GEVHER NESIBE JOURNAL OF MEDICAL & HEALTH SCIENCES | ISSN 2717-7394

Arrival Date: 13.11.2021 | Published Date: 25.01.2022 | 2022, Vol: 7, Issue: 16 | pp: 69-74 | Doi Number: http://dx.doi.org/10.46648/gnj.320

Cancer Screening Tests, Diagnostic Methods and Cancer Vaccines

Kanser Tarama Testleri, Tanı Yöntemleri ve Kanser Aşıları

Gizem Polat[1], Hatice Kübra Yılmaz[2], Çiğdem Yıldırım Maviş[3]

ABSTRACT

Cancer is one of the most common causes of death in the world, observed with the uncontrolled growth of abnormal cells in any part of the body. Early diagnosis with screening programs in individuals with no suspicion of cancer or with the precancerous is important in terms of increasing the quality of life of the patient and taking precautions against the risks that may occur in the future. Early diagnosis of cancer using various diagnostic methods increases the success of treatment. Immunotherapy methods that strengthen the immune system and initiate a new era in anticancer therapy are used in the treatment. This method involves changing a patient's immune cells using biotechnology. Cancer vaccines are one of the therapeutic methods that are frequently studied recently and can develop a clinical response that can completely cure the disease. The vaccine creates an antitumor immune response in individuals with cancer, prevents cancer-causing viruses and infections, and reduces the risk of cancer development in some high-risk individuals.

Keywords: Cancer, screening tests, diagnostic methods, immunotherapy, cancer vaccines

ÖZET

Kanser, vücudun herhangi bir bölgesinde anormal hücrelerin kontrolsüz büyümesi ile gözlemlenen, dünyada en sık rastlanan ölüm nedenlerinden biridir. Kanser şüphesi bulunmayan veya prekanseröz bireylerde tarama programlarıyla erken teşhisin sağlanması, hastanın hayat kalitesinin artırılması ve ileri dönemlerde oluşabilecek risklere karşı önlem alınması açısından önem taşır. Kanserin çeşitli tanı yolları kullanılarak erken teşhisi tedaviye olan başarıyı artırır. Tedavide immün sistemi güçlendiren ve antikanser tedavide yeni bir çağ başlatan immünoterapi yöntemlerinden yararlanılmaktadır. Bu yöntem biyoteknoloji kullanılarak hastaların kendi bağışıklık hücrelerinin değiştirilmesini içerir. Kanser aşıları, son dönemde üzerinde sıklıkla çalışılan, hastalığı tamamen tedavi edebilecek klinik yanıt geliştirebilen terapötik yöntemlerden biridir. Aşı, kanserli bireylerde antitümör bağışıklık tepkisi oluşturmakla beraber kansere neden olan virüs ve enfeksiyonları önler ve bazı yüksek riskli bireylerde kanser gelişim riskini azaltır.

Anahtar kelimeler: Kanser, tarama testleri, tanı yöntemleri, immünoterapi, kanser aşıları

1.Introduction

Cancer is a chronic disease for which there is no definitive cure, with more than 14 million people diagnosed each year, mostly in low- and middle-income countries. It is among the leading causes of death in the world after cardiovascular diseases (1). Early diagnosis is important to ensure success in the treatment process of cancer and to offer a better quality of life to the individual. Early diagnosis is possible with the use of correct diagnostic methods and regular participation in screening programs (2). A comprehensive National Cancer Control Program conducts cost-effective studies covering the majority of the population to control the disease. The principles of the National Cancer Control Program include giving importance to cancer prevention programs, early detection and treatment of cases, development of treatment guidelines, symptom control, and providing high comfort life quality to advanced patients (3). Studies on cancer treatment are continuing rapidly today, and cancer vaccines have recently become one of the most studied therapeutic methods. The preference for this method, which aims to destroy cancer cells by strengthening the immune system of the individual, is increasing day by day. The study aims to examine the diagnostic and therapeutic

[1] Undergraduate Student, Haliç University, Faculty of Health Sciences, Department of Nutrition and Dietetics, İstanbul/Turkey, info@gizempolat.com, ORCID: 0000-0003-2036-9633

[2] Lecturer, Haliç University, Faculty of Health Sciences, Department of Nutrition and Dietetics, İstanbul/Turkey, kubrayilmaz@halic.edu.tr, ORCID: 0000-0001-7750-6024

[3] Asst. Prof. Dr., Haliç University, Faculty of Health Sciences, Department of Nutrition and Dietetics, İstanbul/Turkey, cigdemyildirim@halic.edu.tr, ORCID: 0000-0002-5442-5851

methods that play an important role in the treatment process within the current knowledge.

