up have been researched. Studies have shown high serum CEA and CA 19.9 levels in 15-72% of patients with stomach cancer (2).

Some research has also evaluated CA 72.4 as a tumor determinant for stomach cancer, comparing it with CEA and CA 19-9, and showing that the level of CA 72.4 is strongly related to tumor stage and the presence of lymph node involvement. The consensus, however, is that CA 72.4 should not be used for early assessment, but it can be useful in evaluating cancer recurrence (3).

This study shows that high serum CA 72.4 levels were found in half of the recurring stomach cancer cases before surgical intervention, compared to approximately 24% of patients with no recurrence. Considering these findings, the importance of examining CA 72.4 levels for early detection of recurrence is emphasized (4). Another recent study demonstrated that the serum levels of CA 19.9 and CA 72.4 did not have a significant difference in terms of gender, age, and histological classification (5). Therefore, we aim to conduct a comprehensive review of the CA 72.4 tumor marker using data from the Turkish Ministry of Health. This study will enable us to better understand the applications, efficacy, and limitations of the marker, especially in the context of patients in Türkiye. Additionally, considering this information, we will discuss what can be done to optimize the use of tumor markers and provide more effective treatment and monitoring strategies for cancer patients.

Materials and Methods

Data from a five-year period (2017-2021) were analyzed, including a total of 911.834 tests from 141.974 individuals. The test counts, test rates per population, and rates of exceeding the reference range were assessed based on gender, age groups, geographic regions, and healthcare institution types.

Health net studies in Türkiye started in the 2000s and have

been provided as a database service through the e-Pulse system since 2015. While Health Level 7 (HL7) Version 3 standard was initially used for sending health data set packages, Extensible Markup Language (XML) web services have been employed since 2015. This database includes data from all public, private, and university healthcare institutions in Türkiye. The health data comprises records of demographic characteristics, laboratory data, medication usage, and comorbidities for more than eighty-four million individuals. The CA 72.4 levels consist of results obtained through the immunoassay method in laboratories across Türkiye.

Database and e-Pulse

e-Pulse is a platform developed by the Ministry of Health in Türkiye, allowing individuals to store and manage their health information digitally. For this study, patient information and health records were collected from the e-Pulse system. It allows users to use 30 different services for prevention, treatment, health promotion and health-related fields. In addition, some statistics belonging to the relevant categories are included in the e-Pulse system (6). During the data collection process, personal information was protected, and the principle of privacy was fully respected.

SKRS and ICD Codes

Health Coding Reference Server (SKRS) is a data recording and reporting system used by the Ministry of Health in Türkiye. This system aids in the more effective management of health services. In this study, data pulled from the SKRS and ICD codes were used to analyze disease diagnoses, treatment plans, and the overall state of health services. International Statistical Classification of Diseases and Related Health Problems (ICD) codes are a standard disease and health problem classification system created by the World Health Organization and used worldwide. These codes are an important tool for identifying, monitoring, and treating diseases.

Study Design

This retrospective study utilized data from the Ministry of Health, covering a five-year period from 2017 to 2021. The data included information on CA 72.4 tests requested from individuals across different regions and healthcare institutions in the country.

Data Collection

The data were collected from medical records and laboratory databases. The information included demographics (gender, age), test requests, test results, cancer diagnoses, and healthcare institution types.

Study Population

The study population consisted of individuals who underwent CA 72.4 testing during the study period. Both men and women were included in the analysis.

Data Analysis

Descriptive statistics were used to analyze the data. The test counts, test rates per population, rates of exceeding the reference range, and cancer diagnosis rates were calculated and compared across different variables, including gender,

age groups, geographic regions, and healthcare institution types. The study data were transferred to SPSS Statistics version 26.0 (IBM Corp., Armonk, NY) program, and the analyses were completed.

