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Original Article

Nationwide analysis of the breast cancer guidelines adherence in Bulgaria

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ABSTRACT

Introduction: The diagnosis and treatment of breast cancer have tremendously changed in the last decades improving the survival and quality of life of the patients. Adherence to clinical practice guidelines in oncology significantly improves patients' recurrence-free and overall survival. Nowadays, no national registry/database for breast cancer patients is available. This study aims to perform a nationwide analysis of the breast cancer guidelines adherence in Bulgaria, in particular regarding the diagnostic methods for histological confirmation and the types of radical surgery performed using an artificial intelligence (AI) powered software.

Materials and methods: We analyzed data from January 2019 to August 2023 nationwide using the platform with access to anonymized medical information from Bulgaria's leading territorial oncology hospitals. A total of 13,790 patients met the inclusion criteria.

Results: The gold standard diagnostic tool, CNB, was done in 5427 patients (39.35%), an intraoperative frozen section was performed as a method for confirmation of breast cancer in 6257 patients (45.37%) and the standard technique for lymph node evaluation, sentinel lymph node biopsy, was done in 357 patients (2.99%).

Conclusion: In Bulgaria, there are still difficulties in achieving comparable rates of core-needle biopsy for the diagnosis of breast cancer and we have demonstrated unacceptably high rates of frozen section use for intraoperative diagnosis of breast cancer. Breast-conserving surgery is widely accepted and available, but still, the rates are lower than usual for developed countries. The rates of sentinel lymph node biopsy, however, are unreasonably low.

1. Introduction

Breast cancer is diagnosed in about 1 in 8 patients throughout their lifetimes worldwide. In 2020 breast cancer ranked first in the world in the incidence in both sexes with 2 261 419 new cases (11.7%) and fourth in mortality (6.9%) according to GLOBOCAN (Sung et al., 2021). According to the last update of the Bulgarian Cancer Registry database breast cancer ranks first in the incidence of new cancer cases in women in Bulgaria with 26.8% and is first in cancer-related mortality in women with 17.4% (Valerianova et al., 2017).

The diagnosis and treatment of breast cancer have tremendously changed in the last decades improving the survival and quality of life of the patients. Adherence to clinical practice guidelines in oncology significantly improves patients' recurrence-free and overall survival (Wang, 2017; Shieh et al., 2017; Cedolini et al., 2014; Jafari et al., 2018). Early detection of breast cancer plays a crucial role in improving survival rates, and this can be achieved through methods such as clinical examination, mammography, ultrasound and breast MRI, and biopsy with pathological examination (Shieh et al., 2017; Morris et al., 2015).

The mammography used as the reference examination for breast cancer screening allowing an early detection of small, non palpable tumors at an early stage is classified into 6 ACR categories (American College of Radiology BI-RADS Classification) (Mercado, 2014). While the European Society of Medical Oncology (ESMO) Guidelines for quality assurance in breast cancer recommend the introduction of breast screening programs in all European countries (Cardoso et al., 2019),

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Bulgaria has not yet fully implemented a national breast cancer screening program.

Core-needle breast biopsy (CNB) is the undisputed gold standard for breast cancer diagnosis in all available guidelines. Histological and IHC evaluation of the CNB sample allows proper diagnosis and correct treatment planning, with certain molecular subtypes being forwarded to neoadjuvant systemic treatment and others for primary surgery. Unfortunately, in Bulgaria it is still quite popular to skip CNB, to plan excision of a suspicious breast lump and to use a frozen section (FS) of the excised tumor as a method for histological confirmation of cancer. In case FS confirms cancer, the surgeon proceed with "radical surgery". This practice is not recommended in the international guidelines as a breast cancer diagnostic tool due to sampling errors, challenges in interpretation, lack of pathologists in many countries, and most of all because in the era of tailored cancer treatment the lack of proper diagnosis before the start of any treatment leads to incorrect treatment planning and dis-improves the results.

CNB has replaced fine-needle aspiration cytology (FNAC) as the modality of choice for breast cancer diagnosis showing better sensitivity and giving information about the tumor biology. Nevertheless, it is still used in some lower- and middle-income countries (Wang et al., 2017; Kazi et al., 2017).

