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Improvement of surgical method of breast cancer therapy by s. m. bektursynov's technique

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Abstract: The technology of breast cancer surgical therapy of radical sector resection and radical mastectomy with inclusion stepped section of a greater pectoral muscle is developed and introduced. The stepped section of the greater pectoral muscle as an element of organ preserving operation allows performing adequately lymphodissection of axillary, subscapular and subclavian regions. During the process of standard adjuvant schemes of chemo drugs the immune stimulating therapy with thymalin was carried out, such therapy protects patients from expressed leukopenia and increases duration of their life for 8-14 months. Possibility of breast cancer surgical therapy with minimal injury is shown for the first time both as at sector and radical resection, in the form of decrease specific complications frequency.

Key words: *Mammary Gland; Breast Cancer; Anticoagulant Therapy; Lymphodissection; Mastectomy; Axillary Lymphodissection*

1. Introduction

Surgical method of treatment was always and remains as basic method of breast cancer therapy (DeMoulin, D., 2004).

In treatment of breast malignant neoplasms for the last 10-15 years new approaches were outlined, they generally connected with reconsideration of surgical principles towards reduction the volume of surgery without violation of treatment radicalism.

Halsted operation for the last years has been undergone serious reconsideration as it is traumatic and followed by rather large blood loss, most patients who had this operation became depressed with feeling of their own inferiority, etc. (Gerassimenko, V.N., 1992; Pronin, V. I., 2000; Demidov, V.P., 1997).

Patey-Dyson operation from oncological points of view is not estimated as radical one (Yessenkulov, A.E., 1993).

Improvement of results of patients survival by the way of perfection surgical technique of breast cancer therapy at combined and complex therapy is thought to be topical. Searching and introduction of both highly effective pharmacological means and ways directed on decrease of cytostatic therapy complications including such method as immunotherapy are gaining particular importance (Novikov, V. K., etc., 1999).

At the present time there are some attempts of more reasonable carrying out of anticoagulant therapy without and on the base of chemo drugs introduction in the early postoperative period for the purpose of decrease frequency of thromboembolic complications, such therapy at the same time can have antirecurrent character (Avdeyeva, N. I., 2001; Baluda, V.P., 2001; Barkagan, Z.S., 2001).

Thus, it is still not clear when and in what circumstances this or that volume of surgery is prescribed as well as its true role in combined and complex treatment of breast cancer (BC).

1.1. Purpose of the research

Improvement of direct and follow-up results of surgical treatment of breast cancer patients in combination with chemoimmunotherapy therapy.

1.2. Tasks of the research

1. To conduct thymalin therapy course along with chemo drugs at breast cancer surgical treatment having defined indices of cellular immunity and hematologic components of blood.
2. To carry out anticoagulant therapy course in the early postoperative period of breast cancer patients along with standard chemo drugs.
3. To study direct results of the improved surgical technique at combination of breast cancer chemo-radiotherapy and anticoagulant therapy treatment.

2. Material and methods

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The researches were conducted on clinical base of Taldykorgan Regional Oncologic Dispensary during the period from 1995 to 2013. Clinical records of 521 patients with breast cancer were examined and analyzed.

All patients were divided into two research groups: first – control, it consisted of 203 patients with breast cancer, they were operated under standard traditional techniques; second – basic group, 318 breast cancer patients that were operated by own technique.

Own technique of mastectomy is radical sector resection and radical mastectomy with removal of the small pectoral muscle and lymphodissection of axillary, subscapular and subclavian regions by stepped section of the greater pectoral muscle. Operations of 95 patients of the basic group out of 318 breast cancer patients had ultra preserving economical character – radical sector resection (removal of the part of the mammary gland with a tumor, small pectoral muscle and lymphodissection by stepped section of the greater pectoral muscle). 223 patients had radical mastectomy (removal of the mammary gland, small pectoral muscle and lymphodissection by stepped section of the greater pectoral muscle).

The first variant of surgeries corresponded to traditional ones carried out in the volume of radical classical segmental mastectomy with preservation either pectoral muscles or the greater pectoral muscle (first control group – 135 patients).