Ethical Considerations

The study adhered to ethical guidelines and protected the privacy and confidentiality of the individuals included in the data. Institutional review board approval was obtained, and all data were anonymized to ensure privacy. Relevant approval was obtained from the Turkish Ministry of Health with the waiver of informed consent for retrospective data analysis (95741342-020/27112019).

Results

Between 2017-2021, CA 72.4 testing was requested for 141.974 individuals with a total of 911.834 tests, resulting in an average of 6,42 tests per person and 1.103 tests per 100.000 population. Among the tumor markers used in our study, CA 72.4 had the second-lowest number of tests per 100.000 population.

When comparing the number of CA 72.4 tests over the years, the number of tests and the tests per 100.000 population have been increasing from 2017 to 2019. However, a significant decrease is observed in 2020 and 2021 (Table 1).

Table 1. Number of tests and the ratio of the population by years

| CA72.4 | 2017 | | 2018 | | 2019 | | 2020 | | 2021 | |
|--------|-----------------|--|-----------------|--|-----------------|--|-----------------|--|-----------------|--|
| | Number of Tests | Number of Tests Per 100.000 Population | Number of Tests | Number of Tests Per 100.000 Population | Number of Tests | Number of Tests Per 100.000 Population | Number of Tests | Number of Tests Per 100.000 Population | Number of Tests | Number of Tests Per 100.000 Population |
| | 188.106 | 233 | 212.939 | 260 | 210.111 | 253 | 138.520 | 166 | 162.158 | 194 |

For women, the number of test requests increases as the year progresses from 2017 to 2019, as with the general population, and then significantly decreases in 2020 and 2021. It ranks sixth among the tumor markers tested in women in all years (Table 2).

In men, as in the general population, the number and rate of test requests increase as the year progresses from 2017 to 2019, and then significantly decreases in 2020 and 2021 (Table 3). When the female-to-male test number ratio is evaluated over the years, it is 1,49 in 2017, 1,43 in 2018, 1,41 in 2019, 1,33 in 2020, and 1,28 in 2021.

When comparing test request numbers by age groups over the years, CA 72.4 is most frequently requested in the 18-64 age range, followed by those over 65, and least frequently in the 0-17 age range. The test request ratio between the 18-64 age group and those over 65 is 2,35 in

2017, 2,08 in 2018, 1,88 in 2019, 1,89 in 2020, and 1,84 in 2021. The test consumption rate per 100.000 people between the 18-64 age group and those over 65 is 1/3,14 in 2017, 1/3,46 in 2018, 1/3,69 in 2019, 1/3,52 in 2020, and 1/3,61 in 2021. Among all tumor markers, CA 72.4 is the second least requested marker in the over-65 group per 100.000 people (Neuron-specific Enolase (NSE) is the least). The number of test requests and the test consumption per 100.000 people in the over-65 group increase as the year progresses from 2017 to 2019 but show a significant decrease in 2020-2021. When comparing the rate of cancer diagnosis at any time in patients who had a CA 72.4 tumor marker request, the cancer detection rate increased as the year progressed from 2017 to 2019, with 30% of individuals in 2017, 33% in 2019, 29% in 2020, and 25% in 2021 diagnosed with cancer 2021 (Table 4).

Table 2. The Number of Test Requests by Years in Women

| CA72.4 | 2017 | | 2018 | | 2019 | | 2020 | | 2021 | |
|--------|-----------------|--|-----------------|--|-----------------|--|-----------------|--|-----------------|--|
| | Number of Tests | Number of Tests Per 100.000 Population | Number of Tests | Number of Tests Per 100.000 Population | Number of Tests | Number of Tests Per 100.000 Population | Number of Tests | Number of Tests Per 100.000 Population | Number of Tests | Number of Tests Per 100.000 Population |
| | 112.686 | 280 | 125.548 | 307 | 123.010 | 297 | 79.272 | 190 | 91.056 | 218 |

Table 3. The Number of Test Requests by Years in Men.