Additionally, breast-conserving surgery and sentinel lymph node biopsy (SLNB) are recommended as a preferred treatment option for the majority of patients by all international guidelines for BC treatment (Cardoso et al., 2019; Bartsch and Bergen, 2017; Telli et al., 2019; Burstein et al., 2021).

1.1. This study aims

To perform a nationwide analysis of the breast cancer guidelines adherence in Bulgaria, in particular regarding the diagnostic methods for histological confirmation and the types of radical surgery performed using artificial intelligence (AI) powered software.

To the best of our knowledge no public data if the breast cancer guidelines are followed for other European middle-income countries is available.

2. Materials and methods

We analyzed data from January 2019 to August 2023 nationwide using an artificial intelligence (AI) powered software solution (Danny platform) that has access to anonymized medical information from the leading territorial oncology hospitals in Bulgaria. Information about diagnostic methods for histological confirmation of breast cancer and the types of radical surgery procedures was analyzed and interpreted.

By advanced SAP HANA in-memory database, use of proprietary machine learning and natural language processing (NLP) algorithms, Danny Platform allows a seamless integration of structured and unstructured data from diverse health data sources The data underwent rigorous preprocessing and normalization to ensure high data quality.

To ensure patients' privacy and data security the platform incorporates various security measures, such as data de-identification to safeguard patient identities, adherence to the General Data Protection Regulation (GDPR) standards, implementation of well-structured authorization policies for different access levels, and data anonymization.

Public data were not used to create this analysis, but rather medical records at the level of an individual patient. The information was completely anonymized before entering the Danny platform and its statistical processing. To ensure patient privacy, the platform does not store any personal information directly. The preparation of the current report was carried out by providing the authors and the relevant scientific institutions with access to specific required parameters and information from the platform.

In this retrospective database analysis, digitized medical records in Bulgaria were used to extract data on patients admitted for breast cancer surgery in the period between January 2019 and August 2023. According to data from Danny platform, during this period there were 16 986 newly diagnosed breast cancer cases. The current publication analyzes surgical interventions in 12,989 of the patients in the same period, which represents 76.47% of all newly diagnosed patients during this period in Bulgaria.

A considerable portion of the incoming data was unstructured, consisting of free text manually entered by healthcare professionals. To make this unstructured data useable, additional preprocessing and extraction steps during the data import phase were done. Our objective was to consolidate the transactional-level data into a unified structure that could be easily understood and processed using Natural Language Processing (NLP) entity extraction techniques.

We employed a comprehensive, multi-tiered strategy for data extraction. Initially, the data underwent normalization to reconcile significant syntactical variations across diverse data sources. Subsequently, we utilized a custom-developed NLP algorithm, specifically designed for structuring medical text, to extract the data. This was followed by a thorough verification of the data using regular expressions, string matching, word similarities, and cross-referencing with ICD procedure codes used for reimbursement purposes. In the event of any discrepancies across these checks, a data scientist manually reviews the parameters. For instance, if a single patient record indicates both a core-needle biopsy and radical mastectomy in a single procedure, our quality-checking algorithms flag it as a potential error, prompting a manual review.

Various approaches were employed to extract specific parameter values from the free text, including regular expressions, string matching, word similarities, and advanced NLP methods.

A rule-based approach was adopted to normalize each parameter to address significant variations in syntax across different data sources. For laboratory results, the international system of units and the officially recognized measuring units of each laboratory test were utilized.

For disease coding, the ICD-10 system was employed, and for procedures coding, the ICD-9-CM system was used, as mandated by the National Health Insurance Fund in Bulgaria.

Where the system couldn't find a suitable normalization rule for a specific parameter, it was flagged for further attention by quality control experts to create new regulatory rules specific to that parameter. By standardizing the data across different sources, it became possible to conduct meaningful and reliable analyses.

As we enter the digital age, artificial intelligence (AI) has permeated various aspects of clinical practice, offering new avenues for enhancing diagnostics, treatment, and healthcare management. Despite the slow adoption of AI in healthcare, a report from the Brookings Institution dated March 9th, 2022 indicates an increasing number of healthcare organizations, insurers, and pharmaceutical companies are beginning to implement AI to address issues such as chronic diseases, workforce shortages, and hospital readmissions.

