Original Research Article: full paper

(2020), «EUREKA: Health Sciences»
Number 1

EARLY COMPLICATIONS AFTER RADICAL OPERATIONS IN BREAST CANCER PATIENTS

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Abstract

Breast cancer is one of the most common malignancies in women. In many cases, a major component of complex treatment for breast cancer is surgery – radical mastectomy or radical breast resection.

The aim of the work – to investigate the frequency and structure of complications after radical surgery with dissection of axillary lymph nodes in breast cancer patients.

Material and methods. The baseline and surgical results of 147 women with breast cancer who underwent radical mastectomy or radical breast resection with lymph node dissection were analysed.

Results. Complications in the early period after surgery for breast cancer were found in 76 (51.7 %), including postoperative extremity edema in 60 (40.8 %); lymphorrhea – in 37 (25.2 %), seroma – in 33 (22.4 %); wound infection in 18 (12.2 %), necrosis of the wound edges – in 15 (10.2 %) patients. Correlation of postoperative edema with almost all other complications was found, lymphorrhea and seroma were most associated with swelling and with each other; necrosis of edges with postoperative edema. Wound infection was significantly associated with lymphorrhea. Patients' age, stage of disease, and immunohistochemical type of tumour did not affect the development of complications. With increasing BMI, the incidence of complications increased significantly (χ^2=9.530; p=0.009). The tendency to decrease the frequency of complications during reconstructive surgery was revealed (42.6 % versus 58.1 %, p=0.064), and adjuvant radiotherapy, on the contrary, contributed to the increase of complications (57.8 % versus 43.8 %, p=0.090).

Conclusion. Radical operations with lymph node dissection in patients with breast cancer are characterized by a high frequency of early postoperative complications, mainly associated with disorders of lymphatic outflow, which indicates the need for a set of measures of preoperative preparation, improvement of surgical technique.

Keywords: breast cancer, radical surgery, lymph node dissection, complications.

DOI: 10.21303/2504-5679.2020.001119

1. Introduction

Breast cancer is one of the most common malignancies in women [1, 2]. In many cases, a major component of complex treatment for breast cancer is surgery – radical mastectomy (RME) or radical breast resection (RBR) [3]. In addition to extensive tissue removal of the mammary gland, radical surgery is facilitated by lymph node dissection (LND) in the areas of potential metastasis, which leads to damage to the elements of lymphatic outflow and is one of the leading causes of complications of early and late postoperative period [4, 5]. In the early period after surgery, the most common complications are the formation of lymphocele (seroma), lymphorrhea, postoperative edema, wound infections and impaired wound healing [6, 7], whose frequency increases during reconstructive operations especially using autoplastic methods [8]. The most common complication is seroma, the frequency of which reaches 85 %. Their development is associated both with the features of surgical interventions, and with the individual characteristics of patients [9]. No less relevant are wound complications, which not only worsen the cosmetic results of the operation, but also increase the cost of treatment [10].

These complications lead to an increase in the duration and cost of treatment, may cause other post-mastectomy complications and impairment of quality of life [11, 12]. Therefore, it is very important to study the factors contributing to the development of postoperative complications and to develop measures for their prevention.

The aim of the work – to investigate the frequency and structure of complications after radical surgery with axillary lymph nodes dissection in breast cancer patients.

2. Material and methods

We analysed the baseline condition and results of surgical treatment of women with breast cancer who underwent radical surgery (RME or RBR with LND) from 2010 to 2019 at the Kharkiv Regional Oncology Center or at Medical Center "Molecule" (Kharkiv) and met the following criteria: histologically confirmed breast cancer, operable tumour without distant metastases (M0), presence of results of clinical, instrumental and immunohistochemical (IHC) research, in prospective study - consent of the patient to participate in the study and processing of personal data.

The study design was considered by Ethics Committee of the Kharkiv Medical Academy of Postgraduate Education at the planning stage of the study and found to be in conformity with the principles of the Helsinki Declaration of General Assembly of the World Medical Association (1964–2000), the Council of Europe Convention on Human Rights and Biomedicine (1997), the relevant provisions of WHO, the International Council of Medical Scientific Societies, the International Code medical ethics (1983) and the laws of Ukraine.

The final analysis included 147 women, middle-aged (49.1±11.6) years (from 26 years to 82 years), including those aged up to 39 years – 32 (21.8 %), 40–49 years – 46 (31.3 %), 50–59 years – 42 (28.6 %), more than 59 years – 27 (18.4 %). Overweight (body mass index (BMI) – 25–39 kg/m^2) was found in 49 (33.3 %) patients, obesity (BMI from 30 kg/m^2) in 10 (6.8 %) cases.

