Available online at www.medicinescience.org

ORIGINAL ARTICLE

Medicine Science International Medical Journal

Medicine Science 2025;14(3):864-9

Assessment of tumor biomarkers based on a Turkish city hospital's data

Gamze Gok[1], Salim Neselioglu[2]

[1]Ankara Bilkent City Hospital, Department of Medical Biochemistry, Ankara, Türkiye
[2]Ankara Yıldırım Beyazıt University, Faculty of Medicine, Department of Medical Biochemistry, Ankara, Türkiye

Received 03 March 2025; Accepted 20 May 2025
Available online 01 September 2025 with doi: 10.5455/medscience.2025.02.058

Abstract

Biomarkers can be objectively measured and evaluate the processes of normal biological pathogenic, and pharmacological answers to medications. This study aimed to evaluate the Cancer antigen 15-3 (CA 15-3); Cancer antigen 19-9 (CA 19-9); Cancer antigen 72-4 (CA 72-4); Cancer antigen 125 (CA 125); Carcinoembryonic antigen (CEA); Neuron-specific enolase (NSE), and their test requests in Ankara Bilkent City Hospital. All the results recorded between 01/01/2022 and 31/12/2022 were acquired from our hospital laboratory information system.136,043 tests, consisting of 28,132 CA 15-3, 37,543 CA 19-9, 3135 CA 72-4, 29,996 CA125, 36,788 CEA, and 449 NSE tests, were enrolled. The frequency of positive tumor markers were as follows: CA 15-3 U/mL (N=996, 3.5%), CA 19-9 U/mL (N=4716,12.6%), CA 72-4 U/mL (N=174, 5.6 %), CA125 U/mL (N=3488, 11.6%), CEA ng/mL (N=1699, 4.6%), NSE IU/ mL (N=396, 88.2%). Statistical differences in CA 15-3 U/mL(p<0.001), CA 19-9 U/mL (p=0.016), CA125 U/mL(p<0.001), CEA ng/mLp<0.001), and NSE IU/ Ml (p<.001) tests among genders, and statistical differences in CA 15-3(p<0.001), CA19-9 (p<0.001), CA 72-4 (p=0.038), CA125(p<0.001), CEA(p<0.001), NSE(p<0.01) among age intervals were observed. Our findings may indicate that; tumor biomarker tests may be requested with a low specific diagnosis purpose. Inappropriate testing orders for tumor biomarkers may increase the risk of false above-reference results. patient may experience fear and anxiety, hospital costs may increase. Clinicians should consider all these circumstances before requesting tumor biomarker tests.

Keywords: Cancer antigen 15-3, cancer antigen 19-9, cancer antigen 72-4, cancer antigen 125, carcinoembryonic antigen, neuron-specific enolase

Introduction

Clinical laboratories are health centers that provide modern and quality services [1]. Laboratory tests, an integral part of contemporary medicine, affect 70% of medical diagnoses [2]. The effectiveness of laboratory tests, an essential part of the healthcare system, is increasing daily [3]. The increase in the specificity and sensitivity of the tests, and decrease in turnover time, and being less invasive than other methods cause the laboratory test utilization increment [4].

Cancer usually occurs when normal cells transform into tumor cells, in their multistage period resulting in the lesions to malignant tumor progress [5]. The uncontrollable cell growth exceeds normal limits and may spread to other organs. In 2018, there were 9.6 million new cancer patients and nearly 8.2 million people died due to cancer [6]. Early diagnosis of cancer reduces cancer-related deaths [7]. New technological developments are making great efforts to detect it early. Cancer biomarkers can be any tumor cells of the body fluids and can assess the risk, diagnosis, and prognosis of the disease [8]. Showing cancer risk, early cancer diagnosis and tumor classification are aimed by biomarkers [7].