AI plays a role in improving data flow, recognizing and processing both structured and unstructured data. For instance, the Children's Hospital of Philadelphia turned to AWS's AI services to integrate and share genomic, clinical, and imaging data, aiding researchers in analyzing diseases, developing new hypotheses, and making discoveries.

However, the introduction of AI into clinical practice faces several challenges, including the need for regulatory approval from bodies like the FDA, integration into clinical workflows, incorporation into electronic health records and other systems, and securing funding from health insurers.

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3. Results

A total of 13,790 surgical interventions were performed during the study period into so-called "clinical pathway (CP)" 193 and "CP" 194 to patients diagnosed with – breast cancer (ICD C50). A "clinical pathway" is a type of health service that is included in the package of health activities guaranteed by the national healthcare system budget. It is based on the current European and global standards for the quality of medical care. The surgical treatment of breast cancer in the Bulgarian national healthcare system is only possible and paid for following "CPs" 193 and 194 protocols.

A total of 9287 patients (67.35%) were diagnosed with stage I and II breast cancer, and 828 patients (6.2%) were diagnosed with stage IV. The peak of breast cancer incidence in this cohort was in the 60–79 age group. However, a significant number of patients (522 patients – 3,79%) were diagnosed before the age of 40 and an almost equal number of patients (531 patients – 3,85%) were diagnosed at senior age (>85 years) (Figs. 1 and 2).

To confirm the diagnosis a breast biopsy was performed in 9439 patients (68.45% of all patients in the cohort) as follows: CNB in 5427 patients (39.35%), excisional biopsy in 3322 patients (24.09%), and incisional biopsy in 751 patients (5.45%).

Intraoperative frozen section was performed as a method for confirmation of breast cancer in 6257 patients (45.37%), detected as the word used in Bulgaria for a frozen section in the operative report (free-text search algorithms).

The total number of patients per group in Table 1 is higher than the number of unique patients because in 1967 of them, initial biopsy (excisional or incisional) and subsequent intraoperative frozen section was performed (text in operative report matched the free-text algorithm criteria for two groups). Probably in these patients frozen section was performed and the word "excisional" or "incisional" was included in the operative report. We did not find a way to distinguish these patients and put them in only one group.

The number and types of breast cancer surgeries are shown in Table 2. The total number of records identified is less than all the patients in the cohort because some patients have not yet undergone surgery (time from biopsy to surgery or receiving neoadjuvant treatment). Another possible reason for this could be patients that receive simple excision, under 85.21 ICD-9-CM: local excision of lesion of the breast, and no further surgery.

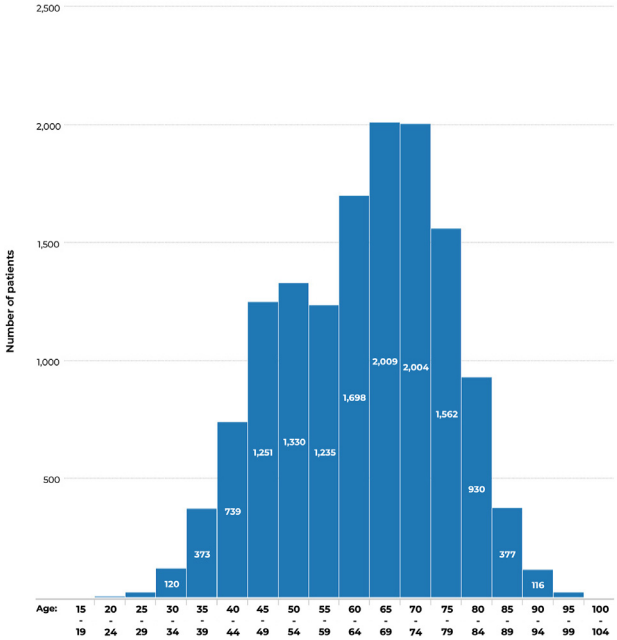

Fig. 1. Distribution of patients by age.