| CA72.4 | 2017 | | 2018 | | 2019 | | 2020 | | 2021 | |
|--------|-----------------|--|-----------------|--|-----------------|--|-----------------|--|-----------------|--|
| | Number of Tests | Number of Tests Per 100.000 Population | Number of Tests | Number of Tests Per 100.000 Population | Number of Tests | Number of Tests Per 100.000 Population | Number of Tests | Number of Tests Per 100.000 Population | Number of Tests | Number of Tests Per 100.000 Population |
| | 75.420 | 186 | 87.391 | 212 | 87.101 | 209 | 59.248 | 141 | 71.102 | 170 |

Table 4. Percentage Distribution of Who Required Tumor Markers were Diagnosed with Cancer at Any Time.

| CA72.4 | 2017 | | 2018 | | 2019 | | 2020 | | 2021 | |
|--------|------------------------|---------------------|------------------------|---------------------|------------------------|---------------------|------------------------|---------------------|------------------------|---------------------|
| | No Diagnosis of Cancer | Diagnosis of Cancer | No Diagnosis of Cancer | Diagnosis of Cancer | No Diagnosis of Cancer | Diagnosis of Cancer | No Diagnosis of Cancer | Diagnosis of Cancer | No Diagnosis of Cancer | Diagnosis of Cancer |
| | 70% | 30% | 68% | 32% | 67% | 33% | 71% | 29% | 75% | 25% |

When analyzing the timing of test requests relative to diagnosis in individuals who had a tumor marker request, it was found that in all years except 2017, tests were requested more often before the diagnosis, second most at the same time as the diagnosis, and least often after the diagnosis. The pre-diagnosis test request rate increased as the year progressed until 2020, with a rate of 11,31% in 2017, 17,53% in 2020, and 16,37% in 2021. When comparing test request rates by diagnosis times (before/at the same time/after diagnosis), the ratio was 1,65/1,77/1 in 2017, 3,17/1,78/1 in 2018, 3,62/1,54/1 in 2019, 3,65/1,43/1 in 2020, and 5,43/1,93/1 in 2021.

In 2017, 6,74% of the patients who underwent the CA 72.4 test were diagnosed with CA 72.4 related cancer, while 56% were diagnosed with cancer unrelated to CA 72.4. This ratio increased until 2020, when 10,61% of patients were diagnosed with CA 72.4 related cancer and 86,47% were diagnosed with cancer unrelated to CA 72.4.

In 2021, these rates were 8,81% and 74,42% respectively. When the ratio of patients diagnosed with CA 72.4 related cancer to those diagnosed with unrelated cancer was compared, the ratios were 1/8,30 in 2017, 1/8,12 in 2018, 1/8,18 in 2019, 1/8,14 in 2020, and 1/8,44 in 2021.

The CA 72.4 test was most frequently requested in the Central Anatolia region in all years. It was requested second most frequently in the Mediterranean region, with a ratio of 2,47 between the two regions in 2021. The region with the least test requests was the Eastern Anatolia region in 2017, the Black Sea region in 2018-2019, and the Southeastern Anatolia region in 2020-2021. When the first and last regions were compared in 2021, the ratio was 162,79. Like the general trend in Türkiye, the number of test requests increased in all regions between 2017 and 2019, but significantly decreased in 2020 and 2021 (Table 1).

Table 5. CA 72.4 Geographical Distribution According to Years and Test Requests.