Biomarkers are "an objectively measurable and evaluated property that indicates normal biological processes, pathogenic processes, or pharmacological responses to a therapeutic intervention" [9]. A biomarker may be any kind of measurable thing that takes place in any part of the body and may help the disease prediction [10]. Tumor biomarkers are the substances produced by or in response to a tumor. They can be measured quantitatively or qualitatively by immunological, genomic, proteomic, and chemical methods. It can identify a tumor's presence and distinguish it from normal tissue. It may be helpful for the early diagnosis of cancer [11]. Concentrations of tumor biomarkers in body fluids may be high in levels [12].

Cancer antigen 15-3 (CA 15-3) is the favorite biomarker in breast cancer, it is valuable in monitoring treatment in patients who cannot be visualized by radiology. In metastasis, CA 15-3 should be accompanied by physical examination, diagnostic imaging, and clinical history [13]. Cancer antigen 19-9 (CA 19-9), is synthesized in pancreatic and bile duct cells, saliva, endometrium, stomach, and colon epithelial cells. It is found in small amounts in serum. It increases some benign gastrointestinal system diseases, and a

CITATION
Gok G, Neselioglu S. Assessment of tumor biomarkers based on a Turkish city hospital's data. Med Science. 2025;14(3):864-9.

Corresponding Author: Gamze Gok, Ankara Bilkent City Hospital, Department of Medical Biochemistry, Ankara, Türkiye
Email: gamze_gok@outlook.com

DOI: 10.5455/medscience.2025.02.058

dramatic increment of CA19-9 takes place in neoplastic diseases [14]. Increased levels of Cancer antigen 72-4 (CA 72-4), have an effective role in diagnosing cancers of the ovary, cervix, and endometrium [15]. Evaluating CA72-4 potentially presents information about cancer recurrence however its measurement is not helpful enough for the early stage of cancer [16].

Cancer antigen 125 (CA125) is synthesized in the peritoneum, pleura, endometrium, and pericardium lining epithelial cells. It is also synthesized in epithelial ovarian cancers. This marker is used in the suspicion of ovarian neoplasm and the follow-up of treatment in epithelial ovarian cancer patients [17]. In preoperative endometrial cancer patients, it presents information about the disease's spread [18]. Carcinoembryonic antigen (CEA) plays a role in diagnosing colorectal cancer and evaluating response to treatment. The elevation in CEA is in line with colorectal cancer progression and a decrease in CEA is expected after surgical treatment [19]. Neuron-specific enolase (NSE), exists in specific tissues but its levels increase in malignancy, it is valuable for the diagnosis, determining the stage, and following-up treatment of neuroendocrine tumors. It is the most reliable tumor marker for small-cell lung cancer. NSE levels increase in all stages of neuroblastomas [20].

The increased demand for laboratories and workload in laboratories has brought about the Ùpossibility of inappropriate use of laboratory tests [1]. The purpose of our study is to evaluate the tumor biomarkers requested in Ankara Bilkent City Hospital. To the best of authors knowledge, our study is the first to include the test results of CA 15-3, CA 19-9, CA 72-4, CA 125, CEA, and NSE together and presenting their big data.

Material and Methods

The data of CA 15-3, CA 19-9, CA 72-4, CA 125, CEA, and NSE tests recorded from 01/01/2022 to 31/12/2022 were acquired the laboratory information system. CA 15-3, CA 19-9, CA125, and CEA tests were performed in our hospital with Atellica® (Siemens Healthineers, Erlangen, Germany) device. CA 72-4 and NSE tests were performed at the external laboratory contracted with our hospital. CA 15-3, CA 19-9, CA 125 and CEA were all measured with a two-step sandwich immunoassay method using direct chemiluminescence technology. All measurements show a direct proportion between the analyte and the light amount detected by the system.

The present study evaluated the test results according to the reference ranges specified in our hospital's laboratory information system. For each test, values over its reference range's upper value were considered positive. The cancer biomarkers' upper values of their references were as follows 32.4 U/mL for CA 15-3, 30.9 U/mL for CA 19-9, for CA 72-4, 30.2 U/mL for CA125, 5ng/mL for CEA, 6.9 IU/ mL for NSE. The present stuy is conducted in line with the Declaration of Helsinki. Ethics Committee of the Ankara Bilkent City Hospital approved the present study (Date: 09/08/2023, Number: E2-23-4617).