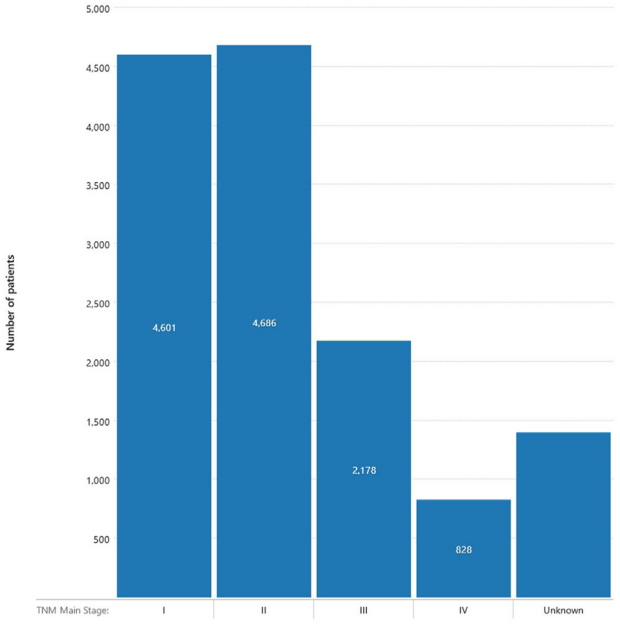

Fig. 2. Distribution of patients by TNM stage.

Table 1
Breast cancer diagnostic procedures for the study period.

Total number of patients	13 790 patients
Core-needle biopsy	5427 patients (39,35%)
Excisional biopsy	3322 patients
Incisional biopsy	751 patients
Frozen section	6257 patients (45,37%)

Table 2
Type of breast cancer surgery by ICD-9-CM.

Code	Number of records
85.22: Resection of quadrant of breast	5706
85.45: Unilateral radical mastectomy	4177
85.43: Unilateral extended simple mastectomy	1187
85.41: Unilateral simple mastectomy	708
85.23: Subtotal mastectomy	69
85.46: Bilateral radical mastectomy	35
85.42: Bilateral simple mastectomy	26
85.44: Bilateral extended simple mastectomy	21
85.47: Unilateral extended radical mastectomy	1
Total:	**11 930**

The breast-conserving surgery (code 85.22 – no other code available on ICD-9-CM for breast conservation) rate was as high as 47.83% (5706 out of 11 930) while the remaining 52.17% of surgeries were unilateral or bilateral mastectomies.

Implant-based breast reconstruction was recorded in 83 patients (1.33% of patients underwent mastectomy) and autologous breast reconstruction in 31 patients (0.5% of patients underwent mastectomy). Therapeutic mammaplasty (unilateral or bilateral breast reduction) was recorded in 21 patients which is 0.37% out of 5706 patients who underwent breast-conserving surgery (Table 3).

SLNB was found to be performed in 357 patients (2.99% of all patients that received surgery for breast cancer) by keyword search algorithms in free text. The same algorithm was used to distinguish the different types of SLNB (Table 4).

Table 3
Autologous, implant-based breast reconstruction, and therapeutic mammaplasty.

Code	Number of records
85.53: Unilateral breast implant	47
85.54: Bilateral breast implant	36
85.85: Muscle flap graft to breast	30
85.31: Unilateral reduction mammoplasty	16
85.32: Bilateral reduction mammoplasty	5
85.82: Split-thickness graft to breast	1

Table 4
Sentinel lymph node tracer used.

Sentinel lymph node tracer	Number of records
Indocyanine green	82
Patent blue V dye	71
Technetium-99 m	20
Unknown	184

4. Discussion

In Bulgaria, there's a noticeable change towards earlier breast cancer detection, with 67.35% of patients being diagnosed at stages I and II in the current cohort. This is likely attributed to improved patients' breast awareness and the increased use of mammography. However, for some stage I and II patients and for all stage III patients neoadjuvant therapy is recommended. It is most appropriate to initiate therapy following a diagnosis through CNB.

In Bulgaria, in most hospitals surgeons are responsible not only for breast cancer treatment but the diagnosis as well. CNB is the gold standard for breast cancer diagnosis (9–12). Over the years, it has demonstrated numerous advantages over alternative biopsy methods such as incisional, excisional, and FNAC (Mercado, 2014; Cardoso et al., 2019; Wang et al., 2017; Kazi et al., 2017). CNB allows minimally invasive tissue sampling while providing information about tumor histological type, receptor status, and subtyping. Given the era of neoadjuvant therapy in breast cancer treatment, CNB serves as the optimal tool for identifying potential candidates. Performing an excisional biopsy of the tumor with or without a frozen section before considering neoadjuvant therapy is not recommended and worsens patient's prognosis.

