



Histopathological pathogenesis of gastric adenocarcinoma in comparison with breast cancer

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Abstract

There are numerous serious varieties of cancer that are extremely difficult to treat. As a result, understanding the origins of cancer, as well as the practical application of cancer in terms of its role of diagnosis and therapy. Detecting Gastric cancer early and correctly diagnosing it histopathologically increases the odds of an effective treatment. Histopathological expertise can help speed up and simplify oncological examinations in this method. According to their various natures, breast and gastric cancers have different tissues and rates. Gastric cancer is still one of the most lethal cancers with a dismal prognosis. New gastric cancer classification based on histologic characteristics, genotypes, and molecular phenotypes aids in better understanding the peculiarities of each subtype and improves early detection, prevention, and treatment. The goal of this essay is to go over the new gastric and breast cancer classifications so that they can be used in management and therapy.

Keywords: Histopathological pathogenesis, Gastric adenocarcinoma, Breast cancer

Introduction

Breast cancer is the most common cancer in women, and unfortunately, the age of onset of this disease has decreased. The reason for this is the referral of patients in the advanced stages of the disease so that still the most common cause of death and severe disability due to breast cancer late diagnosis (1). Cancerous and non-cancerous masses in the breast are also different. Fibroadenoma is also an important tissue mass in the breast (2). The most common benign breast mass is a fibroadenoma, which is usually a painless, circular mass with a rubbery or cartilaginous consistency. Fibroadenomas are usually solitary, but in 10-25% of cases can be multiple.

The disease is more common at younger ages but can occur in all age groups 3. In most cases, these lumps are 2-3 cm at the time of diagnosis but can grow within a few months. When the fibroadenoma is larger than 5 cm, it is called Giant fibroadenoma. Definitive diagnosis of fibroadenomas is made by a combination of physical examination, ultrasound, and postoperative Fine needle aspiration (FNA) examination. On physical examination, these lumps are firm with a smooth, round wall with a rubbery consistency, there is no inflammatory reaction around them, they are fully mobile, they do not cause sagging of the back or nipple, they are often palpable, and a groove is felt when touched (3-5).

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Received: 2021.06.17, Accepted: 2021.07.04

In the classical form, a mass with definite soft and solid boundaries is seen whose craniocerebral length is less than transverse length. In the diagnosis between a cyst and a fibroadenoma, mammography cannot help much, but ultrasound clearly shows the cyst cavity. The presence of fibroadenomas does not increase the risk of breast cancer (4). Of course, neoplasms may occur in the epithelial elements of a fibroadenoma - like the epithelium of other parts of the breast - but overall cancer is very rare in a newly discovered fibroadenoma. Half of the neoplasms that occur in fibroadenomas are ICSI (in situ lobular carcinoma), 25% are infiltrative carcinomas, and 15% are intraductal carcinomas (5). The possible diagnosis of fibroadenoma in the breast must be confirmed by FNA and CNB (Core needle biopsy). Unfortunately, this stage is not well established in our country, and due to the lack of sufficient facilities for needle aspiration with ultrasound guidance and the lack of CNB in all centers, there is a strong desire to remove a fibroadenoma. Simple and digital mammography and, if necessary, magnification mammography - performed in one day for the patient. In the case of benign masses such as fibroadenoma, after a thorough and accurate history and appropriate physical examination, the patient is sent to a special doctor's room for ultrasound and simultaneous needle aspiration with ultrasound guidance (6). Ultrasound is performed with a 14 and 16 MHz probe and in addition to accurately determining the volume and nature of the mass, a new and very interesting elastography method is used to better identify the accompanying masses and the consistency of the mass. At the same time, the orthopedic surgeon solids the mass (Cystic) with the help of ultrasound, and the sample is immediately taken to the pathologist for observation. In less than an hour, the pathology and cytology results are known and the patient is sent to the CNB room to confirm the diagnosis. Core sampling is performed carefully and after examining and determining the benign nature of the mass, even in cases of large fibroadenomas, the patient is scheduled for further control and large incisions and resection of the mass are not performed (7).