Statical Analyses

IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp., Armonk, NY, USA), was used for statistical analyses. Numbers and percentages were used, and chi-square tests were performed for categorical analyses. A p-value <0.05 was considered statistically significant.

Results

136,043 tests, consisting of 28,132 CA 15-3, 37,543 CA 19-9, 3135 CA 72-4, 29,996 CA125, 36,788 CEA, and 449 NSE tests, were enrolled. The numeral variables are presented in Table 1, Frequency of test requests in benign and malign diseases in Table 2, Tumor biomarker tests among genders in Table 3, and Tumor biomarker tests among age intervals in Table 4. In the present study the most requested malign preliminary diagnoses for positive tumor markers were as follows: breast malign neoplasm (N=152, 41.8%), over malign neoplasm (N=52, 14.3%) endometrium malign neoplasm (N=16, 4.4%) for CA 15-3, colon malign neoplasm (N=189, 20.3 %), gastric malign neoplasm (N=141, 15.1%), pancreatic malign neoplasm (N=113, 12.1%) for CA 19-9, gastric malign neoplasm (N=2, 40%), over malign neoplasm (N=1, 20%), prostate malign neoplasm (N=1, 20%) for CA 72-4, over malign neoplasm (N=142, 23.8%), endometrium malign neoplasm (N=60, 10%), breast malign neoplasm (N=56, 9.4%) for CA 125, colon malign neoplasm (N=167, 21.4%), gastric malign neoplasm (N=12015.4%), breast malign neoplasm (N=106, 13.6%) for CEA, and peripheral nerves malignant neoplasm (N=19, 35.2%), adrenal gland malignant neoplasm (N=8, 33.3%), connective and soft tissue malignant neoplasm (N=3, 5.6%) for NSE. Figures 1, 2, 3, 4, 5, and 6 show test results for gender, age, and frequency of CA 15-3, CA 19-9, CA 72-4, CA 125, CEA, and NSE, respectively.

Table 1. Numeral variables

		N	%
Gender	**Female**	96544	71
	Male	39499	29
Age (years)	**0-14**	486	0.4
	15-35	18324	13.5
	36-56	52094	38.3
	57-77	54576	40.1
	Over 78	10563	7.7
CA 15-3 U/mL	**Negative**	27136	96.5
	Positive	996	3.5
CA 19-9 U/mL	**Negative**	32827	87.4
	Positive	4716	12.6
CA 72-4 U/mL	**Negative**	2961	94.4
	Positive	174	5.6
CA125 U/mL	**Negative**	26508	88.4
	Positive	3488	11.6
CEA ng/mL	**Negative**	35089	95.4
	Positive	1699	4.6
NSE IU/ mL	**Negative**	53	11.8
	Positive	396	88.2

CA 15-3: cancer antigen 15-3, CA19-9: cancer antigen 19-9, CA 72-4: cancer antigen 72-4, CA125: cancer antigen 125, CEA: carcinoembryonic antigen, NSE: neuron-specific enolase

DOI: 10.5455/medscience.2025.02.058

Table 2. Frequency of test requests in bening and malign diseases

		Frequency of test requests			
		Benign diseases		Malign diseases	
		N	%	N	%
CA 15-3 U/mL	Negative	22658	97.3	4478	92.5
	Positive	632	2.7	364	7.5
CA 19-9 U/mL	Negative	28380	88.2	4447	82.7
	Positive	3783	11.8	933	17.3
CA 72-4 U/mL	Negative	2943	94.6	18	78.3
	Positive	169	5.4	5	21.7
CA125 U/mL	Negative	23355	89.0	3153	84.1
	Positive	2893	11.0	595	15.9
CEA ng/mL	Negative	28030	96.8	7059	90
	Positive	919	3.2	780	10
NSE IU/mL	Negative	46	11.9	7	11.5
	Positive	342	88.1	54	88.5