CNB is a simple, feasible, safe, and reliable method with high sensitivity and specificity. It's commonly performed under manual or ultrasound guidance, and those performed with ultrasound guidance significantly enhance success rates (Bartsch and Bergen, 2017; Telli et al., 2019; Burstein et al., 2021). During the study period in Bulgaria, only 39.35% of the patients received a breast cancer diagnosis via CNB.

Frozen section (FS) analysis of the excised breast lump for breast cancer diagnosis is highly discouraged in the international guidelines. Its utility lies in evaluating resection margins (except the accuracy of margins assessment on FS for DCIS is rather low) and sentinel lymph nodes. Attempting tumorectomy, waiting for the FS intraoperatively, and deciding on the extent of the surgery in one stage depending on the result of FS is unacceptable in the 21st century. Besides all other disadvantages, this practice does not allow a proper pre-operative injection of radioisotope or a dye for SLN identification and excision. The current study demonstrated that in 45,37% of newly diagnosed BC patients, FS was the method for histological confirmation of the diagnosis.

Nowadays, SLNB is recommended in clinically negative lymph nodes (no palpable lymph nodes) or less than 2 suspicious lymph nodes on imaging. The method has proven its benefits over axillary lymph node dissection (ALND) with the same oncological safety but with significantly fewer complications and side effects for patients with pN0(sn), pN1(1-2sn) and ypN0(sn) (Hunt et al., 2012; Galimberti et al., 2013; Donker et al., 2014; Sávolt et al., 2017; Lyman et al., 2005; Kim et al., 2006; Tee et al., 2018). Furthermore, suggestions based on data that the preservation of healthy axillary lymph nodes may have survival benefits are made (Veronesi et al., 2010). New tracers, such as ICG, magnetic tracer and carbon dye are reasonable alternatives to the standard techniques using radioisotope and/or blue dye (Sugie et al., 2016; Zada et al., 2016; Wei et al., 2021). SLNB has shown evidence to be safe and effective also after neoadjuvant therapy (Sávolt et al., 2017; Lyman et al., 2005; Tee et al., 2018; Sugie et al., 2016; Sanchez et al., 2021). Regardless of the fact that SLNB is recommended for the majority of BC patients, this procedure is not routinely performed in Bulgaria even in territorial cancer centers. The documented rate of less than 3% in our study is unacceptably low. No specific coding is used for SLNB. A free-text search in the operative report was used, so no or few procedures could be missed.

Probably, the reasons for the low rates of CNB and SLNB, and the high rates of frozen section in Bulgaria are all connected and similar. There is a lack of trained and experienced surgeons; guidelines are available, but no control is obtained if they are followed; payment is received for all types of procedures and last but not least no fully developed continuous medical education system is implemented and it is not obligatory to follow it. Especially for SLNB, regulations and availability of the tracers are a problem due to the cost and the small market.

Breast-conserving surgery (BCS) has improved significantly the quality of life of breast cancer patients with no worsening of disease-free (DFS) and overall survival (OS) (Veronesi et al., 2002; Fisher et al., 2002; Krag et al., 2010; Zwakman et al., 2022; Li et al., 2022). The estimated rates of BCS in Europe at the beginning 21st century were around 50% of all cancer surgeries and nowadays the suggested rates in the Western countries are 60–75% (Tyldesley et al., 2003). However, rates as low as 11–23% are reported in India and 17–54% in Malaysia (Hassan Ali et al., 2019; Wong et al., 2019). Our data analysis demonstrates BCS rates of 47.83% in Bulgaria between 2019 and August 2023. ***The rates of BCS are still to be improved even for middle-income county.*** Over the last decade, multiple emerging data from retrospective analysis of large population databases in various countries demonstrated that BCS plus radiotherapy may have a survival benefit (BCSS, OS) over mastectomy with or without radiotherapy (Burstein et al., 2021; de Boniface et al., 2021; Gentilini et al., 2017; Chen et al., 2023). Furthermore, some authors suggest that “if both interventions (BCS and mastectomy) are valid options, mastectomy should not be regarded as equal to breast conservation” (Gentilini et al., 2017; Onitilo et al., 2015).