The anatomical structure of the breast

Each breast is made up of lobes and lymphatics. Each breast is made up of 15 to 20 sections called lobes. Each

of these lobes is made up of several smaller parts called lobes. The lobes and lobular are connected by tiny ducts called lymphatics. There are also several blood vessels and lymph vessels in each breast. Each of these lymph vessels carries a colorless fluid called lymph. All of these lymph vessels lead to small organs and beans in a shape called lymph nodes. These lymph nodes help the body fight disease and infection. Lymph nodes are present all over the body. Lymph nodes are found in groups near the breast, under the armpits, above the clavicle, and in the chest (8, 9).

Morphological and histological signs of breast cancer include the presence of a swollen or firm mass inside or near the breast or under the armpit, changes in the shape or size of the breast, the presence of wrinkles or dimples on the skin of the breast, and the release of any fluid. Apart from nipple milk, especially if this fluid is bloody, scaling, redness, or swelling on the breast, nipple, the presence of depressions in the skin of the breast, so that these depressions look like orange peel. In this case, this complication is called *Peau d'orange*. These symptoms may occur in some normal people and are not necessarily "specific to breast cancer" (10, 11).

Breast cancer is often very difficult to diagnose in pregnant or breastfeeding women, who usually have tender and swollen breasts. Women who are pregnant, breastfeeding, or giving birth often have sensitive and swollen breasts. In this case, the diagnosis of small tumors is very difficult and often the diagnosis of breast cancer is delayed. Because of these delays, cancer is usually diagnosed in this group of women in the advanced stages of the disease (12).

Biopsy

A tissue sample from a suspicious mass and examined by a pathologist under a microscope to look for cancer cells is called a biopsy (13).

Factors affecting the chances of recovery and treatment of breast cancer

Factors influencing recovery include the stage of cancer (mass size, axillary lymph node involvement, and distant metastasis), the status of the estrogen and progesterone receptors in the cancer cells, the status of the HER2 receptor cancer cells, the presence of general cancer symptoms, and the patient's general health (14,

15). Once breast cancer is diagnosed, tests are done to see if the cancer is present only in the breast itself or if it has spread to other organs. Some ways of spreading breast cancer include spreading through adjacent tissues, invading adjacent tissues, spreading through the lymphatic system, cancer also invading the lymphatic system and spreading through the lymph vessels to other parts of the body, and finally Through the blood, cancer invades the blood vessels and spreads through the blood to other parts of the body (16).

When cancer cells are isolated from the primary tumor and spread to other parts of the body through the blood or lymph, another (secondary) tumor forms. This process is called metastasis. The second (metastatic) tumor is the same as the first tumor. For example, if breast cancer spreads to the bones, the cancer cells in the bone are the same as the breast cancer cells. In this case, the disease is metastatic (17).

Staging of breast cancer

The stage of breast cancer represents the rate of progression of the disease in breast tissue and other organs of the body and directly indicates the survival rate of the patient following cancer. The more advanced the disease, the shorter the patient's lifespan. Breast cancer stages include Stage 0 to stage four (Stage IV) It is worth noting that the choice of treatment is based on the stage of the disease (18).

Stage 0 or intraductal carcinoma (in situ)

There are two types of breast cancer in the in-situ stage.

1. Ductal carcinoma in situ (DCIS)

At this stage of breast cancer, abnormal cells are seen non-invasively exclusively in the lining of the ducts of the breast and have not invaded the basement membrane and other parts of the breast. If the disease is not detected and treated in the DCIS stage, the cancer cells continue to grow and invade the basement membrane and other breast tissues (19).

2. Lobular Carcinoma in situ (LCIS)

At this stage of the disease, cancer cells are found only in the lips of the breast. LCIS rarely become invasive cancer, but having LCIS in one breast can increase the risk of developing cancer in the other breast (20).

Stage I

In Stage I, cancer has formed and this stage is divided into two stages: Stage IA and Stage IB.

Stage IA and Stage IB.

1. Stage IA

The tumor is less than 2cm or 2cm in size and the cancer cells have not spread outside the breast tissue.

2. Stage IB

No disease or tumor is found in the breast at this stage, and only small clusters of cancer cells (larger than 0.2 and smaller than 2 mm) are seen in the lymph nodes. Or, the tumor is 2 cm or smaller, and small clusters of cancer cells (larger than 0.2 and smaller than 2 mm) are found in the lymph nodes.