CA 15-3: cancer antigen 15-3, CA19-9: cancer antigen 19-9, CA 72-4: cancer antigen 72-4, CA125: cancer antigen 125, CEA: carcinoembryonic antigen, NSE: neuron-specific enolase

Table 3. Tumor biomarker tests among genders

		Gender		p
		Female	Male	
		n (%)	n (%)	
CA 15-3 U/mL	Negative	21632 (97)	5504 (94.6)	<.001*
	Positive	679 (3)	317 (5.4)	
CA 19-9 U/mL	Negative	21387 (87.7)	11440 (86.9)	.016*
	Positive	2988 (12.3)	1728 (13.1)	
CA 72-4 U/mL	Negative	1582 (94.8)	1379 (94.1)	.378
	Positive	87 (5.2)	87 (5.9)	
CA125 U/mL	Negative	20773 (88.6)	5735 (87)	<.001*
	Positive	2632 (11.2)	856 (13)	
CEA ng/mL	Negative	23753 (96.7)	11336 (92.8)	<.001*
	Positive	820 (3.3)	879 (7.2)	
NSE IU/mL	Negative	37 (17.5)	16 (6.7)	<.001*
	Positive	174 (82.5)	222 (93.3)	

CA 15-3: cancer antigen 15-3, CA19-9: cancer antigen 19-9, CA 72-4: cancer antigen 72-4, CA125: cancer antigen 125, CEA: carcinoembryonic antigen, NSE: neuron-specific enolase, p: Chi-squared test, *: a statistically significant p-value

Table 4. Tumor biomarker tests among age intervals

		Age intervals					p
		0-14	15-35	36-56	57-77	Over 78	
		n (%)	n (%)	n (%)	n (%)	n (%)	
CA 15-3 U/mL	Negative	37 (100)	3833 (99.3)	10952 (97.5)	10312 (95)	2002 (92.7)	<.001*
	Positive		27 (0.7)	277 (2.5)	534 (5)	158 (7.3)	
CA 19-9 U/mL	Negative	40 (83.3)	4200 (85.5)	12743 (90.4)	13504 (86.8)	2340 (79.6)	<.001*
	Positive	8 (16.7)	710 (14.5)	1347 (9.6)	2050 (13.2)	601 (20.4)	
CA 72-4 U/mL	Negative	1 (100)	524 (96.7)	963 (95.1)	1135 (93.4)	338 (92.9)	.038*
	Positive		18 (3.3)	50 (4.9)	80 (6.6)	26 (7.1)	
CA125 U/mL	Negative	48 (85.7)	3919 (87.4)	10876 (90)	9927 (88.9)	1738 (78.4)	<.001*
	Positive	8 (14.3)	563 (12.6)	1203 (10)	1235 (11.1)	479 (21.6)	
CEA ng/mL	Negative	46 (100)	4387 (99.6)	13281 (97.2)	14794 (93.7)	2581 (89.7)	<.001*
	Positive		17 (0.4)	389 (2.8)	997 (6.3)	296 (10.3)	
NSE IU/ mL	Negative	19 (6.4)	22 (17.5)	4 (30.8)	4 (50)	4 (100)	<.001*
	Positive	279 (93.6)	104 (82.5)	9 (69.2)	4 (50)		

CA 15-3: cancer antigen 15-3, CA19-9: cancer antigen 19-9, CA 72-4: cancer antigen 72-4, CA125: cancer antigen 125, CEA: carcinoembryonic antigen, NSE: neuron-specific enolase, p: Chi-squared test, *: a statistically significant p-value