I stage of breast cancer was diagnosed in 31 (21.1 %) patients; IIA – in 46 (31.1 %); IIB – in 23 (15.6 %); IIIA – 21 (14.3 %); IIIB – in 20 (13.6 %); IIIC – in 6 (4.1 %). In 81 (55.1 %) patients the left breast was affected, in most cases the process was localized in the central part of the breast – 54 (36.7 %) and in the upper-outer quadrant – 53 (36.1 %). Less frequently in the upper-inner quadrant – 19 (12.9 %), lower-outer – 10 (6.8 %), lower-internal – 9 (6.1 %), in two or more quadrants – 2 (1.4 %). By IHC type: luminal A – 53 (36.1 %), luminal B – 19 (12.9 %), HER2+ – 9 (6.1 %), three-negative BC (TNBC) – 66 (44.9 %). The degree of histological differentiation: G1 – 21 (14.3 %), G2 – 57 (38.8 %), G3 – 69 (46.9 %).

All patients received treatment according to current clinical guidelines [3]. In 113 (76.9 %) patients performed RME, in 34 (23.1 %) RBR. In all patients performed LND 2–3 order. Reconstructive surgery was performed in 61 (41.5 %) patients, including 3 (2.0 %) primary allograft using a silicone implant, 52 (35.4 %) implanting a silicone prosthesis after dermotension using expander, in 6 (4.1 %) cases – two-stage prosthesis of the breast a year or more after RME.

Chemotherapy (CT) was received 139 (94.6 %) patients, while in the neoadjuvant mode (NCT) – 49 (33.3 %) patients; hormone therapy – 17 (11.6 %) women (12 of them after the course of CT). 83 (56.5 %) women received adjuvant radiotherapy.

The frequency and pattern of postoperative complications in the entire sample of patients were analyzed. The main focus is on the complications most characteristic of the surgery for the BC: seroma (fluid accumulation in the surgical area after removal of drainage), lymphorrhea (serous discharge from the drainage more than 100 ml in the first day after surgery, then more than 50 ml for more than 3 days), postoperative edema (the difference of the circumference of the shoulder above the elbow joint between the upper extremities up to 2 cm – 1 st., 2–6 cm – II st., more than 6 cm – III st.) and wound complications (infection and necrosis of the wound edges).

The obtained results were processed with statistical programs PSSP (open program, which does not require a license) with the use of methods of descriptive statistics, criterion χ^2, correlation analysis according to Spearman criterion.

3. Results

Complications in the early period after breast surgery were detected in 76 (51.7±5.2 %). The most common complication was postoperative extremity edema, which was observed in 60 (40.8±4.6 %) patients, of whom I st. – 23 (38.3±7.1 %), II st. – 33 (55.0±8.5 %) and III st. – 4 (6.7±2.9 %). Intensive and/or prolonged lymphorrhea was observed in 37 (25.2±3.7 %) patients, seroma (lymphocele) in 33 (22.4±3.5 %). Wound infection was detected in 18 (12.2±2.5 %) patients, wound necrosis (WN) in 15 (10.2±2.3 %).

Most complications of the early postoperative period were associated: in 24 (16.3±2.9 %) patients there were one complication, in 53 (36.1±4.4 %) patients a combination of two or more complications was found.

The correlation of complications is illustrated by the results of correlation analysis (**Table 1**).

It was revealed strong correlation of postoperative edema with almost all other complications, first of all, with the manifestations of lympho-venous outflow disorders: lymphorrhea (r_S=0.546; p<0.001); seroma (r_S=0.525; p<0.001). In a lesser extent, but also significantly, this complication was correlated with the development of wound necrosis (r_S=0.311; p<0.001). Lymphorrhea and seroma were most associated with edema (r_S=0.546; p<0.001 and r_S=0.525; p<0.001) and with each other (r_S=0.239; p =0.004); wound necrosis with postoperative extremity edema (r_S=0.311; p<0.001). Wound infection was significantly associated with lymphorrhea only (r_S=0.167; p=0.043).