The second variant of surgery corresponded to operations performed in the volume of classical radical mastectomy by Halsted – removal of the greater and small pectoral muscles (second control group – 30 patients).

The third variant of surgery corresponded to operations carried out in the volume of sector resection with axillary lymphodissection (third control group - 38 patients).

The greatest number of breast cancer patients of the age 40 – 60 years old. Patients age fluctuated within 23 – 75 years. Average age was 59,7 ±3,2 (Tables 1-2)

Table 1: Methods of surgical treatment of breast cancer patients in the basic and control groups

Groups of patients	Volume of operation at breast cancer	Total	
		Abs. number	%
Basic (n=318)	-radical sector resection of mammary gland, removal of the small pectoral muscle and lymphodissection of axillary, subscapular and subclavian regions with stepped section of the greater pectoral muscle;	95	29,8
	- radical mastectomy, removal of the small pectoral muscle and lymphodissection of axillary, subscapular and subclavian regions with stepped section of the greater pectoral muscle.	223	70,1
Control (n=203)	- radical sector resection with lymphodissection of the axillary region	38	18,7
	- modified radical mastectomy with preservation of the greater pectoral muscle	67	33,0
	- radical mastectomy with preservation of both pectoral muscles by Madden	68	33,4
	- radical mastectomy by Halsted	30	14,7
Source: Bektursynov S.M., (2012)			

Table 2: Classification of the patients according to the stages of tumor process in the experimental group

Groups of patients	Stages of disease	Number	%
Basic (n=318)	I stage	37	11,6
	II stage	135	42,4
	III – IIIa stage	146	45,9
Control (n=203)	I stage	20	9,8
	II stage	83	40,3
	III – IIIa stage	100	49,2
Source: Bektursynov S.M., (2012)			

As it is seen from the table, the greatest number of patients arrives for treatment with the third stage of tumor process.

3. Results of the research

Improvement of surgery of mammary gland resection at cancer is thought to be radical sector resection and radical mastectomy with removal of the small pectoral muscle and lymphodissection of axillary, subscapular and subclavian regions by stepped section of the greater pectoral muscle.

Traditional section of skin, the greater pectoral muscle at the level of VI rib at the place of outer edge attachment is dissected cross with length 4-5 cm (pictures 1, 2). Parallel sections are made on fibers of the greater pectoral muscle with 3-5 cm distances between them before emergence of the small pectoral muscle (pictures 3, 4). We continue section vertically with the length of 4-5 cm. It allows maximum access to the small pectoral muscle (Bektursynov, S.M., 2007).

Thus, the technique of mammary gland resection offered by us differs from nowadays conventional operations in the following:

1. In conventional sector resection it is not possible to remove radically subclavial lymph nodes, first of all due to lack of access.

2. At operation by Halsted the mammary gland is removed as well as the greater and the small pectoral muscles for the purpose of guaranteed section of axillary and subclavial lymph nodes.

3. At operation by Madden modified radical mastectomy is performed (total mastectomy with axillary dissection of 1-2 levels).

4. Operation by Bektursynov consists of radical mastectomy, removal of the small pectoral muscle and lymphodissection of subclavial, axillary and subscapular regions with stepped section of the greater pectoral muscle.

3.1. Complications and results of the improved operation at breast cancer

Frequency and nature of postoperative complications emerging in the compared basic and control groups are presented in Table 3.

Table 3: Frequency and nature of postoperative complications

Extension of patients mammary gland resection	Number of patients	Lymphorrhea		Haematoma		Suppuration		Edema of upper extremity		Thrombophlebitis		Thrombosis		Pain in upper extremity	
		abs	%	abs	%	abs	%	abs	%	abs	%	abs	%	abs	%
***Basic group**-Radical sector resection with stepped section of the greater pectoral muscle and removal of the small pectoral muscle*	95	4	4,2	2	2,1	5	1							4	4,2
- Radical mastectomy with stepped section of the greater pectoral muscle and removal of the small pectoral muscle	223	8	3,5	1	0,4			2	0,9	2	0,9			4	1,5
TOTAL:	318	14	43	3	0,9	1	0,4	2	0,6	2	0,6			8	2,4
***Control group** sector resection of axillary lymphodissection*	38	2	5,2	3	7,9	4	10,5	2	5,2	4	10,5	1	0,5	1	2,6
Radical mastectomy with both muscles preservation	68	4	5,8	2	2,8	1	1,4	6	8,8	10	14,6			4	5,8
Radical mastectomy with section of the greater pectoral muscle and removal of the small pectoral muscle continuation under Patey	67	4	5,9	2	2,9	1	1,5	4	5,9	12	17,8	2	2,9	6	8,9
Halstead Operation	30	6	20	2	6,6	2	6,6	8	26,6	5	13,3			11	36,6
TOTAL:	203	16	7,8	9	4,3	8	3,9	20	9,8	31	15,2	2	0,9	22	10,8