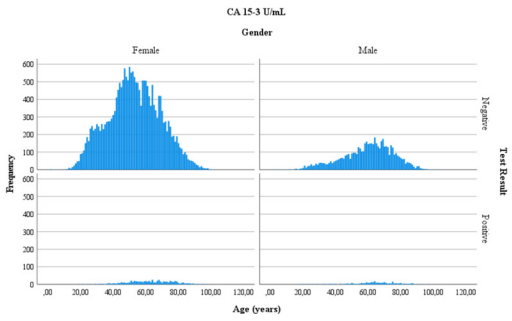

Figure 1. Cancer antigen 15-3 (CA 15-3) tests by tests by gender, age, and frequency

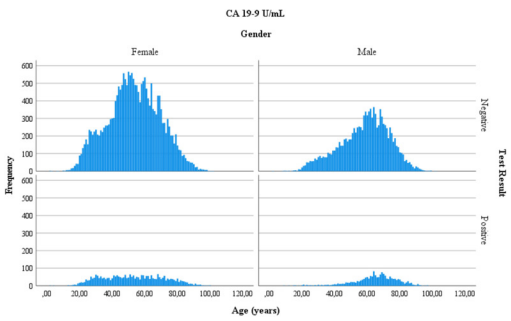

Figure 2. Cancer antigen19-9 (CA 19-9) tests by gender, age, and frequency

DOI: 10.5455/medscience.2025.02.058

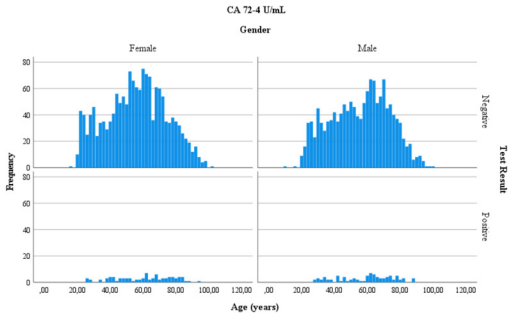

Figure 3. Cancer antigen 72-4 (CA 72-4) tests by gender, age, and frequency

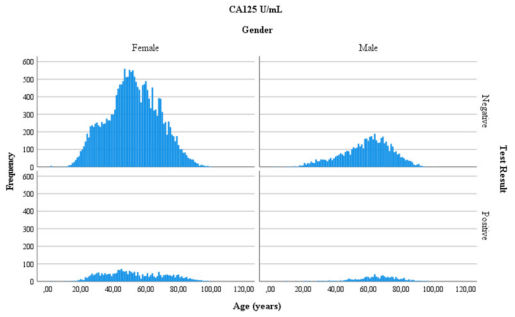

Figure 4. Cancer antigen 125 (CA125) tests by gender, age, and frequency

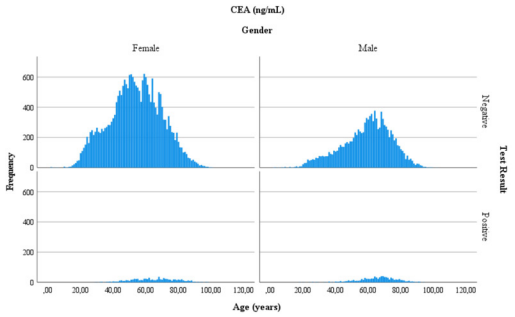

Figure 5. Carcinoembryonic antigen (CEA) tests by gender, age and frequency

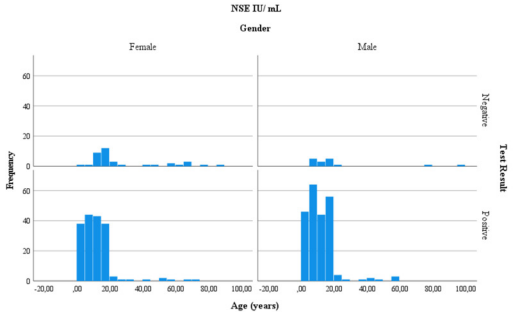

Figure 6. Neuron-specific enolase (NSE) tests by gender, age, and frequency

Discussion

Tumor markers are rarely diagnostic and cannot replace biopsy for primary cancer diagnosis [21]. The targets of tumor biomarkers are as follows: they must be synthesized at a minimum level in other tissues and cancers, they must show different immunological properties when synthesized in other tissues and cancers, they must be synthesized in proportion to the tumor mass and tumor activity, and they must be in measurable amounts even in a minimal cancer mass [22]. However, no ideal tumor biomarker exists [23].