Table 1

Correlation analysis of surgery complications for breast cancer

Complications	Lymphorrhea	Postoperative extremity edema	Seroma	Wound infection	Wound necrosis
Lymphorrhea	–	0.546** <0.001	0.239** 0.004	0.167* 0.043	0.115 0.165
Postoperative extremity edema	0.546** <0.001	–	0.525** <0.001	0.122 0.140	0.311** <0.001
Seroma	0.239** 0.004	0.525** <0.001	–	0.152 =0.067	0.043 0.605
Wound infection	0.167* 0.043	0.122 0.140	0.152 =0.067	–	0.109 0.188
Wound necrosis	0.115 0.165	0.311** <0.001	0.043 0.605	0.109 0.188	–

*Note: * – Spearman correlation coefficient (r_S), p<0.05; ** – Spearman correlation coefficient (r_S), p<0.001*

The foregoing testifies to the common pathogenesis of postoperative complications, which are mainly associated with disorders of lymphatic outflow due to extensive LND. However, the development of postoperative edema can also be a manifestation of inflammatory-infectious processes in the wound area and a consequence of the inflammatory reaction in the necrosis of the wound edges.

A very important issue is the general background that contributes to the development of complications, i.e. the initial risk factors. The most available indicators for a long observation period were epidemiological data, features of the underlying disease and treatment modalities (**Tables 2, 3**).

Number of complications not depended from patients' age (χ^2=2.169; p=0.538), stage of the disease (χ^2=1.886; p=0.868), and IHC type of the tumour (χ^2=2.446; p=0.485). Nevertheless, there is some increase in the incidence of complications with Her2 + (66.7 %) and TNBC (56.1 %) compared with luminal A (47.2 %) and luminal B (42.1 %) types. Significant differences were found in the analysis of the frequency of complications depending on BMI: with increasing BMI, the frequency of complications significantly increased (χ^2=9.530; p=0.009) (**Table 2**).

In addition, the frequency of complications was affected by treatment modalities (**Table 3**).

Table 2

Number of patients with complications after breast cancer depending of baseline data

Indicator	Number – n (%)		χ^2	p
	No complications (n=71)	With complications (n=76)		
Age groups:				
30–39 y. (n=32)	19 (59.4 %)	13 (40.6 %)		
40–49 y. (n=46)	20 (43.5 %)	26 (56.5 %)	2.169	0.538
50–59 y. (n=42)	20 (47.6 %)	22 (52.4 %)		
>59 y. (n=27)	12 (44.4 %)	15 (55.6 %)		
BMI:				
<25 kg/m^2	50 (56.8 %)	38 (43.2 %)	9.530	0.009
25–29.9 kg/m^2	20 (40.8 %)	29 (59.2 %)		
≥30 kg/m^2	1 (10.0 %)	9 (9 (90.0 %)		
IHC type:				
Luminal A	28 (52.8 %)	25 (47.2 %)		
Luminal B	11 (57.9 %)	8 (42.1 %)	2.446	0.485
Her2+	3 (33.3 %)	6 (66.7 %)		
TNBC	29 (43.9 %)	37 (56.1 %)		
Stage:				
I	16 (22.5 %)	15 (19.7 %)		
IIA	24 (33.8 %)	22 (28.9 %)		
IIB	9 (12.7 %)	14 (18.4 %)	1.886	0.865
IIIA	11 (15.5 %)	10 (13.2 %)		
IIIB	8 (11.3 %)	12 (15.8 %)		
IIIC	3 (4.2 %)	3 (3.9 %)		

Note: BMI – body mass index; IHC – immunohistochemistry; TNBC – three-negative breast cancer; p – by the criterion χ^2

Table 3

Dependence of the incidence of postoperative complications depending on the method of treatment

Method of treatment	Number – n (%)		χ^2	p
	No complications (n=71)	With complications (n=76)		
Type of operation:				
RME (n=113)	59 (52.2 %)	54 (47.8 %)	2.996	0.083
RBR (n=34)	12 (35.3 %)	22 (64.7 %)		
Reconstruction:				
No (n=86)	36 (41.9 %)	50 (58.1 %)	3.441	0.064
Yes (n=61)	35 (57.4 %)	26 (42.6 %)		
Reconstruction method:				
primary implant (n=3)	2 (66.7 %)	1 (33.3 %)	5.423	0.143
Expander implant (n=52)	28 (53.8 %)	24 (46.2 %)		
delayed implant (n=6)	5 (83.3 %)	1 (16.7 %)		
Adjuvant radiotherapy:				
No (n=64)	36 (56.3 %)	28 (43.8 %)	2.869	0.090
Yes (n=83)	35 (42.2 %)	48 (57.8 %)		
NCT:				
No (n=98)	44 (44.9 %)	54 (55.1 %)	1.362	0.243
Yes (n=49)	27 (55.1 %)	22 (44.9 %)		

Note: RME – radical mastectomy; RBR – radical breast resection; NCT – neo-adjuvant chemotherapy

No significant differences were found depending on the treatment modality, although there were some patterns. First of all, increase of complications rate in RBR compared to RME was found (64.7 % vs. 47.8 %, p=0.083), but it should be noted that, regardless of the volume of surgery, all patients had LND in similar volume. Performing reconstructive surgery reduced the incidence of complications (42.6 % versus 58.1 %, p=0.064), with the smallest number of complications observed during the breast reconstruction a year or more after the initial operation. In patients with NCT, there was a slight decrease of complications rate (44.9 % versus 55.1 %, p=0.243), and adjuvant radiotherapy, on the contrary, contributed to increase of complications rate (57.8 % versus 43.8 %, p=0.090).