| 2017 | | 2018 | | 2019 | | 2020 | | 2021 | |
|---------------------------|-----------------|---------------------------|-----------------|---------------------------|-----------------|---------------------------|-----------------|---------------------------|-----------------|
| Region | Number of tests | Region | Number of tests | Region | Number of tests | Region | Number of tests | Region | Number of tests |
| Central Anatolia Region | 85.568 | Central Anatolia Region | 98.593 | Central Anatolia Region | 103.111 | Central Anatolia Region | 75.066 | Central Anatolia Region | 89.539 |
| Mediterranean Region | 40.328 | Mediterranean Region | 45.788 | Mediterranean Region | 44.707 | Marmara Region | 32.195 | Marmara Region | 36.177 |
| Marmara Region | 34.496 | Marmara Region | 35.096 | Marmara Region | 43.876 | Mediterranean Region | 26.854 | Mediterranean Region | 31.302 |
| Southeast Anatolia Region | 19.279 | Southeast Anatolia Region | 271 | Southeast Anatolia Region | 13.661 | Aegean Region | 218 | Aegean Region | 2.281 |
| Aegean Region | 5.206 | Aegean Region | 4.448 | Aegean Region | 3.502 | Eastern Anatolia Region | 1.065 | Eastern Anatolia Region | 1.694 |
| Black Sea Region | 2.234 | Eastern Anatolia Region | 1.029 | Eastern Anatolia Region | 667 | Black Sea Region | 584 | Black Sea Region | 615 |
| Eastern Anatolia Region | 995 | Black Sea Region | 885 | Black Sea Region | 587 | Southeast Anatolia Region | 570 | Southeast Anatolia Region | 550 |

When regions were analyzed according to the number of tests per 100.000 population, the Central Anatolia region had the highest number of requests in all years. The lowest region was Eastern Anatolia in 2017, the Black Sea region in 2018-2019, and Southeastern Anatolia in 2020-2021. In 2021, when the Central Anatolia region, which had the highest test rate, was compared with the second-place Mediterranean region, the ratio was 2,30, and when compared with the lowest region, Southeastern Anatolia, the ratio was 111,83 (Table 5).

When clinics were compared according to the number of test requests, the clinic that requested the most tests was the Medical Oncology clinic in 2018, while in other years it was the Internal Medicine clinic. In second place was Internal Medicine in 2018, the Medical Oncology clinic in 2017 and 2019, and the Gastroenterology clinic in 2020 and 2021. Medical oncology was in 2nd place in 2017, 1st place in 2018; 2nd place in 2019, and 5th place in 2020 and 2021. Family medicine did not enter the top 10 clinics in all years.

The Emergency Medicine clinic was in 6th place in 2017, 8th place in 2018, 6th place in 2019, 8th place in 2020, and 7th place in 2021 (Table 6).

When examining the rates of exceeding the reference range by geographic region, the highest rate belonged to the Southeastern Anatolia region, which had the lowest number of test requests and the lowest number of test requests per 100.000 population between 2020-2021, at a rate of 11%. The second highest rate was in the Black Sea region, which had the lowest number of tests per 100.000 population between 2018-2019, with a rate of 10,2%. The Marmara region was third with a rate of 9,9%. The lowest rate belonged to the Aegean region with 8,6%.

When examining the rates of exceeding the reference range by gender, overall, 9,20% tested positive. However, the rate for men was 9,61%, and for women, it was 8,89%. When examining the rates of exceeding the reference range by age group, the highest rate was in those over 65 with 10,65%. This was followed by the 18-64 age group with 8,45%, and

then the 0-17 age group with 5,01%. When the age groups were compared, the rates were 2,12/1,68/1 for the positive findings.

When examining the rates of exceeding the reference range by admission status, the highest rate was seen in inpatients at 11,72%, followed by day-patients at 8,99%, and outpatients at 8,78%. When these rates are compared, the ratio is 2,01/1,13/1. When examining the rates of exceeding the reference range by cancer diagnosis status, a total of 9,22% of individuals tested positive. Among the patients who tested positive, 15,02% have a cancer diagnosis, while 6,26% do not have a cancer diagnosis.