Source: Bektursynov and Bayduvaliyev (2012)

Presented material shows that surgery at breast cancer under offered by us techniques do not burden seriously postoperative period and do not cause increase frequency of postoperative complications.

From the table it is seen that at performance surgery in the volume of sector resection on frequency and nature of postoperative complications the difference in the compared groups is not so essential, at increase the operation volume till radical mastectomy more sparing character is distinctly noticed in the technique offered by us. At the same time the average duration of a lymphorrhea decreases for 4-5 days (Bektursynov, S.M. and others, 1998). Edema of the upper

extremity had less widespread character. Patients complained very seldom of pain in the upper extremity caused mainly by clinical edema progressing (2,4%). Complications in the form of hypodermic bruises and thrombophlebitis of the upper extremity (pictures 7, 8) were observed at 13% of patients after operation by Halsted. We connect it not only with smaller injury of our operations, but also with patients involvement into preoperative preparation of anticoagulant therapy (Bektursynov, S.M. 2003).

The presented material shows that breast operations by offered by us techniques do not seriously burden the course of the postoperative period, they do not lead to increase the frequency of postoperative complications (Bektursynov, S.M. 2003).

Frequency of emergence of local recurrence and metastasises after surgical treatment under offered by us technique and similar data at traditional operations are presented in the table 4a, 4b, 4c.

Table 4a: Cancer recurrences and metastasises after breast cancer surgical treatment

Operations	Cancer recurrences		Cancer metastasises	
	3 years	5 years	3 years	5 years
I. Sector resection				
Average statistical literary data	35,5%		42,9%	39,3%
Our data	3,1%	3,3%	5,2%	7,7%
II. Radical mastectomy				
Halsted	4,6%	4,9%		
Madden	8,5%		19,1%	20,4%
Our data	0,9%	0,4%	4,6%	5,3%

Table 4b: Improved operations of mammary gland resection

Operations	Number of the operated patients	Cancer recurrences				Cancer metastasises			
		3 years		5 years		3 years		5 years	
		Our %	lit. %	our %	lit. %	our %	lit. %	our %	lit. %
Radical sector resection	95	3,1	35,5	3,3	42,9	5,2	32,3	7,7	39,3
Radical mastectomy	223	0,9	8,5	0,4	4,9	4,6	19,1	5,3	20,4

Table 4c: Cancer recurrences and metastasises after breast cancer surgical treatment

Operations	Cancer recurrences		Cancer metastasises	
	3 years	5 years	3 years	5 years
I. Sector resection				
Average statistical literary data	35,5%		42,9%	39,3%
Our data	3,1%	3,3%	5,2%	7,7%
II. Radical mastectomy				
Halsted	4,6%	4,9%		
Madden	8,5%		19,1%	20,4%
Our data	0,9%	0,4%	4,6%	5,3%

Frequency of recurrence and metastasises after 3 years of breast cancer surgical treatment according to literature data has the following picture: at wide electrosurgical sector resection – 35,5%, MRME by Madden – 8,5%, RME by Halsted – 4,6%. Remote metastasises were noticed less often at patients with MRME by Madden of 19,1%, more often after organ-preserving operations (32,3%).

After similar treatment after 5 years local recurrences and remote metastasises of the tumor were also met in group with wide sector resection (42,9% and 39,3%, respectively). Local recurrences were less revealed after RME by Halsted (4,9%), and the remote metastasises – after MRME by Madden (20,4%).

The survival of the breast cancer patients operated by the offered by us technique in comparison to similar data at traditional operations is presented in Table 5.