Stage II

The second stage is divided into two stages, Stage II A and Stage II B.

Stage II A

No tumors are found in the breast, but cancer is found in the axillary lymph nodes. The tumor is 2 cm or smaller in size and has spread to the axillary lymph nodes. Or the tumor size is larger than 2 cm and smaller than 5 cm and has not spread to the axillary lymph nodes.

Stage II B

The tumor is larger than 2 cm and smaller than 5 cm and has spread to the axillary lymph nodes. The tumor is larger than 5 cm but has not spread to the axillary lymph nodes.

Stage III

The third stage is divided into three stages, Stage III A, Stage III B and Stage III C.

Stage III A

No tumors are found in the breast at this stage. And only cancer is found in the axillary lymph nodes, glands that are either attached or to other parts of the breast, or cancer may even be found in the lymph nodes near the breastbone (10). The tumor is 2 cm or smaller. In this case, cancer may spread to the axillary lymph nodes,

which are either connected or to other parts of the breast, and cancer may even spread to the lymph nodes near the breastbone. The tumor is larger than 2 cm and smaller than 5 cm. In this case, cancer has spread to the axillary lymph nodes, glands that are connected or to other parts of the breast, or may even have spread to lymph nodes located near the breast bone (11). The tumor is larger than 5 cm. In this case, cancer has spread to the axillary lymph nodes, glands that are connected or to other parts of the breast, or may even have spread to the lymph nodes near the breast bone.

Stage III B

At this stage, the tumor may be of any size and cancer has spread to the chest wall or breast skin, or cancer has spread to the axillary lymph nodes, glands that are connected or to parts of the breast. It may or may not have spread to the lymph nodes near the breastbone. This stage of the disease is called inflammatory breast cancer, which is associated with skin involvement (12).

Stage III C

At this stage, there may be no signs of breast cancer or a breast tumor of any size. Or cancer may have spread to the chest wall or even to the skin of the breast. Cancer has also spread to the lymph nodes above or below the collarbone. It has spread to the axillary lymph nodes and lymph nodes near the sternum. Stage IIIC Breast cancer itself is divided into operable and non-surgical. In the operative stage, the cancer is found in 10 or more lymph nodes. The cancer is found in the lymph nodes below the clavicle. Cancer of the axillary lymph nodes is found near the sternum. Inoperable Stage IIIC cancer has spread to the supraclavicular lymph nodes (21).

Stage IV

In stage 4 breast cancer, the disease has spread to other parts of the body. These organs often include bone tissue, lungs, liver and brain (22) (Figure1).