When examining the rates of tests exceeding the reference range by the clinics that requested the CA 72.4 test, the highest rate was in the Medical Oncology clinic with 16,97%, followed by the General Surgery clinic with 9,45%, and the Emergency Medicine clinic with 8,97%. While the Internal Medicine clinic had the highest number of test requests in all years except 2018, the rate in this clinic was 6,98%. In the Medical Oncology clinic, which had the highest number in 2018, the rate was 16,97% (first place). In the Obstetrics and Gynecology clinic, which ranked third between 2017-2020, the rate was 7,60%. Family medicine did not rank among the top 10 clinics (Table 6).

Table 6. CA 72.4 Top 10 Clinics by Years and Number of Test Requests.

| 2017 | | 2018 | | 2019 | | 2020 | | 2021 | |
|---------------------------------|--------|------------------------------|--------|------------------------------|--------|------------------------------|--------|------------------------------|--------|
| Internal Medicine | 30.235 | Medical Oncology | 36.774 | Internal Medicine | 29.657 | Internal Medicine | 22.326 | Internal Medicine | 25.901 |
| Medical Oncology | 29.715 | Internal Medicine | 32.193 | Medical Oncology | 29.627 | Gastroenterology | 19.069 | Gastroenterology | 22.041 |
| Gynecology and Obstetrics | 27.430 | Gynecology and Obstetrics | 24.828 | Gynecology and Obstetrics | 28.186 | Gynecology and Obstetrics | 16.234 | General Surgery | 19.634 |
| Gastroenterology | 18.171 | Gastroenterology | 23.845 | Gastroenterology | 22.989 | General Surgery | 16.093 | Gynecology and Obstetrics | 16.478 |
| General Surgery | 17.603 | General Surgery | 19.806 | General Surgery | 21.968 | Medical Oncology | 10.789 | Medical Oncology | 10.045 |
| Emergency Medicine | 7.022 | Cardiology | 9.689 | Emergency Medicine | 9.637 | Cardiology | 8.471 | Cardiology | 7.983 |
| Endocrinology and Metabolism | 6.595 | Endocrinology and Metabolism | 7.886 | Cardiology | 9.591 | Neurology | 5.446 | Emergency Medicine | 6.888 |
| Neurology | 4.599 | Emergency Medicine | 6.141 | Endocrinology and Metabolism | 787 | Emergency Medicine | 5.305 | Neurology | 5.937 |
| Chest Diseases | 4.488 | Neurology | 5.557 | Neurology | 714 | Endocrinology and Metabolism | 5.265 | Hematology | 59 |
| Immunology and Allergy Diseases | 4.315 | Chest Diseases | 5.301 | Hematology | 4.787 | Hematology | 418 | Endocrinology and Metabolism | 5.823 |

Discussion

Upon reviewing the findings of this study, it is evident that there are substantial differences in the rates of the CA 72.4 test exceeding the reference range based on factors such as diagnosis, clinic type, type of hospital stays, cancer diagnosis status, and geographical location. The variability underscores the need for a more tailored approach to requesting this test, especially considering the cost implications and the potential impact on patient management. The continuous assessment of the need for and the cost-effectiveness of the CA 72.4 test is crucial to ensure efficient use of healthcare resources. Understanding the determinants of these variations could lead to more efficient allocation of resources, possibly leading to better patient outcomes and improved overall healthcare efficiency.

The crucial findings revolving around the use of the CA 72.4 test need to be highlighted. One of the key results of the study was the pronounced overuse of the test in inpatients, with a rate of 11,72%, compared to day patients and outpa-

tients at rates of 8,99% and 8,78% respectively. This highlights a potentially excessive reliance on this test for inpatients, which may not necessarily result in improved patient outcomes. Furthermore, the significant presence of the test exceeding reference range in cancer patients (15,02%) compared to those without a cancer diagnosis (6,26%) suggests a potential overuse in cancer diagnostics and monitoring. Our data also indicated significant geographical variation in the usage of the CA 72.4 test. Such variations and potential overuse could have considerable implications in terms of cost-efficiency, with the cost of the test exhibiting a decreasing trend over the years, which might indicate potential resource wastage. These findings underline the necessity for judicious use of the CA 72.4 test and call for an in-depth evaluation of the diagnostic strategies to ensure optimum resource allocation and patient care.