General 3-year survival after breast cancer St. II-111a surgical treatment was 84,4%. 3-year survival by Halsted – 90,7%. General 5-year survival after breast cancer surgical treatment was on average 79,7%. The best indicators of survival were reached after RME by Halsted – 87,8%, the smallest – after wide electrosurgical sector resection of mammary gland with axillary lymphadenectomy (67,9%). At RME by Madden – 75%.

3.2. The results of application improved operation at breast cancer in combination with chemotherapy

80 patients with breast cancer of the II-IIIA disease stages were examined. Thymolin treatment

course was carried out along with polychemotherapy, also quantitative parameters were studied regarding absolute content of leukocytes, lymphocytes and monocytes in peripheral blood, thymolin treatment course and course without it was applied in groups of patients with immunotherapy. It was established that prevention of hematoimmunologic complications with the help of thymolin maintains the level of blood leukocytes, lymphocytes and monocytes (Bektursynov, 2003).

Table 5: 3-year and 5-year survival of patients after breast cancer surgical treatment

Operations	3- year survival	5- year survival
I. Sector resection		
Average statistical literary data	74,2%	67,9%
Our data	94,7%	87,4%
II. Sector resection		
Halsted	90,7%	87,8%
Madden		83,7%
Our data	90,7%	86%

Table 6: Survival of breast cancer patients operated by the offered technique depending on the disease stage

Stage of breast cancer	Number of the operated patients	3- year survival		5- year survival	
		abs.number	%	abs.number	%
I	37	37	100	36	97,3
II	135	128	94,7	120	88,3
III	146	129	89,5	119	79,6

As a result of use advanced surgical equipment for breast cancer operational therapy the duration of recurrence-free period of the patients with IIIa stage of tumoral process at carrying out chemotherapy with thymolin immunotherapy increased on 12 months in comparison with the group of patients whose chemotherapy was carried out without thymolin introduction.

After combined breast cancer of St II-IIIa (picture 1) therapy the general 3-year survival of patients was on average 87,1%, at the same time higher results were reached after RME carried out under our technique (94,0%), lower results of survival were observed in groups of patients with organ-preserving operations (81,1%) ($p < 0.05$).

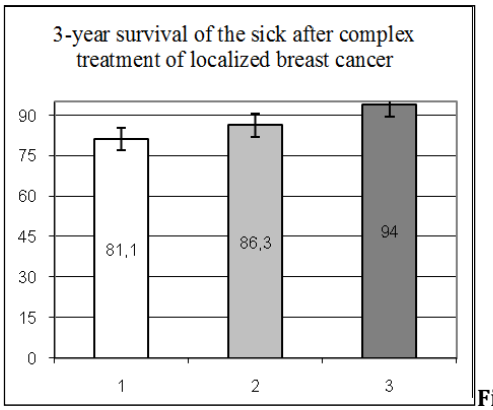

Fig. 1: Abscissa axis: – methods of operations: 1 - wide electrosurgical sector resection, 2 – RME by Halsted, 3 - by Bektursynov; ordinate axis –general survival of patients in %

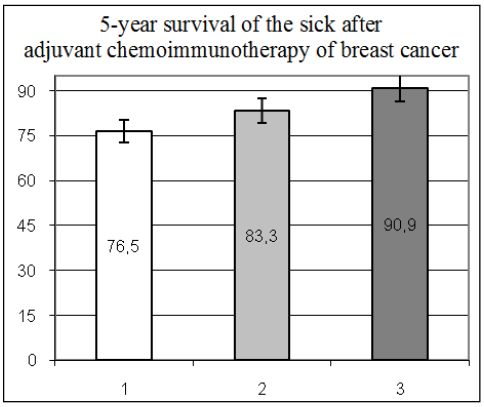

Fig. 2: Abscissa axis: – methods of operations: 1 - wide electrosurgical sector resection, 2 – RME by Halsted, 3 - by Bektursynov; ordinate axis –general survival of patients in %

The results of therapy of patients with breast cancer that had adjuvant chemo immunotherapy and further surgery under techniques developed by us, general 3-year survival on average reached 94.0%.