No consensus was stated for the utilization of CA 15-3 in cancer. Its levels rarely increase in individuals with localized disease or the early stages [13]. CA 15-3 has been reported to be one of the two strongest predictors in primary breast cancer patients [24]. Another study reported that elevated levels of CA 15-3 at baseline were associated with a very poor prognosis in both early and late-stage disease [25]. CA19-9 is a biomarker for the malignancies of the pancreas and stomach but is still not suggested in malignancy diagnoses [26]. In the study conducted by Li et all, it was stated that CA72-4 and CA15-3 levels were high in endometrial, ovarian, and cervical cancers [27].

In the study conducted by Katar, the frequency of positive tumor markers was as follows: 312 (22%) for CEA, 202 (30.1%) for CA 15-3, 204 (23.5%) for CA 19-9, and 113 (19.3%) for CA 125 [28]. In line with Katar's study, we observed lower frequency in all positive tumor markers except NSE and they were as follows: CA 15-3 U/mL (N=996, 3.5%), CA 19-9 U/mL (N=4716,12.6%), CA 72-4 U/mL (N=174, 5.6 %), CA125 U/mL (N=3488, 11.6%), CEA ng/mL (N=1699, 4.6%), NSE IU/mL (N=396, 88.2%) (Table 1).

In the study conducted by Cure et al, 1858 CA 19-9 test requests comprised 10.3% malignant and %89.7 benign diseases, 1710226 CEA test requests comprised 13.2% malignant, and 1484 86.8% benign diseases, 1449 CA 15-3 test requests comprised 12% malignant and 1275 88% benign diseases [29]. In the present study, the frequency of test requests in benign and malign diseases is presented in Table 2. We also want to underline the frequency of malign diseases for positive tumor biomarkers and they were as follows: CA 15-3 U/mL (N=364, 7.5%), CA 19-9 U/mL (N=933, 17.3%), CA 72-4 U/mL (N=5, 21.7%), CA125 U/mL (N=595, 15.9%), CEA ng/mL(N=780, 10.0%), NSE IU/ mL (N=54, 88.5%) (Table 2).

In the study conducted by Katar; statistical difference was stated between genders in CEA ($p<0.001$) and CA 125 ($p=0.033$) tests. The positive and negative CEA ($p<0.001$) and CA 125 ($p<0.001$) test results presented significant differences among age intervals [28]. Some of our findings aligned with the previous study [28]. We observed statistical differences in CA 15-3 U/mL ($p<0.001$), CA 19-9 U/mL ($p=0.016$), CA125 U/mL ($p<0.001$), CEA ng/mL $p<0.001$), and NSE IU/Ml ($p<.001$) tests among genders (Table 3). We observed statistical differences in all tumor biomarkers among age intervals and they were as follows: CA 15-3 ($p<0.001$), CA19-9 ($p<0.001$), CA 72-4 ($p=0.038$), CA125 ($p<0.001$), CEA ($p<0.001$), NSE ($p<0.01$) (Table 4).

In the present study, the most requested malign preliminary diagnoses for positive tumor markers were aligned with some previous studies [13-20].

The strong properties of our work are as follows: The data were obtained from one of the biggest medical biochemistry laboratories in Europe. The most requested malign preliminary diagnoses for positive tumor biomarkers and the frequency of

DOI: 10.5455/medscience.2025.02.058

test requests in benign and malignant diseases were shared. Big data including different tumor biomarkers were evaluated according to age intervals gender, and positivity. The limitations of the present study are as follows: 2.5 ng/mL is the limit value for smokers while 5 ng/mL is the limit value for non-smokers for positive CEA, in our study, there was not enough information about smoking in the hospital information system, so CEA was accepted as positive if it was above 5ng/mL. Patients' medication information could not be accessed.