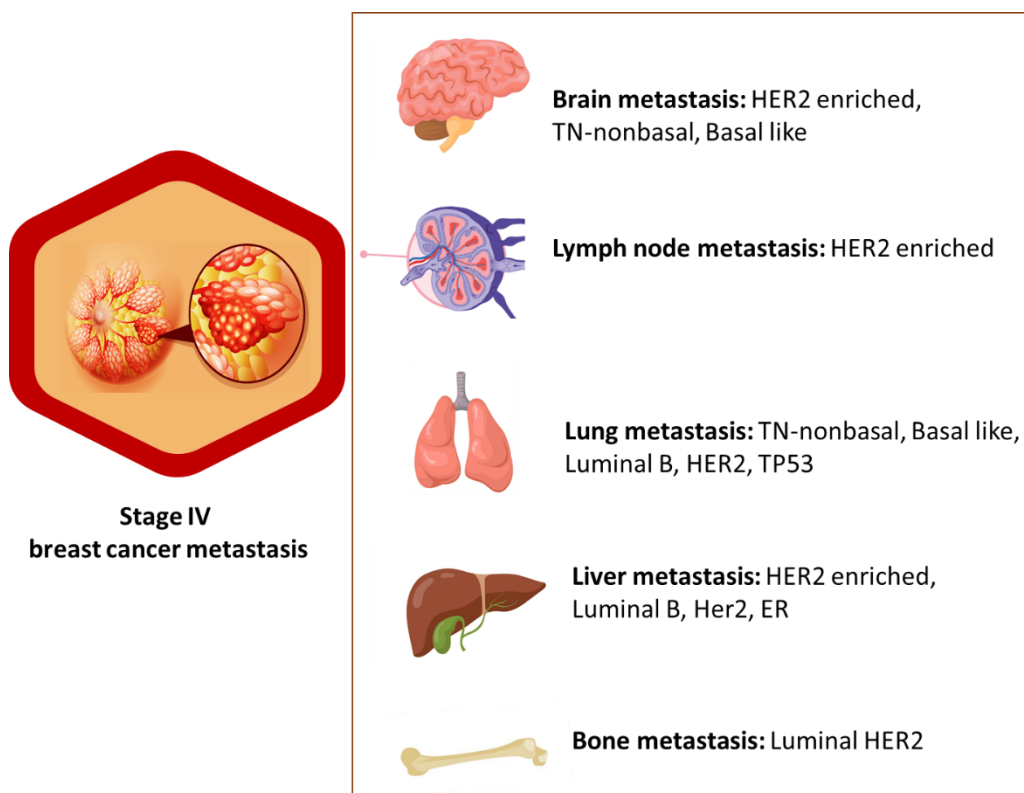


Figure 1. Advanced (metastatic) breast cancer.

Inflammatory breast cancer

At this stage, cancer invades the lymph vessels of the breast skin, causing them to become blocked and the breast to become red and swollen, and the person may feel warmth at this point. It is called d'orange. In this case, a certain mass in the chest may not be touched due to severe swelling. This condition of breast cancer can occur in any of the stages of Stage III B, Stage III C, Stage IV (23, 24).

Recurrent breast cancer

Recurrent breast cancer is cancer that has come back after a full course of treatment. Cancer may come back in the breast tissue, chest, or any part of the body (25).

Gastric cancer

Gastric cancer (GC) is a type of cancer and its most common form is adenocarcinoma or glandular cancer of the stomach (26).

Other less common types of stomach cancer include lymphoma (cancer of the lymphatic system) and sarcoma (cancer of connective tissue such as muscle, fat, or blood vessels). Gastric cancer kills about one million people worldwide each year (27).

It kills many people around the world and is twice as common in men as women and is the fourth most common cancer in the world. It is more common in people with blood type A. Embryonic cell debris in the esophagus and upper third of the stomach is a risk factor for gastric cancer. Embryonic cell debris has the potential to become cancerous with routine diagnostic tests, X-rays and CT scans that are not detectable (26, 28).

Gastric cancer, also known as abdominal cancer, is cancer that occurs in the stomach and upper abdomen. The prevalence of gastric cancer is relatively low in the United States, and it is more common in countries such as China and Japan. Gastric cancer is divided into several types, and the most common type (about 90 to 95% of all types) is cancer that occurs in the glandular area of the stomach. Gastric cancer may be cured if diagnosed early, but unfortunately in the advanced stages of the disease the result is not very satisfactory (29, 30). It should be noted that the presence of risk

factors does not always mean getting the disease and only increases the conditions for getting the disease. *Helicobacter pylori* infection leading to chronic gastritis. Of course, many people who carry this germ will never get stomach cancer (31).

Helicobacter pylori (H. pylori)

Helicobacter pylori is a curved gram-negative bacillus that lives in the labia of the gastric mucosa and sometimes in the duodenum and esophagus. This bacterium is by no means part of the natural flora but causes chronic superficial and diffuse inflammation in infected people in the stomach (32).

The biochemical properties of this bacterium are the production of the enzyme urease. The disease is usually transmitted through oral feces. This is because the bacterium is more common in people who are in poor health or in people who live in groups. The prevalence of *Helicobacter pylori* is primarily dependent on age and geographical area and its prevalence are the same in men and women (33).

Helicobacter pylori can survive in the gastric mucosa, where many bacteria are unable to survive. But when the acidity of the stomach decreases, other bacteria can survive because it may compete with other bacteria. Diagnosis is based on radiology, endoscopy, urease test, and medical history. But these methods are time-consuming and sometimes aggressive, and their sensitivity is not entirely clear. However, the ELISA method has eliminated this problem by identifying specific antibodies so that the desired results can be achieved in a short time with a non-invasive method (34).

Various studies have shown the presence of antibodies against *Helicobacter pylori* and gastric disease. There is a clear relationship between serum IgM antibody levels and clinical tissues so that an increase in serum immunoglobulin levels is seen in acute gastritis. This test is very useful as a rapid screening test and also in the early detection of *Helicobacter pylori* infection because the immune response often occurs before clinical signs (Figure 2) (35, 36).