The survival of patients after complex treatment of the localized breast cancer during 5-year observation on average estimated 86.0% (picture 2). It should be noted that the results of survival of patients after complex treatment in groups with modified mastectomies at this prevalence of tumoral process were not worse than the results of complex treatment of patients with RME by Halsted (90,9%) ($p > 0,05$). After wide electrosurgical section resection of the mammary gland survival of patients was 76.5% ($p < 0,05$).

Thus, comparative analysis of 3 methods of treatment of the localized breast cancer showed that better results of patients survival were received

after combination of operation with chemo immunotherapy in comparison with single surgical or combined (operation + radiation therapy) methods. Modified mastectomy at this prevalence of tumoral process was not worse in its efficiency than RME by Halsted and Madden, and even it was more effective.

3.3. Frequency of emergence of local recurrence and remote metastasises after combined treatment

Application of system treatment (chemo immunotherapy) led to considerable decrease of rates of tumor recurrence and metastasises emergence in comparison with other medical influences (operation, radiation therapy). Local recurrences and remote metastasises at 3-year observation were revealed themselves more often after a wide sector resection of the mammary gland (8,1% and 16,2%, respectively). In groups of patients with RME by Halsted local recurrences were not noticed (Figs. 3, 4)

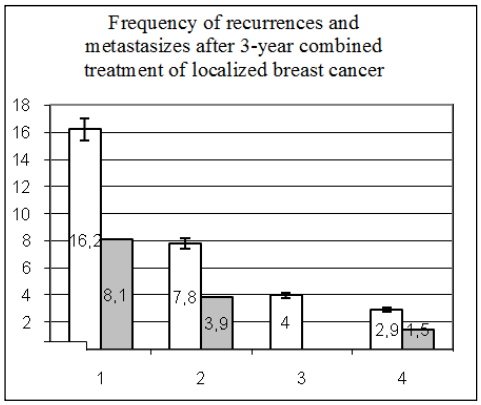

Fig. 3: Abscissa axis: 1 - wide electrosurgical sector resection, 2 – MRME by Madden, 3 – RME by Halsted, 4 – our data (metastasises, recurrences); ordinate axis – frequency in %

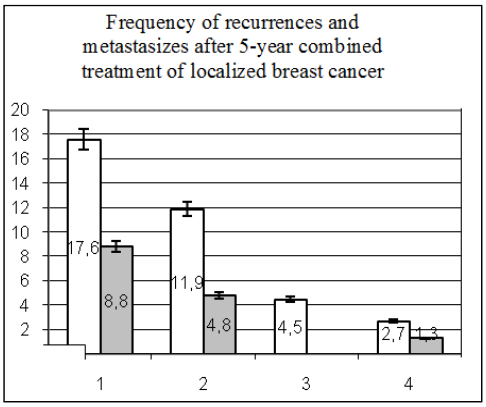

Fig. 4: Abscissa axis: 1 - wide electrosurgical sector resection, 2 – MRME by Madden, 3 – RME by Halsted, 4 – our data (metastasises, recurrences); ordinate axis – frequency in %

5 years after complex treatment (picture 5) remote metastasises and local recurrence were noticed considerably more often after organ-preserving operations (17,6% and 8,8%, respectively) RME by Halsted (4,5% of metastasises, no recurrences).

According to our data, complex treatment of localized breast cancer leads to considerable decrease in frequency of emergence both local recurrence and remote metastasises in comparison with surgical methods (on average by 4,4-3,1 times) and combined (on average by 1,3-2,8 times) methods ($p < 0,05$).

3.4. The results of application improved operation at breast cancer in combination with radiation therapy

Preoperative radiation therapy was made on the tumoral center and zones of regional lymphatic outflow (axillary and retrosternal) by method of large fractionation with a single basic dose of 5 Gray, bringing it to total basic dose 20-25 Gray.

Operative interventions were carried out by improved by us methods of mammary gland resection: At operations performing the same two advanced methods of mammary gland resection were adhered:

1 variant (23 patients) – radical sector resection (removal of the part of the mammary gland with tumor and lymphodissection by the stepped section of the greater pectoral muscle).

2 variant (57 patients) – radical mastectomy (removal of the mammary gland, small pectoral muscle and lymphodissection by section of the greater pectoral muscle).