Conclusion

Laboratory tests are part of clinical decision-making but may not always be appropriate [30]. Laboratories are among the units that use technology best in the hospital. The increased demand for laboratories and workload in laboratories has brought about the possibility of inappropriate use of laboratory tests [1]. Test orders for tumor biomarkers are not standardized [1]. Many studies have shown that utilizing laboratory tests with low diagnostic value is widespread and constitutes a significant portion of health expenditures [31-33]. Inappropriate testing orders for tumor biomarkers may increase the risk of false above-reference results. Retesting may be performed for confirmation of the high results and procedures such as imaging and surgical intervention may be applied to the patient to exclude the disease. While the patient may experience fear and anxiety, hospital costs may increase [34]. Our findings may indicate that; tumor biomarker tests may be requested with a low specific diagnosis purpose. Clinicians may request unnecessary tests for defensive medical practices, legal self-protection purposes, or malpractice lawsuits [35] but they should consider all these circumstances before requesting tumor biomarker tests.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical Approval
Ethic Committee of the Ankara Bilkent City Hospital approved the present study (Date:09/08/2023, Number: E2-23-4617).

References

1. Gion M, Franceschini R, Rosin C, et al. An epidemiology-based model to estimate the rate of inappropriateness of tumor marker requests. Clin Chem Lab Med. 2014;52:889-97.
2. Signorelli H, Straseski JA, Genzen JR, et al. Benchmarking to identify practice variation in test ordering: a potential tool for utilization management. Lab Med. 2015;46:356-64.
3. Forsman RW. Why is the laboratory an afterthought for managed care organizations?. Clinical Chem. 1996;42:813-6.
4. Liang BA, Mackey T. Direct-to-consumer advertising with interactive internet media: global regulation and public health issues. JAMA. 2011;305:824-5.
5. Baran Deniz E. Cancer epidemiology. SOYD. 2022;3:102-11.
6. Crulhas BP, Basso CR, Castro GR, Pedrosa VA. Recent advances based on a sensor for cancer biomarker detection. ECS J. Solid State Sci. Technol. 2021;10:047004.
7. Tuncer Z. Biomarkers. Gevher Nesibe Journalof Medical & Health Sciences. 2023;8:366-70.
8. Wu L, Qu X. Cancer biomarker detection: recent achievements and challenges. Chem Soc Rev. 2015;44:2963-97.
9. Fuentes-Arderiu X. What is a biomarker? It's time for a renewed definition. Clin Chem Lab Med. 2013;51:1689-90.
10. Lassere MN. The Biomarker-Surrogacy Evaluation Schema: a review of the biomarker-surrogate literature and a proposal for a criterion-based, quantitative, multidimensional hierarchical levels of evidence schema for evaluating the status of biomarkers as surrogate endpoints. Stat Methods Med Res. 2008;17:303-40.
11. Srinivas PR, Kramer BS, Srivastava S. Trends in biomarker research for cancer detection. Lancet Oncol. 2001;2:698-704.
12. Chan DW, Schwartz M. Tumor markers: Introduction and general principles. In: Diamandis EP, Fritsche H, Jr Lilja H, et al. eds. Tumor markers: physiology, pathobiology, technology, and clinical applications. Washington, D.C.: AACC Press. 2002;9–18.
13. Duffy MJ, Evoy D, McDermott EW. CA 15-3: uses and limitation as a biomarker for breast cancer. Clin Chim Acta. 2010;411:1869-74.
14. Scarà S, Bottoni P, Scatena R. CA 19-9: biochemical and clinical aspects. Adv Exp Med Biol. 2015:247-60.
15. Xu Y, Zhang P, Zhang K, Huang C. The application of CA72-4 in the diagnosis, prognosis, and treatment of gastric cancer. Biochim Biophys Acta Rev Cancer. 2021;1876:188634.
16. Roşu MC, Ardelean A, Moldovan SD, et al. The importance of CA 72-4 and CA 19-9 dosing in gastric cancer. Journal of medicine and life. 2023;16:186-8.
17. Gandhi T, Zubair M, Bhatt H. Cancer Antigen 125. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024.
18. Powell JL, Hill KA, Shiro BC, et al. Preoperative serum CA-125 levels in treating endometrial cancer. J Reprod Med. 2005;50:585-90.
19. Campos-da-Paz M, Dórea JG, Galdino AS, et al. Carcinoembryonic antigen (CEA) and hepatic metastasis in colorectal cancer: update on biomarker for clinical and biotechnological approaches. Recent Pat Biotechnol. 2018;12:269-79.
20. Isgrò MA, Bottoni P, Scatena R. Neuron-specific enolase as a biomarker: biochemical and clinical aspects. Adv Exp Med Biol. 2015:125-43.
21. Rifai N. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics-E-Book. 5th edition. Elsevier Health Sciences. 2011;616-61.
22. Onat T, Emerk K, Sözmen EY. İnsan biyokimyası. Palme Publishing. Ankara. 2002;711.
23. Duffy MJ. Tumor markers in clinical practice: a review focusing on common solid cancers. Med Princ Pract. 2012;22:4-11.
24. Kumpulainen EJ, Keskikuru RJ, Johansson RT. Serum tumor marker CA 15.3 and stage are the two most powerful predictors of survival in primary breast cancer. Breast Cancer Res Treat. 2002;76:95-102.
25. McLaughlin R, McGrath J, Grimes H, Given H. The prognostic value of the tumor marker CA 15–3 at initial diagnosis of patients with breast cancer. Int J Biol Markers. 2000;15:340-2.