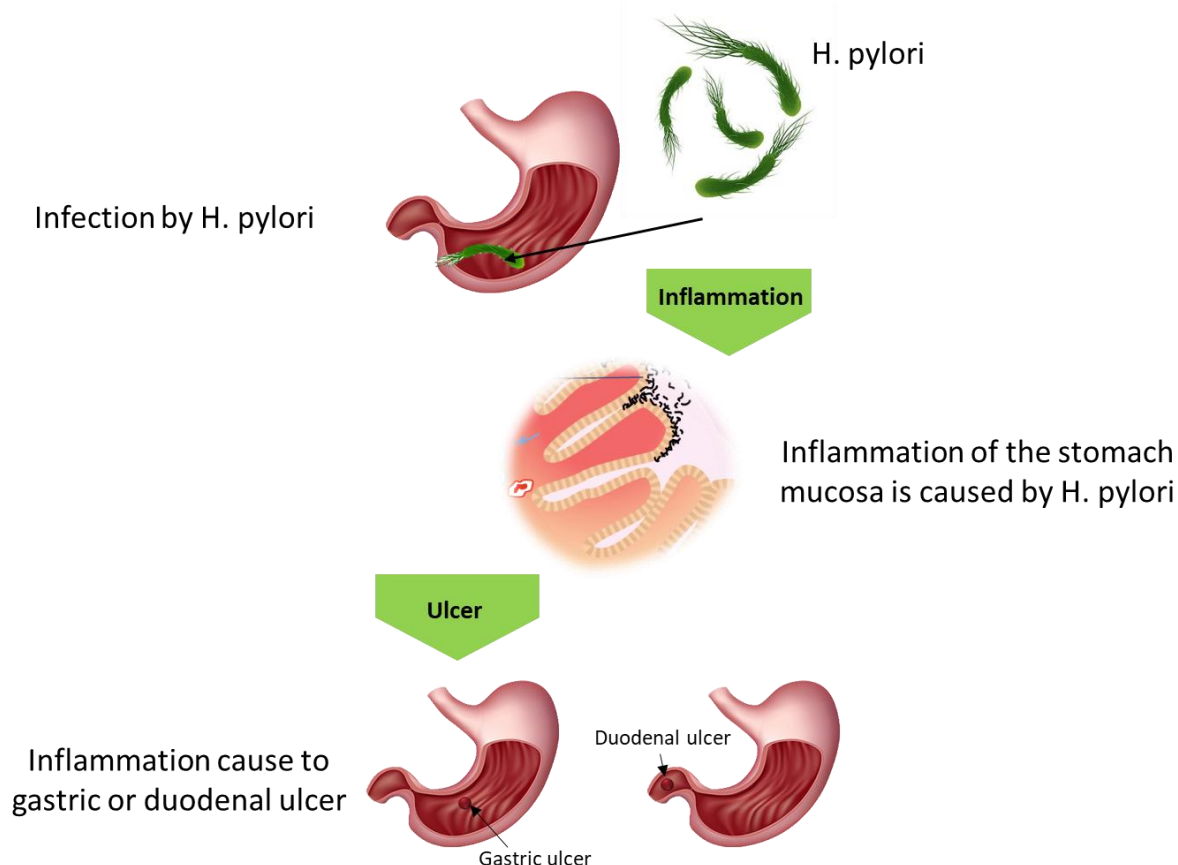


Figure 2. The process of gastric cancer by *Helicobacter pylori*.

Conclusion

Globally, GC is the second leading cause of mortality from cancer. Clinical behavior, the biology of tumor and outcome may all be predicted by histologic categorization. The disease is split into two forms, diffuse and intestinal, based on the current Lauren classification, with the latter having a better prognostic. Diffuse-type GC is the most common subtype in the general population, and it is linked to a poorer prognosis. BC is the most frequent cancer in the world, with a high mortality rate, particularly among women. Early detection and proper medical care might raise the chances of survival. Because the diagnosis procedure is time-consuming and the results may differ amongst pathologists, the computer-Assisted Diagnosis (CAD) system is critical for enhancing precision.