2. Cancer

Cells constantly renew themselves for the sustainability of life. Cells that have expired of their life are removed from the body by apoptosis and replaced by new cells. Genes control this balance. While some genes are responsible for the division and proliferation of cells, another part prevents excessive cell reproduction. Sometimes, one or more of the cell control mechanisms are disrupted as a result of some environmental factors or changes in DNA and genes and begin to divide uncontrollably. Thus, it produces a pathology that is not normal and much more cells than necessary. The condition that develops with the uncontrolled growth and spread of these abnormal cells is defined as cancer (4). Healthy cells have limited dividing potential. After dividing 20-40 times on average, it loses its ability to divide. Tumors must divide more than this number for cancer to occur. Tumor cells gain immortality by developing mechanisms that increase their ability to divide. Tumor cells can be benign or malignant. Benign tumors are tumors that can be removed from the body, often do not recur, do not show metastasis, and are rarely life-threatening. For cancer to occur, it must also have malignant features such as invasion (invasion of other healthy tissues) and metastasis (spread to other healthy tissues either directly or through blood-lymph vessels) (5). Malignant tumors require the initiation of the treatment process for the individual as soon as possible.

2.1. Diagnosis in Cancer

Accurate diagnosis is crucial for detecting cancer at an early stage. Early diagnosis defines as the early detection of cancer in patients with symptoms of the disease. Thanks to early diagnosis, the probability of success in cancer treatment are increased (2,6). The focus of early detection of cancer is on people with symptoms and signs consistent with cancer. The aim is to detect the disease at the earliest possible opportunity and start diagnosis and treatment without delay. When done promptly, cancer can be detected at a potentially curable stage. This condition can improve survival and quality of life (2). Screening tests used in diagnosing cancer and determining the stages are diverse and vary according to the type of cancer. Staging defines where cancer is located, where it has metastasized, and whether it affects other organs in the body. Knowing the stage of cancer helps the physician to determine the right treatment method and to predict the course of the disease. Various systems are used for staging today. The most widely used of these is the TNM (tumour-node-metastasis) system prepared and approved by AJCC (American Joint Committee on Cancer) and IUCC (Cancer Control Organization). The functioning of the TNM system is described in Table.1 (4,7).

Table 1. TNM (tumor-node-metastasis system) (4,7)

T (tumor)	It describes the size of the primary tumor and where it is located.
N (node)	Categorize the spread of the tumor to the axillary lymph nodes.
M (metastasis)	Indicates whether cancer has spread (metastasized) to other parts of the body.

TNM results are combined and, the stage of cancer from 1 to 4 (I, II, III, IV) is determined. A diagnosis of stage 0 means that cancer is limited to where it started and has not spread to surrounding tissues (7).

2.1.1 Screening tests

Screening tests aim to identify unrecognized cancer or its precursor lesions in a healthy, asymptomatic population through procedures, examinations (e.g. VIA visual inspection with acetic acid), imaging (e.g. mammography), or tests that are rapidly applicable and widely available to the target population (e.g. HPV testing). Screening differs from early detection because the entire target population is evaluated for unspecified cancer or precancer, and most of the individuals tested do not have the disease. It has been noted that cancer screening programs reduce incidence and mortality. Screening should be viewed as a process, not as administering a particular test, exam, or procedure. Screening tests are managed in 3 stages:

i. follow-up of test results and referral for further testing among those with abnormal test results,
ii. timely pathological diagnosis with routine evaluation to improve the process,
iii. staging and ensuring access to effective treatment.