Complications of the next postoperative period: lymphorrhea (3,2%); skin necrosis (0,7%); wound abscess (0,5%);

Late postoperative complications: lymphostasis of the upper extremity (3,2%); restriction of mobility of the shoulder joint from the side of mammary gland resection (2,2%).

At comparison the frequency of these complications to similar indicators during carrying out only surgical treatment reliable distinctions were not revealed. Radiation therapy in the dose of 20-25 Gr at preoperative stage did not lead to increase of frequency and complication of postoperative complications.

Data on detection edema of the upper extremity of patients with breast cancer after combined treatment method are presented in Table 7.

In control group – only at radiation therapy (21 patients) these indicators are 3 times higher than generally. It is possible to suppose that patients who experienced radiation therapy have edema of upper extremity more often. Radiation influence promotes fabrics fibrosis, especially after operation by Halsted (removal of the greater and small pectoral muscles, it naturally negatively affects their blood supply).

The 3-year survival of patients after combined treatment of our patients was 89,9%. According to the data of literature, 3-year survival after organ-preserving operations consists 75,7%.

Table 7: Frequency of detection edema of the upper extremity at breast cancer combined therapy depending on disease stage, in %

Breast cancer	Number of the cured patients	Edema of the upper extremity	
		Early (<1 year)	Late (1 year >)
I stage	10	1	2,7
II stage	25	0,7	2,1
III stage	46	1,3	2,06
Total	81		

After combined treatment 80,6% of our patients lived for 5 years. After radical mastectomy by Halsted the indicators of 5- year survival shoed 86,7%, after wide electrosurgical sector resection with lymphadenectomy of the axillary zone – 70,0%.

Frequency of local recurrence and the remote metastasises emergence after combined treatment of our patients in comparison to similar data at traditional operations are reflected in the form of Figs. 5 and 6.

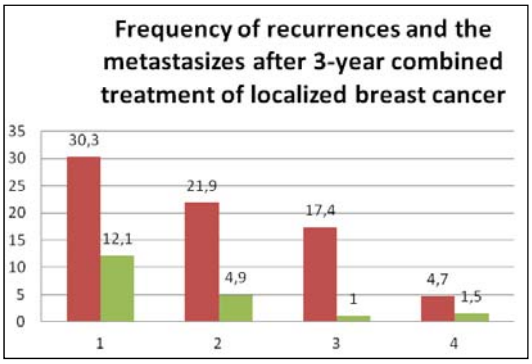

Fig. 5: Abscissa axis: 1 - wide electrosurgical sector resection, 2 – MRME by Madden, 3 – RME by Halsted, 4 – our data (metastasises, recurrences); ordinate axis – frequency in %

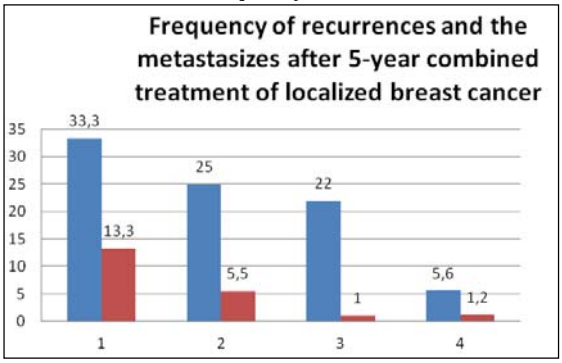

Fig. 6: Abscissa axis: 1 - wide electrosurgical sector resection, 2 – MRME by Madden, 3 – RME by Halsted, 4 – our data (metastasises, recurrences); ordinate axis – frequency in %

Thus, application of the technique of preoperative radiation therapy of 5Gr to SOD 20 Gr in comparison with surgical method of treatment led to some increase of general survival without improving indicators of local recurrence and data of the remote metastasis.

Frequency of local recurrences and remote metastasises emergence after combined treatment according to literary data: the greatest indicators of disease return (12,1%-13,3% of local recurrences and 30,3%-33,3% of remote metastasises) are noted in the group of patients with organ-preserving operations, the smallest – of patients with RME by Halsted (17,4% of OM, lack of MR).