CA 72.4 is a tumor marker primarily used in gastrointestinal system tumors, especially stomach cancer, and ovarian cancer.

According to GLOBOCAN data, stomach cancer is the fifth most common cancer worldwide and ranks third in cancer-related deaths. It is more prevalent in men, with a rate of 15,7/100.000 in men and 7/100.000 in women (7). In our study, when the ratio of female to male test numbers is compared by year, the ratio was 1,49 in 2017, 1,43 in 2018, 1,41 in 2019, 1,33 in 2020, and 1,28 in 2021. When the rates of exceeding the reference range were examined by gender, it was found to be positive at a rate of 9,20% overall, 9,61% in men, and 8,89% in women.

Although the incidence of stomach cancer increases with older age, the median age is 70, and only 10% of patients receive a diagnosis under the age of 45. H. pylori infection status, gastric polyps, atrophic gastritis and gastric ulcer are other causes of increase (8). In our study, when test request numbers by age groups were compared by year, CA 72.4 was most frequently requested in the 18-64 age range, second most frequently in those over 65, and least frequently in the 0-17 age range.

The consensus on the use of CA 72.4 as a tumor marker is that it should be used in the evaluation of cancer recurrence (9). As for stomach cancer, studies have been conducted on its usability for diagnosis, prognosis determination, preoperative metastasis prediction, and postoperative recurrence assessment. However, no results demonstrating high clinical benefit have been found. In our study, the timing of test requests was examined, and except for 2017, the test was most frequently requested before diagnosis in other years, second most frequently at the same time as diagnosis, and least frequently after the diagnosis. In a study of Chinese origin, the sensitivity and specificity of serum CA 72.4 levels for the diagnosis of gastric cancer were calculated to be 49% and 96%, respectively. Sensitivity has been evaluated in the range of 40-80% in other studies (10).

In our study, when comparing the rate of receiving a cancer diagnosis at any time among patients who requested the CA 72.4 tumor marker, the cancer detection rate increased as the year progressed between 2017-2019, with 30% of people in 2017, 33% in 2019, 29% in 2020, and 25% in 2021 receiving a cancer diagnosis (Table 4). In 2017, 6,74% of the individuals who had the CA-72.4 test received a CA 72.4 related cancer diagnosis, while 56% received a diagnosis of a cancer unrelated to CA 72.4. This rate has been increasing until 2020, when 10,61% of patients received a CA 72.4 related cancer diagnosis, and 86,47% received a diagnosis of cancer unrelated to CA 72.4. These rates in 2021 are 8,81% and 74,42%, respectively. When comparing the rates of exceeding the reference range by year, the highest rate was in 2020, at 9,69%, and the lowest rate was in 2018, at 8,71%. When the rates of exceeding the reference range according to whether a cancer diagnosis has been received are examined, a total of 9,22% of people have tested positive, with a cancer diagnosis being present in 15,02% of the patients who tested positive, and no cancer diagnosis in 6,26%.