The screening program includes the process from the beginning of screening to treatment and requires planning, coordination, monitoring, and evaluation. Before starting or scaling up a program for early cancer detection or screening an evidence-based assessment of existing capacity and potential benefits should be made (2).

Table 2. Evaluation of early diagnosis and screening tests within specific parameters (2)

Parameter	Early Diagnosis	Screening
The number of participants	It is restricted to individuals with suspected symptoms of cancer.	Entire target population (50-100 times more participants than early diagnosis)
Health system requirements	Facilities for timely clinical diagnosis, pathology, radiology, staging, access to rapid treatment	Health system requirements for early detection, significant additional resources to invite and test the entire target population, recall mechanism, systematic evaluation, and additional diagnostic testing for all people who screen positive
Potential benefits	Reduction in disease stage at diagnosis Death, usually within three to five years, when associated with treatment	Potential reduction in target population if the precursor is detected and treated by screening (e.g, cervical and colorectal cancers) In the target population, reduction in disease stage at diagnosis (usually earlier than early diagnosis) Reduction in mortality when screening is effective and linked to treatment (usually >10 years)

Colorectal cancer early detection programs have been shown to reduce the death rate and incidence of this cancer (8). Pandemic processes can affect cancer screenings. In 2020, it was reported that in a group that underwent selective colorectal cancer screening (CRCS) during the COVID-19 pandemic and quarantine process, more colorectal cancers were detected with less examination during the quarantine process and general compliance with CRCS decreased (9).

2.1.2. Diagnostic methods

There are many methods to diagnose cancer. These methods are constantly being developed and revised by researchers. The first step is to request appropriate tests to confirm the diagnosis. Laboratory tests, pathological results and imaging methods are the most common diagnostic methods.

1. Physical examination: The physical examination method can be used for changes in skin color, enlargement or shrinkage of a specific area, or pain sensation.

2. Laboratory tests: Cancerous cells can increase or decrease the blood values of some molecules in our body. The physician may request that samples be taken from blood, urea, sputum or other body fluids in order to check the values of these compounds. Although laboratory tests are one of the primary methods used for diagnosis, they cannot be used alone as a competent method.

3. Complete Blood Count (Hemogram): It is especially used in the diagnosis of leukemia. In this method, known as complete blood count, the number and type of unusual white blood cells, percentage of total blood volume, hemoglobin, number, and size of red blood cells are determined (4).

4. Genetic tests: The cause of cancer is mutations in our genes for various reasons. Predisposition to cancer types can be determined by genetic tests. Since cancer types can develop due to specific gene mutations, each type of cancer is associated with a different gene mutation. BRCA-1 and BRCA-2 gene mutations ovarian and breast cancer, EGFR-1 gene mutation pancreatic, lung, head and neck cancer, HER-2 gene mutation ovarian, lung, stomach, uterus, breast cancer, RAS gene mutation colorectal (large intestine), head and neck cancer, EML4-ALK fusion gene lung cancer, BRAF gene mutation colorectal, malignant melanoma, lung cancer, MDR1, MDR2, MRP1, MRP2, cytidine deaminase, thymidylate synthase gene expression analysis are used as a marker for lung cancer (10).

5. Cytogenetic Analysis: Chromosomes taken from different tissues are analyzed. Routine cytogenetic analysis method should be used in diagnosis, determination of prognosis, and treatment in cases with suspected leukaemia or which may develop into leukaemia. The diagnosis is made by observing the changes in the number and structure of existing chromosomes in bone marrow cells and white blood cells taken from the patient, and their roles in heredity. FISH (Fluorescent In Situ Hybridization) technique, which was developed as an alternative due to the limitations of the cytogenetic analysis method, is an effective method in the pre-diagnosis of both haematological and solid tumors and in determining the chromosomal aberrations of the cases under follow-up. rRNA Using probes targeting rRNA allows phylogenetic identification of mixed-state microorganisms from direct samples by epifluorescent microscopy, confocal laser scanning microscope or flow cytometry without resorting to culture methods. The application of the FISH method is easy and practical, the cost per patient is cheaper than PCR and conventional culture methods, the identification time is relatively short (approximately 2-3 hours), and it is a more effective method (4,11).