DOI: 10.5455/medscience.2025.02.058

26. Galli C, Basso D, Plebani M. CA 19-9: handle with care. Clinical chemistry and laboratory medicine. 2013;51:1369-83.

27. Li M, Men X, Zhang X. Diagnostic value of carbohydrate antigen 72-4 combined with carbohydrate antigen 15.3 in ovarian cancer, cervical cancer and endometrial cancer. J BUON. 2020;25:1918-27.

28. Katar M. Evaluation of tumor marker test requests in a hospital setting. International Journal of Medical Biochemistry. 2021;4:8-13.

29. Cure MC, Cure E, Kirbas A, Yazici T, Yuce S. Requests for tumor marker tests in Turkey without indications and frequency of elevation in benign conditions. Asian Pacific Journal of Cancer Prevention. 2012;13:6485-9.

30. Müskens JL, Kool RB, van Dulmen SA, Westert GP. Overuse of diagnostic testing in healthcare: a systematic review. BMJ Qual Saf. 2022;31:54-63.

31. Yeh DD. A clinician's perspective on laboratory utilization management. Clin Chim Acta. 2014;427:145-50.

32. Bruce Alexander C. Message from the President: reducing healthcare costs through appropriate test utilization. Critical Values. 2012;5:6-9.

33. Xu S, Hom J, Balasubramanian S, et al. Prevalence and predictability of low-yield inpatient laboratory diagnostic tests. JAMA Netw Open. 2019;2:e1910967. Erratum in: JAMA Netw Open. 2019;2:e1914190.

34. Gion M, Rampazzo A, Mione R, Bruscagnin G. Cost/effectiveness ratio of carcinoembryonic antigen-importance of adequacy of routine requests of tumor markers. Int J Biol Markers. 1992;7:179-82.

35. Fidan Y, Öztürk YE, Özdemir M, Ayan U. Retrospective analysis of unnecessary test prompts in terms of rational use of laboratory: serology laboratory case. İşletme Bilimi Dergisi. 2016;8:283-305.