The present study carries several limitations that need to be

acknowledged. Firstly, the sample size and diversity of representation could limit the generalizability of the findings, as it may not accurately represent the broader population with different demographics. Secondly, being a retrospective study, it relies heavily on the accuracy and completeness of past records, and it may not definitively establish cause-effect relationships as precisely as prospective studies. The absence of a control group could further make it challenging to attribute the outcomes directly to the factors being investigated. The lack of randomization may also introduce a selection bias, potentially affecting the results' representativeness. Furthermore, the variability in the timing of test requests could introduce confounding factors. Our study's focus on the single tumor marker, CA 72.4, may oversimplify the complexity of cancer diagnosis, and not considering other important variables like lifestyle or diet could impact the findings. Lastly, our outcome measure relying on the single factor of whether the CA 72.4 test exceeds the reference range may not fully encapsulate the multifaceted nature of cancer detection. Despite these limitations, our findings contribute valuable insights to the existing body of research. In conclusion, our study contributes significant insights into the utilization and potential relevance of the CA 72.4 tumor marker in the diagnosis of certain types of cancer, particularly gastric cancer. Despite the limitations mentioned, our findings underscore the fact that the CA-72.4 test's request frequency and subsequent results correlate with cancer diagnoses and may play a pivotal role in early detection. Our study also highlights the increasing trend of CA 72.4 associated cancer diagnosis over the years, shedding light on the test's increasing importance in cancer detection. Therefore, further in-depth research and more comprehensive studies are crucial to substantiate these preliminary findings and explore the full potential of the CA 72.4 test in cancer diagnosis and management. It is hoped that these findings will encourage more thorough investigations into the role of tumor markers in the broader field of oncology.

Ethical Approval: Scientific Commissions have been established to analyze the National Ministry of Health database of the Ministry of Health, develop health policies and transfer this study to scientific platforms. For this purpose, the Approval of the Ministry dated and numbered 95741342-020/27112019 has been received. Data studied All data studied are anonymized data whose information belongs to has been blacked out. Since these data are National Data, it was not found correct to obtain the approval of the Ethics committee and permission was not granted.

Author Contributions:

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Literature Review: S. B., M.M.

Design : S.B.

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Analysis and interpretation: S. B., M.M.

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Critical revision of manuscript: S. B., M.M.

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References

1. Liang Y, Wang W, Fang C, Raj SS, Li QW, Zhou ZW. Clinical significance and diagnostic value of serum CEA, CA19-9 and CA72-4 in patients with gastric cancer. *Oncotarget* 2016;7:49565–73.
2. Molina R, Auge JM, Alicarte J, Filella X, Vinolas N, Ballesta AM. Pro-gastrin-releasing peptide in patients with benign and malignant disease. *Tumor Biol* 2004;25:56–61.
3. Guadagni F, Roselli M, Cosimelli M, Mannella E, Tedesco M, Cavaliere F. TAG-72 (CA 72-4 assay) as a complementary serum tumor antigen to CEA in monitoring patients with colorectal cancer. *Cancer* 1993;72(7):2098–106.
4. Yu J, Zhang S, Zhao B. Differences and correlation of serum CEA, CA19-9 and CA72-4 in gastric cancer. *Mol Clin Oncol* 2016;4(3):441–49.
5. Guadagni F, Roselli M, Cosimelli M, Ferroni P, Spila A, Casaldi V, et al. Correlation between positive CA 72-4 serum levels and lymph node involvement in patients with gastric carcinoma. *Anticancer Res* 1993;13(6B):2409–13.
6. Birinci Ş. A Digital Opportunity for Patients to Manage Their Health: Turkey National Personal Health Record System (The e-Nabız). *Balkan Med J* 2023;40(3):215.
7. gco.iarc.fr [homepage on the Internet]. WHO: GLOBOCAN [updated 19.05.2020]. Available from: <https://gco.iarc.fr/today/data/factsheets/cancers/7-Stomach-fact-sheet.pdf>
8. Hu PJ, Chen MY, Wu MS, Lin YC, Shih PH, Lai CH, Lin HJ. Clinical evaluation of CA72-4 for screening gastric cancer in a healthy population: a multicenter retrospective study. *Cancers* 2019;11(5):733.
9. Li TT, Liu H, Yu J, Shi GY, Zhao LY, Li GX. Prognostic and predictive blood biomarkers in gastric cancer and the potential application of circulating tumor cells *World J. Gastroenterol* 2018;24(21):2236-46.
10. Chen XZ, Zhang WK, Yang K, Liu J, Wang L, Hu JK, et al. Correlation between serum CA724 and gastric cancer: multiple analyses based on Chinese population. *Mol Biol Rep* 2012;39(9):9031-39