Therapeutic mammaplasty following BCS is not widely available and performed because no breast cancer centers and onco/plastic surgeons are present. Furthermore, breast reconstruction is not covered by the national health insurance system.

The Danny platform in Bulgaria, along with similar analytical platforms globally, processes and analyzes vast medical data sets to identify patterns and trends for improving patient care. Modern oncology relies on the analysis of big data, starting with the discovery of target molecules like trastuzumab in HER2+ breast cancer and imatinib in chronic myeloid leukemia. Experts anticipate that the future of oncology and medicine as a whole hinges on data processing and analysis, ultimately leading to highly personalized medicine and improved outcomes.

Using the Danny platform, which employs artificial intelligence for analysis, a comprehensive evaluation of breast cancer diagnostic methods and treatment in Bulgaria between 2019 and August 2023 has been conducted. This information is invaluable as an audit and a way for further implementing standardized practices to treat breast cancer and enhance healthcare. However, concerns about anonymizing information have been raised by medical ethics specialists. Thus far, no articles based on data analysis using similar or the same AI-based software have been found. This may be attributed to the existence of national cancer registries and databases in developed countries which might be used to run the analysis.

The latest available data in the Bulgarian cancer registry is from 2015. No other national registry is available. No control if the national, European and world guidelines are followed is obtained.

5. Conclusion

In Bulgaria, there are still difficulties in achieving comparable rates of core-needle biopsy for the diagnosis of breast cancer and we have demonstrated unacceptably high rates of frozen section use for intra-operative diagnosis of breast cancer. Breast-conserving surgery is widely accepted and available, but still, the rates are lower than usual for developed countries. The rates of sentinel lymph node biopsy, however, are unreasonably low. There is still much to be improved in the adherence to breast cancer diagnostics and treatment guidelines in Bulgaria.

The use and declaration of AI and AI-assisted technologies in scientific writing

Artificial intelligence was not used in the writing process.

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Declaration of competing interest

Authors have no conflict to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cson.2024.100044.

References

Bartsch, R., Bergen, E., 2017. ASCO 2017: highlights in breast cancer. memo - Mag Eur Med Oncol 10 (4), 228–232. https://doi.org/10.1007/s12254-017-0368-7.

Burstein, H.J., Curigliano, G., Thürlimann, B., et al., 2021. Customizing local and systemic therapies for women with early breast cancer: the St. Gallen International Consensus Guidelines for treatment of early breast cancer 2021. Ann. Oncol. 32 (10), 1216–1235. https://doi.org/10.1016/j.annonc.2021.06.023.

Cardoso, F., Kyriakides, S., Ohno, S., et al., 2019. Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†. Ann. Oncol. 30 (8), 1194–1220. https://doi.org/10.1093/annonc/mdz173.

Cedolini, C., Bertozzi, S., Londero, A.P., et al., 2014. Type of breast cancer diagnosis, screening, and survival. Clin. Breast Cancer 14 (4), 235–240. https://doi.org/10.1016/j.clbc.2014.02.004.

Chen, Y., Qi, Y., Wang, K., 2023. Neoadjuvant chemotherapy for breast cancer: an evaluation of its efficacy and research progress. Front. Oncol. 13, 1169010. https://doi.org/10.3389/fonc.2023.1169010.

de Boniface, J., Szulkin, R., Johansson, A.L.V., 2021. Survival after breast conservation vs mastectomy adjusted for comorbidity and socioeconomic status: a Swedish national 6-year follow-up of 48 986 women. JAMA Surg 156 (7), 628–637. https://doi.org/10.1001/jamasurg.2021.1438.

Donker, M., van Tienhoven, G., Straver, M.E., et al., 2014. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial. Lancet Oncol. 15 (12), 1303–1310. https://doi.org/10.1016/S1470-2045(14)70460-7.

Fisher, B., Anderson, S., Bryant, J., et al., 2002. Twenty-Year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N. Engl. J. Med. 347 (16), 1233–1241. https://doi.org/10.1056/NEJMoa022152.