Author contribution

SAN accomplished the data processing, investigated, wrote the whole manuscript, revised and managed the manuscript.

Acknowledgments

I thank all the people who helped me in this article.

Conflict of interest

There are no conflicts of interest.

References

1. Sun Y-S, Zhao Z, Yang Z-N, Xu F, Lu H-J, Zhu Z-Y, et al. Risk factors and preventions of breast cancer. *International journal of biological sciences*. 2017;13(11):1387.
2. Lee M, Soltanian HT. Breast fibroadenomas in adolescents: current perspectives. *Adolescent health, medicine and therapeutics*. 2015;6:159.
3. Abe M, Miyata S, Nishimura S, Iijima K, Makita M, Akiyama F, et al. Malignant transformation of breast fibroadenoma to malignant phyllodes tumor: long-term outcome of 36 malignant phyllodes tumors. *Breast Cancer*. 2011;18(4):268-72.
4. Namazi A, Adibi A, Haghighi M, Hashemi M. An evaluation of ultrasound features of breast fibroadenoma. *Advanced biomedical research*. 2017;6.

5. Wu Y-T, Chen S-T, Chen C-J, Kuo Y-L, Tseng L-M, Chen D-R, et al. Breast cancer arising within fibroadenoma: collective analysis of case reports in the literature and hints on treatment policy. *World Journal of Surgical Oncology*. 2014;12(1):1-8.
6. Mitra S, Dey P. Fine-needle aspiration and core biopsy in the diagnosis of breast lesions: A comparison and review of the literature. *Cytojournal*. 2016;13.
7. Youk JH, Gweon HM, Son EJ. Shear-wave elastography in breast ultrasonography: the state of the art. *Ultrasonography*. 2017;36(4):300.
8. Colleluori G, Perugini J, Barbatelli G, Cinti S. Mammary gland adipocytes in lactation cycle, obesity and breast cancer. *Reviews in Endocrine and Metabolic Disorders*. 2021:1-15.
9. Zucca-Matthes G, Urban C, Vallejo A. Anatomy of the nipple and breast ducts. *Gland surgery*. 2016;5(1):32-36.
10. Sharma GN, Dave R, Sanadya J, Sharma P, Sharma K. Various types and management of breast cancer: an overview. *Journal of advanced pharmaceutical technology & research*. 2010;1(2):109.
11. Stachs A, Stubert J, Reimer T, Hartmann S. Benign breast disease in women. *Deutsches Ärzteblatt International*. 2019;116(33-34):565.
12. Joshi S, Dialani V, Marotti J, Mehta TS, Slanetz PJ. Breast disease in the pregnant and lactating patient: radiological-pathological correlation. *Insights into imaging*. 2013;4(5):527-38.
13. Elfgen C, Papassotiropoulos B, Varga Z, Moskovszky L, Nap M, Güth U, et al. Comparative analysis of confocal microscopy on fresh breast core needle biopsies and conventional histology. *Diagnostic pathology*. 2019;14(1):1-8.
14. Ahmed AR. HER2 expression is a strong independent predictor of nodal metastasis in breast cancer. *Journal of the Egyptian National Cancer Institute*. 2016;28(4):219-27.
15. Pondé N, Brandão M, El-Hachem G, Werbrouck E, Piccart M. Treatment of advanced HER2-positive breast cancer: 2018 and beyond. *Cancer treatment reviews*. 2018;67:10-20.
16. Martin TA, Ye L, Sanders AJ, Lane J, Jiang WG. Cancer invasion and metastasis: molecular and cellular perspective. *Madame Curie Bioscience Database [Internet]: Landes Bioscience*; 2013.
17. Seyfried TN, Huysentruyt LC. On the origin of cancer metastasis. *Critical Reviews™ in Oncogenesis*. 2013;18(1-2).
18. Feng Y, Spezia M, Huang S, Yuan C, Zeng Z, Zhang L, et al. Breast cancer development and progression: Risk factors, cancer stem cells, signaling pathways, genomics, and molecular pathogenesis. *Genes & diseases*. 2018;5(2):77-106.
19. Salvatorelli L, Puzzo L, Vecchio GM, Caltabiano R, Virzi V, Magro G. Ductal carcinoma in situ of the breast: An update with emphasis on radiological and morphological features as predictive prognostic factors. *Cancers*. 2020;12(3):609.
20. van Seijen M, Lips EH, Thompson AM, Nik-Zainal S, Futreal A, Hwang ES, et al. Ductal carcinoma in situ: to treat or not to treat, that is the question. *British journal of cancer*. 2019;121(4):285-92.
21. Zhu C, Wu XZ. Proposal of new classification for stage III breast cancer on the number and ratio of metastatic lymph nodes. *Journal of surgical oncology*. 2012;106(6):696-702.
22. Caswell-Jin JL, Plevritis SK, Tian L, Cadham CJ, Xu C, Stout NK, et al. Change in survival in metastatic breast cancer with treatment advances: meta-analysis and systematic review. *JNCI cancer spectrum*. 2018;2(4):pky062.
23. Yamauchi H, Woodward WA, Valero V, Alvarez RH, Lucci A, Buchholz TA, et al. Inflammatory breast cancer: what we know and what we need to learn. *The oncologist*. 2012;17(7):891.
24. Yaghoobi R, Talaizade A, Lal K, Ranjbari N, Sohrabiaan N, Feily A. Inflammatory breast carcinoma presenting with two different patterns of cutaneous metastases: carcinoma telangiectaticum and carcinoma erysipeloides. *The Journal of clinical and aesthetic dermatology*. 2015;8(8):47.
25. Brett EA, Aitzetmüller MM, Sauter MA, Huemer GM, Machens H-G, Duscher D. Breast cancer recurrence after reconstruction: know thine enemy. *Oncotarget*. 2018;9(45):27895.
26. Hu B, El Hajj N, Sittler S, Lammert N, Barnes R, Meloni-Ehrig A. Gastric cancer: Classification, histology and application of molecular pathology. *Journal of gastrointestinal oncology*. 2012;3(3):251.
27. Kumar RK, Raj SS, Shankar EM, Ganapathy E, Ebrahim AS, Farooq SM. Gastric carcinoma: a review on epidemiology, current surgical and

