Immediate Breast Reconstruction in Relation to Women's Age

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ABSTRACT

A modern approach to breast cancer treatment after mastectomy includes immediate breast reconstruction (performed simultaneously with the mastectomy). The understanding of factors that influence women's decisions and appreciation of their satisfaction is as important as the knowledge of medical efficiency of the selected treatment. The influence of women's age on opinion making for immediate breast reconstruction was researched in a monocentric prospective study (N=102). Methods included questionnaires, interviews and medical documentation reviews. Women comply breast reconstruction with silicone implants and autologous tissue equally. Analyzing age distribution it is evident that women age 35–50 and older than 65 would agree to reconstruction with silicone implants more often. This can be explained by the fact that younger women expect to have better shaped breasts after reconstruction then prior to the same, while older women tend to avoid breast reconstruction using muscle flaps because they are more demanding and also require longer hospitalization.

Key words: breast, cancer, immediate breast reconstruction, age

Introduction

Nowadays, conservative breast surgery is a standard in breast cancer treatment of stages 0, I and II, but mastectomy is still the only possible treatment that provides survival in a great number of patients¹. Post-mastectomy breast reconstruction is easily performed procedure, so no woman should ever suffer from the mutilating operation of body part amputation. Breast reconstruction avoids the necessity of external breast prostheses, which cause number of problems in everyday life². Therefore, post-mastectomy breast reconstruction is nowadays an integral part of operative treatment for breast cancer.

Post-mastectomy breast reconstruction, according to the timing of the procedure, can be immediate (performed at the same time after the mastectomy) or delayed. Immediate breast reconstruction is growing more popular in the last decades³⁻⁶. This approach is in many ways better and safer for the patients, for they return to their normal life sooner and undergo only one surgical procedure under general anaesthesia, which significantly reduces the cost of the treatment⁷. At the same time, it is

also important to note that while performing contralateral mastectomy in order to achieve breast symmetry after primary reconstruction, clinically and radiological »hidden« contralateral breast cancer was detected in over 4.5% of all cases⁸.

Major complaint about immediate breast reconstruction was oncological (un)certainty or actually the assumption of delay in diagnostics of disease relapse. Therefore, immediate reconstruction was recommended after the mastectomy due to ductal or lobular carcinoma in situ and for prophylactic purposes. Since carcinoma relapse of stage I and II A is only 0–2% and the implant is positioned subpectoral, superficial relapse of the skin and submammary connective tissue is accessible to palpation and thus not obscure to either clinical or radiological examination. Further complaints about immediate breast reconstruction, also unjustifiable, are the delay of adjuvant therapy due to additional procedure, inaccurate radiation of patients with implant reconstruction and implant capsular contracture after radiation or cyto-

static therapy (Doxorubicin). All disadvantages mentioned earlier can be eliminated by the use of silicone implants (which are not forbidden by the FDA in cases of post-mastectomy reconstruction due to malignancy) or autologous tissue reconstruction. Besides, breast reconstruction is better to be done prior to radiotherapy (PORT) for the reason that reconstructive surgery is much harder to be performed in previously radiated area due to different post radiation complications $^{9-13}$. Therefore, there are no medical contraindications for immediate breast reconstruction, while there is a significant positive effect on women. Early post-mastectomy reconstruction reduces the emotional experience of the mastectomy. The earlier the mastectomy is performed, the less frequent depression rate is 14,15. Other important advantages of the immediate reconstruction are better symmetry of the breast due to lithesome non-contractive skin flap and preservation of the inframammary fold, which is harder to reconstruct later. Furthermore, immediate reconstruction is economically more acceptable because only one operation during a single hospitalization is necessary. Finally, there is no statistically significant difference in complications between immediate and delayed reconstruction.

Immediate post-mastectomy breast reconstruction is a safe procedure from an oncologic point of view. There is much evidence to prove this notion. Relapse of breast cancer after primary reconstruction is noted in 4–11% of patients, especially within the first 5 years, with the incidence of 1% per year, most frequently during the second post-operative year. The incidence of local cancer relapse after mastectomy that was not followed by reconstruction is 0.2–1%, while after non-radical operation 1–2% yearly. Therefore, regardless of the operative technique (non-radical operation vs. mastectomy with or without reconstruction), the incidence of cancer relapse is similar^{16–19}.

The causes of cancer relapse are residue tissue of the carcinoma itself, implantation of tumour cells during operation, sequestration of tumour cells through lymphatic system or new primary tumour in the form of late »relapse«, formed of post-mastectomy normal breast tissue residue²⁰.

The risk of local recurrence of the disease, thereby, does not depend on immediate reconstruction. The complaint can be in-time diagnostics of the relapse. The most common site for cancer recurrence is skin and subcutaneous tissue, less commonly deeper tissue of the chest^{21–24}. Most of them are easy to detect by physical examination due to their superficial location. Besides, because of the subpectoral implant position technique deeper tissue of the chest becomes superficial and thus easier for palpation. Diagnostics of local cancer recurrence of the deepest layers of the chest wall is hard regardless of reconstruction. De facto, there is no time difference in relapse detection of deeper chest wall layers in reconstructed and unreconstructed breast.