Galimberti, V., Cole, B.F., Zurrida, S., et al., 2013. Axillary dissection versus no axillary dissection in patients with sentinel-node micrometastases (IBCSG 23-01): a phase 3 randomised controlled trial. Lancet Oncol. 14 (4), 297–305. https://doi.org/10.1016/S1470-2045(13)70035-4.

Gentilini, O.D., Cardoso, M.-J., Poortmans, P., 2017. Less is more. Breast conservation might be even better than mastectomy in early breast cancer patients. Breast 35, 32–33. https://doi.org/10.1016/j.breast.2017.06.004.

Hassan Ali, S., S, P.S., N, A.K., 2019. Rate of breast-conserving surgery vs mastectomy in breast cancer: a tertiary care centre experience from south India. Indian J Surg Oncol 10 (1), 72–76. https://doi.org/10.1007/s13193-018-0818-7.

Hunt, K.K., Ballman, K.V., McCall, L.M., et al., 2012. Factors associated with local-regional recurrence after a negative sentinel node dissection: results of the ACOSOG Z0010 trial. Ann. Surg. 256 (3), 428–436. https://doi.org/10.1097/SLA.0b013e3182654494.

Jafari, S.H., Saadatpour, Z., Salmaninejad, A., et al., 2018. Breast cancer diagnosis: imaging techniques and biochemical markers. J. Cell. Physiol. 233 (7), 5200–5213. https://doi.org/10.1002/jcp.26379.

Kazi, M., Suhani, Parshad R., Seenu, V., Mathur, S., Haresh, K.P., 2017. Fine-needle aspiration cytology (FNAC) in breast cancer: a reappraisal based on retrospective review of 698 cases. World J. Surg. 41 (6), 1528–1533. https://doi.org/10.1007/s00268-017-3906-x.

Kim, T., Giuliano, A.E., Lyman, G.H., 2006. Lymphatic mapping and sentinel lymph node biopsy in early-stage breast carcinoma. Cancer 106 (1), 4–16. https://doi.org/10.1002/cncr.21568.

Krag, D.N., Anderson, S.J., Julian, T.B., et al., 2010. Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: overall survival findings from the NSABP B-32 randomised phase 3 trial. Lancet Oncol. 11 (10), 927–933. https://doi.org/10.1016/S1470-2045(10)70207-2.

Li, Y., Guo, J., Sui, Y., Chen, B., Li, D., Jiang, J., 2022. Quality of life in patients with breast cancer following breast conservation surgery: a systematic review and meta-analysis. J Healthc Eng 2022, 3877984. https://doi.org/10.1155/2022/3877984.

Lyman, G.H., Giuliano, A.E., Somerfield, M.R., et al., 2005. American Society of Clinical Oncology guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer. J Clin Oncol Off J Am Soc Clin Oncol 23 (30), 7703–7720. https://doi.org/10.1200/JCO.2005.08.001.

Mercado, C.L., 2014. BI-RADS update. Radiol. Clin. 52 (3), 481–487. https://doi.org/10.1016/j.rcl.2014.02.008.

Morris, E., Feig, S.A., Drexler, M., Lehman, C., 2015. Implications of overdiagnosis: impact on screening mammography practices. Popul. Health Manag. 18 (Suppl. 1), S3–S11. https://doi.org/10.1089/pop.2015.29023.mor. Suppl 1.

Onitilo, A.A., Engel, J.M., Stankowski, R.V., Doi, S.A.R., 2015. Survival comparisons for breast conserving surgery and mastectomy revisited: community experience and the role of radiation therapy. Clin. Med. Res. 13 (2), 65–73. https://doi.org/10.3121/cmr.2014.1245.

Sanchez, A.M., Terribile, D., Franco, A., et al., 2021. Sentinel node biopsy after neoadjuvant chemotherapy for breast cancer: preliminary experience with clinically node negative patients after systemic treatment. J Pers Med 11 (3). https://doi.org/10.3390/jpm11030172.

Sávolt, Á., Péley, G., Polgár, C., et al., 2017. Eight-year follow up result of the OTOASOR trial: the Optimal Treatment of the Axilla - surgery or Radiotherapy after positive sentinel lymph node biopsy in early-stage breast cancer: a randomized, single centre, phase III, non-inferiority trial. Eur J Surg Oncol J Eur Soc Surg Oncol Br Assoc Surg Oncol 43 (4), 672–679. https://doi.org/10.1016/j.ejso.2016.12.011.