chemotherapeutic options. *Gastric Carcinoma-New Insights into Current Management*. 2013;12.

28. Dhakras P, Uboha N, Horner V, Reinig E, Matkowskyj KA. Gastrointestinal cancers: current biomarkers in esophageal and gastric adenocarcinoma. *Translational Gastroenterology and Hepatology*. 2020;5:55.

29. Rawla P, Barsouk A. Epidemiology of gastric cancer: global trends, risk factors and prevention. *Przegląd gastroenterologiczny*. 2019;14(1):26.

30. Karimi P, Islami F, Anandasabapathy S, Freedman ND, Kamangar F. Gastric cancer: descriptive epidemiology, risk factors, screening, and prevention. *Cancer Epidemiology and Prevention Biomarkers*. 2014;23(5):700-13.

31. Testerman TL, Morris J. Beyond the stomach: an updated view of *Helicobacter pylori* pathogenesis, diagnosis, and treatment. *World journal of gastroenterology: WJG*. 2014;20(36):12781.

32. Blaser M, Smith P, Ravdin J, Greenberg H, Guerrant R. *Infections of the gastrointestinal tract*. 1995.

33. Huang Y, Wang Q-l, Cheng D-d, Xu W-t, Lu N-h. Adhesion and invasion of gastric mucosa epithelial cells by *Helicobacter pylori*. *Frontiers in cellular and infection microbiology*. 2016;6:159.

34. Ansari S, Yamaoka Y. Survival of *Helicobacter pylori* in gastric acidic territory. *Helicobacter*. 2017;22(4):e12386.

35. Sabbagh P, Mohammadnia-Afrouzi M, Javanian M, Babazadeh A, Koppolu V, Vasigala VR, et al. Diagnostic methods for *Helicobacter pylori* infection: ideals, options, and limitations. *European Journal of Clinical Microbiology & Infectious Diseases*. 2019;38(1):55-66.

36. Zaman A, Shamsuzzaman S, Bhuiyan F, Hasan MR, Saito T. Observation of Changes in *Helicobacter pylori* Antigen and Antibody Positivity According to Non-Invasive Tests Before and After *Helicobacter pylori* Eradication Therapy in Symptomatic Patients. *International Journal of General Medicine*. 2020;13:1093.