The combined treatment of breast cancer St.II-A in comparison with only surgical treatment led to reliable decrease of frequency of local recurrences emergence in the studied patients groups (on average twice, $p < 0,001$), however indicators of identification the remote metastasises after combination of radiation treatment and operation practically did not differ from the results of only surgical treatment.

Prevention of postoperative thromboses of our patients was carried out as follows:

1. Nonspecific (reduction of emotional pressure, struggle against hypodynamia, elastic bandaging of the lower extremities).

2. Nonspecific (medicamental) – a clexane therapy, application of rheopolyglukin (400 ml 2 times with the interval of 2-3 days), application of antiaggregant (aspirin of 0,5 g 2 times before operation and after operation for 3-7 days).

Distinct parallelism becomes apparent in increase of frequency and soverity of postoperative complications with increase of the volume of surgery and absence of terrible thromboembolitic complications such as thrombosis of pulmonary artery and vessels of the lung, thromboses and embolisms of brain vessels and coronary vessels.

Postoperative complications in the form of phlebothrombosis of women who did not receive anticoagulant therapy before operation proceeds more expressed and it requires more long-term treatment. The obtained data do not leave any doubt in provocative role of surgical trauma in development of thromboembolitic complications and embolisms. At the same time during anticoagulant therapy we did not observe any case of clinical implications of bleeding. Thus, it is possible to consider that application of anticoagulant therapy for breast cancer patients who are going to have surgical treatment is thought to be reasonable.

4. Conclusions

1. New technology of surgical treatment at breast cancer–radical sector resection and radical mastectomy with removal of the small pectoral muscle and a lymphadissection by stepped section of the greater pectoral muscle has been developed and recommended to use in practice.

2. The stepped section of the greater pectoral muscle and removal of the small pectoral muscle allows to execute adequately lymphadissection of axillary, subscapular and subclavial regions.

3. The developed technique of surgical therapy of breast cancer possesses technical stages of organ-preserving operation and less traumatic, it reveals in decrease of frequency of specific postoperative complications (lymphorrhea, lymphostasis of upper extremity, rigidity of the shoulder joint) in

comparison with standard operations on average for 17 - 26%.

4. Pathogenetic reasonable measure of prevention tromboembolic episodes at breast cancer surgical therapy is thought to be application of anticoagulant therapy (aspirin 0,5 two times per day, transfusion 400 rheopolyglukin 2 times with the interval 2-3 days, clexane 2 times per day 2-3 days before operation and 3-5 days after operation), frequency and severity of specific complications decreases 15%.

5. Preoperative radiation therapy at breast cancer is carried out daily 5 Gr, in a total dose 25 Gr in comparison with surgical method it led to increase survival only for 8%, without improving indicators of recurrences and metastasises.

6. Standard chemotherapy of breast cancer in combination with parallel thymalin infusion according to the scheme No. 4 of the patients operated by the developed technique is active prevention of hematologic complications, at the same time there is no falling of leukocytes content below critical level ($2,5x9^{10}$) that excludes treatment breaks and cancellation and increases duration of recurrence-free period from 10-12 days to 2, 3 months in comparison with group of patients who received chemotherapy without thymalin application.

7. Improved radical sector resection of mammary gland and radical mastectomy at cancer is not worse in efficiency than operations by Halsted, Madden, 5-year survival reaches 86,7%, 80,6% and 80,2%.

- recurrence - 4,7%, 15,8%, respectively
- metastasises - 1,6%, 17,4%, 18,1%, respectively.

5. Discussion

1. The offered surgical method of breast cancer therapy allows to carry out radical sector resection and radical mastectomy with the smallest injury.

2. Anticoagulant therapy does not raise intraoperative bleeding, it is an adequate measure of prevention tromboembolic episodes.

3. At application radiation therapy in the preoperative period, at application of a single dose equal to 5gr and SOD 20-25 of Gr, operation should be carried out within 7-10 days after the end of radiation.

4. Surgical therapy of breast cancer should be combined with thymalin immunotherapy which is prescribed parallel to the scheme No. 4 that excludes possibility of myelotoxic affect of chemotherapy on cells of white blood and increases antitumoral efficiency of chemotherapy.

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