6. Immunophenotyping: It is the examination performed to examine a specific cell type in blood, bone marrow, lymph node cells. It uses in the diagnosis, observation, and treatment of haematological disorders, lymphoma, leukaemia, myelodysplastic myeloproliferative disorders. With this method, it can be determined whether the cells in the patient are monoclonal (sourced from a single malignant cell) (4).

7. Biopsy: It defines as the pathological examination under the microscope by taking a small tissue sample from the lesion thought to be cancerous by surgical procedure. Depending on the tumor location, different types of biopsy can be performed. Fine needle biopsy is usually in thyroid nodules, trust biopsy (thick needle), which is the most commonly used method, is generally used for lung, breast tumors etc., together with fine needle biopsy, excisional biopsy (removal of the tumor by surgical method) in the removal of the lymph node in suspected lymphoma, vacuum-assisted biopsy (VDB) is increasingly used in the diagnosis of suspicious breast lesions (12).

8. Endoscopy: It is the process of imaging the suspicious area through a tube with a light and camera at the end. It may be possible to provide an early diagnosis with endoscopy, especially in asymptomatic gastrointestinal system diseases. There are different endoscopy methods according to the parts of the body. Rectum and large intestine regions with colonoscopy, abdominal cavity with laparoscopy, endoscopic retrograde cholangiopancreatography (ERCP) method using duodenoscopes and pancreatic duct, double-balloon enteroscopy using gastroscope small intestine between the duodenum and large intestine, rectum with sigmoidoscopy method and colon, and inner part of breast milk ducts are examined by micro endoscopes. A biopsy or polyp may be removed during the procedure. In addition, with the capsule endoscopy method, the digestive system can be visualized and diagnosed using a capsule-shaped wireless camera (13).

9. Imaging Methods: It is a diagnostic method that enables to see of suspected abnormal structures in the body by using various radioactive energies, magnetic fields, or rays. Imaging methods may differ according to the suspected area. It can help with early detection, staging, recurrence (whether cancer recurs after treatment), or treatment planning.

Examples of imaging methods include computed tomography (CT), magnetic resonance imaging (MR), mammography, radiographic studies (normal x-ray and contrast studies), nuclear scans, ultrasound, computed tomography scan (CAT), radiography/fluoroscopy (4).

10. Other Diagnostic Methods: Some diseases can be diagnosed with a single test. For example, the PSA-1 test is used as a prostate cancer marker. The PAP-smear test is an important marker in the detection of cervical cancer.

3. Immunotherapy

There are various treatment methods applied in cancer patients. Immunotherapy is a form of treatment in which certain parts of the patient's immune system are used to combat a group of diseases, including cancer. The purpose of this system is to strengthen the immune system cells and enable them to destroy cancer cells. Monoclonal antibodies, immune system control inhibitors, cancer vaccines, adoptive immunotherapy can be shown as mechanisms that affect these pathways. It is stated that, with the increasing interest in immunotherapy and the increase in studies in this field, since it does not harm healthy cells by directly targeting cancer cells, immunotherapy may replace chemotherapy (14).