4. Discussion

In our study, which combines retrospective and prospective analysis of the results of surgical interventions for breast cancer, complications were found in 51.7 % of patients. The high frequency of complications in our observations can be explained by the lymphatic node dissection, which was performed in all cases. In similar observations. A. Lucci et al. (2007) after RME with LND, adverse surgical events (wound infection, seroma, paresthesia) were reported in 70 %. [13]. M. O. Abass et al (2018) reported about complications in 42 % of women after similar surgery [6].

In the structure of complications in our study, the leading place is occupied by postoperative extremity edema, which was found in 40.8 % of patients. The occurrence of edema of the ipsilateral limb within a month after surgery is more often regarded not as a complication but as a manifestation of other complications or as a normal course of the postoperative period. In our study, postoperative edema was most commonly associated with other complications and was observed in 60.0 % of patients with the presence of wound infection, in 80.0 % of patients with necrosis of the wound edges, in 86.5 % of patients with lymphorrhea, in 84.8 % of patients with seroma. However, in 10.8 % of patients postoperative edema was observed in the absence of other complications, indicating other pathogenetic mechanisms of its development.

Quite often in the postoperative period, lymphorrhea (25.2 %) and seroma (22.4 %) were detected. Most authors attribute these complications to LND, and the frequency reported by other researchers is very variable. M.O. Abass et al (2018) reported what seroma after RME with LND was detected in 15.6 % of cases [6]. In another study, the rate of seroma was dependent from the use of a hemostasis device: 37.5 % of patients were using standard electrosurgical device, while using a new electrosurgical device (PEAK PlasmaBlade) – in 10 % [14]. Srivastava V. et al. reported that the seroma rate come to 85 % and can be considered not a complication but a side effect of the operation [9].

The incidence of wound complications (wound infections and necrosis of the wound edges) was almost indistinguishable from similar studies in other studies [6]. Their development depends on many factors, so the statistics are very variable. In particular, according to a recent review of clinical studies, wound infections after mastectomy were detected in 3–15 % of cases [15]. Researchers from Poland report that infectious complications were detected in 6.2 % of patients, and after alloplastic reconstruction in 14.6 % of cases. [16]. Risk factors for surgical site infections was BMI greater than 25, American Society of Anesthesiology classification of 3 or higher, diabetes mellitus, surgical time 2 hours and greater, and current smoking status [17].

Another line of research to this problem is to study the effectiveness of prevention methods. Patient-specific complication risk factors are not modifiable, therefore a variety of methods for improving surgery techniques are proposed, including advanced hemostasis devices [14.18], optimization of LND technique, ligation of lymph vessels, methods of wound drainage [19]. However, the evidence base for the effectiveness of these methods is limited [20]. Thus, the problem of prevention of complications after radical surgery needs further research.

Study limitations. This study combines the results of a retrospective analysis and a prospective study. The main emphasis is on the clinical and pathological features of patients and methods of surgical treatment. The features of preoperative preparation, the experience of the surgeon, and postoperative treatment were not analysed. However, these indicators may affect the immediate results of surgical treatment.

Perspective of further research. Further studies of the problem of postoperative complications are needed to identify modifiable risk factors and the development of methods to reduce the risk of these complications.

5. Conclusion

Thus, radical breast surgery with LND in patients with breast cancer is characterized by high incidence of early postoperative complications, mainly associated with disorders of lymphatic outflow. Analysis of the incidence of complications based on baseline demographic and clinical data revealed a reliable association with BMI only. There were no reliable associations with therapies, but there was a marked increase in the incidence of complications after RBR, adjuvant radiotherapy, and their decrease after reconstructive surgery and NCT. Although LND leads to the development of these disorders, it remains a necessary element of radical surgery, in particular, with N-positive status, T3-4, TNBC, which indicates the need for a complex preoperative preparation, improvement of surgical equipment and postoperative management of patients.

Conflict of interest

No conflict of interest.

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Received date 17.12.2019
Accepted date 14.01.2020
Published date 31.01.2020