Shieh, Y., Eklund, M., Madlensky, L., et al., 2017. Breast cancer screening in the precision medicine era: risk-based screening in a population-based trial. J Natl Cancer Inst 109 (5). https://doi.org/10.1093/jnci/djw290.

Sugie, T., Kinoshita, T., Masuda, N., et al., 2016. Evaluation of the clinical utility of the ICG fluorescence method compared with the radioisotope method for sentinel lymph node biopsy in breast cancer. Ann. Surg Oncol. 23 (1), 44–50. https://doi.org/10.1245/s10434-015-4809-4.

Sung, H., Ferlay, J., Siegel, R.L., et al., 2021. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 71 (3), 209–249. https://doi.org/10.3322/caac.21660.

Tee, S.R., Devane, L.A., Evoy, D., et al., 2018. Meta-analysis of sentinel lymph node biopsy after neoadjuvant chemotherapy in patients with initial biopsy-proven node-positive breast cancer. Br. J. Surg. 105 (12), 1541–1552. https://doi.org/10.1002/bjs.10986.

Telli, M.L., Gradishar, W.J., Ward, J.H., 2019. NCCN guidelines updates: breast cancer. J Natl Compr Cancer Netw J Natl Compr Canc Netw 17 (5.5), 552–555. https://doi.org/10.6004/jnccn.2019.5006.

Tyldesley, S., Foroudi, F., Barbera, L., et al., 2003. The appropriate rate of breast conserving surgery: an evidence-based estimate. Clin. Oncol. 15 (3), 144–155. https://doi.org/10.1053/clon.2003.0206.

Valerianova, Z., Atanasov, T., Vukov, M. (Eds.), 2017. Cancer Incidence in Bulgaria, 2014 & 2015. Bulgarian National Cancer Registry, Sofia.

Veronesi, U., Cascinelli, N., Mariani, L., et al., 2002. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N. Engl. J. Med. 347 (16), 1227–1232. https://doi.org/10.1056/NEJMoa020989.

Veronesi, U., Viale, G., Paganelli, G., et al., 2010. Sentinel lymph node biopsy in breast cancer: ten-year results of a randomized controlled study. Ann. Surg. 251 (4). https://journals.lww.com/annalsofsurgery/fulltext/2010/04000/sentinel_lymph_node_biopsy_in_breast_cancer_.3.aspx.

Wang, L., 2017. Early diagnosis of breast cancer. Sensors 17 (7). https://doi.org/10.3390/s17071572.

Wang, M., He, X., Chang, Y., Sun, G., Thabane, L., 2017. A sensitivity and specificity comparison of fine needle aspiration cytology and core needle biopsy in evaluation of suspicious breast lesions: a systematic review and meta-analysis. Breast 31, 157–166. https://doi.org/10.1016/j.breast.2016.11.009.

Wei, N., Hou, J., Chen, J., et al., 2021. Sentinel lymph node biopsy with carbon nanoparticle suspension after neoadjuvant chemotherapy for breast cancer patients. Ann. R. Coll. Surg. Engl. 103 (10), 752–756. https://doi.org/10.1308/rcsann.2021.0084.

Wong, W.J., Mosiun, J.A., Hidayati, Z., et al., 2019. Low Breast Conserving Surgery (BCS) rates in public hospitals in Malaysia: the effect of stage and ethnicity. Breast 46, 136–143. https://doi.org/10.1016/j.breast.2019.05.016.

Zada, A., Peek, M.C.L., Ahmed, M., et al., 2016. Meta-analysis of sentinel lymph node biopsy in breast cancer using the magnetic technique. Br. J. Surg. 103 (11), 1409–1419. https://doi.org/10.1002/bjs.10283.

Zwakman, M., Tan, A., Boersma, C., et al., 2022. Long-term quality of life and aesthetic outcomes after breast conserving surgery in patients with breast cancer. Eur. J. Surg. Oncol. 48 (8), 1692–1698. https://doi.org/10.1016/j.ejso.2022.02.011.