3.1. Cancer Vaccines

Therapeutic cancer vaccines are based on stimulating the immune system by creating an attack against cancer cells with the patient's tumor cells or antigens. Vaccines may be in the form of recombinant proteins administered with adjuvants. The purpose of this method is to create an immune defence mechanism against the existing disease, instead of preventing the disease by providing the formation of CTL (cytotoxic T lymphocyte) against the tumor by imitating the normal pathway of cross-presentation of dendritic cells bearing and presenting tumor antigens. Another vaccination method is to give plasmids containing DNAs encoding tumor antigens to the patient and start to express these antigens in the patient's cells and antigen-presenting cells, thus providing an immunity and T cell response against them. The greatest benefit of vaccine studies is that they occur as the basis for studies on the use of monoclonal antibodies in cancer. Some vaccines directly prevent cancer. Vaccines developed against the human papillomavirus (HPV) help prevent cancer (15). It has been observed that co-administration of immunomodulators in biodegradable nanoparticles increases the therapeutic efficacy of cancer vaccines (16). New studies on cancer vaccines continue to be conducted and studied. Adjuvant-protein-antigen protein conjugates function as a novel cancer vaccine strategy. The situated adjuvant of the TLR7 agonist can reduce toxicities and increase immune stimulations, and three-in-one protein conjugates have been found to enhance potent immune responses against cancer cells (17). In a clinical study, a combination of cancer vaccine and immunotherapy drug specific to individuals in different cancer types was administered on patients, and it was observed that while 5 out of 10 patients developed clinical response, the disease was completely cured in 2 patients and their symptoms disappeared (18). Different strategies are applied to the development of cancer vaccines. In recent studies, it has been stated that mucin 1 (MUC1)-based cancer vaccines are a promising strategy to prevent cancer progression and metastasis (19). Sipuleucel-T (Provenge) is a cancer vaccine used in the treatment of advanced prostate cancer where hormone therapy does not help, and Talimogene laherparepvec (T-VEC) is a cancer vaccine used in the treatment of advanced melanoma skin cancer (20). TVEC is a type I herpes simplex virus that has been genetically modified to preferentially replicate in tumor cells, increase antigen loading of MHC class I molecules, and express granulocyte-macrophage colony-stimulating factor to increase tumor-antigen presentation by dendritic cells. It is the first oncolytic virus approved by the FDA with the indication of melanoma. Clinical studies investigating TVEC in melanoma are ongoing (21).

4. Results

When well designed and managed, National Cancer Control Programs (NCCP) help reduce the burden of cancer and improve services for cancer patients and their families. Early diagnosis using accurate diagnostic methods improves the course of cancer by providing prevention at the earliest possible stage, therefore it is an important public health strategy. Cancer treatment requires careful consideration of evidence-based options, which may include more than one of the major therapeutic modalities. Cancer vaccines, which continue to be studied, are promising to stop the disease and prevent the worsening course.

REFERENCES

1. Shao, W., Wang, T., Sun, L., Dong, T., Han, Z., Huang, Z., Zhang, J., Zhang, D., & Huang, K. (2020). Multi-task multi-modal learning for joint diagnosis and prognosis of human cancers. Medical image analysis, 65, 101795. https://doi.org/10.1016/j.media.2020.101795.
2. World Health Organization (2017). "Guide to Cancer Early Diagnosis", https://apps.who.int/iris/handle/10665/254500, (6 December 2020)
3. T.C. Sağlık Bakanlığı (2016). "Türkiye Kanser Kontrol Programı", https://hsgm.saglik.gov.tr/depo/birimler/kanser-db/yayinlar/Kitaplar/TURKIYE_KANSER_KONTROL_PROGRAMI_2016.pdf, (6 December 2020)
4. Akbulut G. (2019). Kanserde Beslenme Tedavisi. Ankara: Ankara Nobel Tıp Kitabevleri
5. Başpınar M. (2015). Kanserli Kolon Hücre Dizisinde Seranib-2 Maddesinin Apoptoz Oluşumuna ve Hücre Yaşamına Olası Etkileri. Tıpta Uzmanlık Tezi. Eskişehir Osmangazi Üniversitesi, Eskişehir.
6. Falborg, A. Z., Vedsted, P., Menon, U., Weller, D., Neal, R. D., Reguilon, I., Harrison, S., Jensen, H., & ICBP Module 4 Working Group (2020). Agreement between questionnaires and registry data on routes to diagnosis and milestone dates of the cancer diagnostic pathway. Cancer epidemiology, 65, 101690. https://doi.org/10.1016/j.canep.2020.101690
7. Halk Sağlığı Genel Müdürlüğü (2017). "Evreleme", https://hsgm.saglik.gov.tr/tr/kanser-tedavisi/kanser-tedavisi-nelerdir/evreleme.html, (6 December 2020)
8. Otero I., Burón A., Macià F., Álvarez-Urturi C., Comas M., Román M., & Castells X. (2018). Adherence to follow-up in high-risk adenoma patients diagnosed by, and excluded from the Barcelona colorectal cancer screening programme, Gastroenterología y Hepatología (English Edition), 41 (4), 226-233, 2018. https://doi.org/10.1016/j.gastre.2018.04.016
9. D'Ovidio, V., Lucidi, C., Bruno, G., Lisi, D., Miglioresi, L., & Bazuro, M. E. (2021). Impact of COVID-19 Pandemic on Colorectal Cancer Screening Program. Clinical colorectal cancer, 20(1), e5–e11. https://doi.org/10.1016/j.clcc.2020.07.006
10. Türk Kanser Derneği (2018). "Kişiye Özel Onkolojik Testler", http://www.turkkanserdernegi.org/tr/faydali-bilgiler/124/kisiye-ozel-genetik-onkolojik-testler.html, (6 December 2020)
11. Börekçi, G., 2010, Flüoresan in situ hibridizasyon (FISH) yönteminin klinik mikrobiyolojide kullanımı, Türk mikrobiyoloji cemiyeti dergisi, 40 (3), 131-142.
12. Çitgez B. (2008). Meme Lezyonu Eksizyon Sistemi ile Doku Örneklemesi (BLES). Uzmanlık Tezi. Şişli Etfal Eğitim ve Araştırma Hastanesi, İstanbul.
13. Sarı R. (2020). Mide Kanseri Tanı Tedavi ve Planlamasında Görüntüleme Yöntemlerinin Yeri. Aytaç H.Ö. (Der) Gastrointestinal Sistem Kanserlerinin Cerrahisi: İçinde 67-78. Ankara: Akademisyen Kitabevi.
14. Özlük, A. A. , Güner Oytun, M. & Günenç, D. (2017). Kanser immünoterapisi . İstanbul Bilim Üniversitesi Florence Nightingale Transplantasyon Dergisi , 2 (1) , 21-23 . Retrieved from https://dergipark.org.tr/tr/pub/ibufntx/issue/28274/300243
15. Barbaros, M. B. & Dikmen, M. (2015). Kanser immünoterapisi . Erciyes Üniversitesi Fen Bilimleri Enstitüsü Fen Bilimleri Dergisi , 31 (4) , 177-182 . Retrieved from https://dergipark.org.tr/tr/pub/erciyesfen/issue/25543/269496
16. Da Silva, C. G., Camps, M., Li, T., Chan, A. B., Ossendorp, F., & Cruz, L. J. (2019). Co-delivery of immunomodulators in biodegradable nanoparticles improves therapeutic efficacy of cancer vaccines. Biomaterials, 220, 119417. https://doi.org/10.1016/j.biomaterials.2019.119417
17. Du, J. J., Wang, C. W., Xu, W. B., Zhang, L., Tang, Y. K., Zhou, S. H., Gao, X. F., Yang, G. F., & Guo, J. (2020). Multifunctional Protein Conjugates with Built-in Adjuvant (Adjuvant-Protein-Antigen) as Cancer Vaccines Boost Potent Immune Responses. iScience, 23(3), 100935. https://doi.org/10.1016/j.isci.2020.100935.
18. The University of Arizona (2020). "Personalized Cancer Vaccine Clinical Trial to Expand Following Promising Early Results", https://opa.uahs.arizona.edu/newsroom/news/2020/personalized-cancer-vaccine-clinical-trial-expand-following-promising-early, (6 December 2020)
19. Gao, T., Cen, Q., & Lei, H. (2020). A review on development of MUC1-based cancer vaccine. Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie, 132, 110888. https://doi.org/10.1016/j.biopha.2020.110888

20. American Cancer Society (2020). “Vaccines to help prevent cancer”, https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy/cancer-vaccines.html, (6 December 2020).

21. Conry, R. M., Westbrook, B., McKee, S., & Norwood, T. G. (2018). Talimogene laherparepvec: First in class oncolytic virotherapy. Human vaccines & immunotherapeutics, 14(4), 839–846. https://doi.org/10.1080/21645515.2017.1412896