Screening mammography is thus recommended in reconstructed breasts (with implants or autologous tissue)

due to early detection of cancer relapse, prior to it becoming palpable. In contribution, routine screening mammography after non-radical breast operations is commonly accepted, while it is also technically carried out in early detection of cancer recurrence after TRAM flap reconstruction²⁵. Commonly recognized trend in relapse therapy of reconstructed breasts is resection of cancer recurrence followed by adjuvant radiotherapy²¹.

The ideal candidate for post-mastectomy breast reconstruction is a young healthy woman in the early stage of the cancer. But, since different options of reconstruction are introduced, all women should be considered potential candidates for reconstruction. The dilemma should only be in choosing the reconstructive technique.

While selecting patients prior to final decision on whether to perform breast reconstruction and how to do it, many physiological and psychological parameters should be taken into consideration. Some of them are major surgical trauma, extended duration of the procedure, major blood loss, extended recovery and the will for reconstruction itself. Determining factors that define (or exclude) a potential patient can be divided into 4 groups: patients characteristics (age, weight, attitude towards the reconstruction, occupation), medical factors (prior abdominal or chest surgery, medications for concomitant diseases, heart disease, chronic pulmonary disease, vascular or systemic disease), disease characteristics (stage, carcinoma type) and technical opportunities (experience of the surgeon, accessibility of equipment).

Evidently, there are many factors that influence the procedure, but the most important to consider are age, weight, smoking, concomitant diseases and psychological/emotional status of the patient²⁶.

The aim of the present study was to survey patients opinion towards primary breast construction in regard to their age.

Patients and Methods

The intent was to process in a prospective study 100 breast cancer patients who are about to undergo surgical treatment at Dubrava University Hospital.

The patients were divided into 3 groups in consideration to their opinion on primary breast reconstruction: A. women who do not agree with primary breast reconstruction, B. women who agree with primary breast reconstruction and C. women who have no opinion on primary breast reconstruction due to inadequate information. These 3 groups were formed into subgroups with regard to age: 1. age 30–39, 2. age 40–49, 3. age 50–59, 4. age 60–69, 5. age 70 and older. Methods of investigation: a questionnaire and an interview. Statistical analysis:

All the data were analyzed with the statistical program Statistica 6.0. Descriptive statistics and χ^2 tests were made. Contingency tables showed quantitative results in absolute number and percentage. Median and range represented qualitative results. The level of statis-

tical significance was set at p<0.05. The Kruskal-Wallis test was also used in the statistical analysis for assessing the significance of the difference between the mean values of three different women groups regarding their attitude towards breast reconstruction.

Results

Out of 102 women in total, 100 of them (98.04%) filled out a questioner and agreed to an interview. The median age of the patients was 52 (30–71). The patients were asked a question on their attitude towards immediate breast reconstruction prior to the operation itself. Total of 46 patients agreed to immediate breast reconstruction, 36 of them denied it and 18 patients stated they were uninformed on the subject.

Women were divided into 3 groups according to their attitude towards primary breast reconstruction: A. women who are against primary breast reconstruction, B. women who are for primary breast reconstruction and C. women who are uninformed and do not have an attitude on primary breast reconstruction. These groups were analyzed according to reconstruction methods in regard to age and divided into subgroups: 1. age 30–39, 2. age 40–49, 3. age 50–59, 4. age 60–69, and 5. age 70 and older.

According to age, there is a statistically significant difference (p=0.005): younger women tend to agree with immediate breast reconstruction (Figure 1). The difference is highly noticeable when the patients are grouped by age (Figure 2). Younger women are better informed and more willing to undergo immediate breast reconstruction. Total of 80% of women aged under 39 agree to immediate reconstruction. The interest for the procedure decreases with age, so the ratio for and pro immediate reconstruction is almost equalized in the age group 50-59 (still a bit in favour of the procedure), while after the age of 60 almost 70% of women do not agree to the operation. In average, the will for reconstructive surgery tends to reduce by 20% per decade (Figure 3). Older women, especially over 70 years of age, are not interested even in the possibility of breast reconstruction so it seems in the charts that they are best informed which is not correct.

Out of 36 patients against breast reconstruction 23 patients (64%) specified fear of relapse as the result for rejection of reconstruction, 6 stated age (they were too old), 5 referred to fear of foreign material and 2 were afraid of additional surgical procedure (Figure 4).

In the group of women who agree to the procedure, 25 out of 46 patients want silicone implant breast reconstruction, while 21 of them want autologous tissue reconstruction (Figure 5). Although there is no statistically significant difference in reconstructive methods, the charts point out that women aged 40–49 prefer silicone implant reconstruction, while women over 50 year of age tend to want autologous tissue breast reconstruction.

Discussion and Conclusion

Surgical treatment of breast cancer includes series of operative methods, ranging from those that preserve the breast to mastectomies with or without reconstruction. Primary breast reconstruction can be preformed after modified radical mastectomy, after skin sparing mastectomy or skin and nipple sparing mastectomy. Cosmetic result is in direct relations with the selected type of operation. By increasing therapeutic possibilities many researchers try to reveal factors that have a direct influence on patient selection. One patient would be appropriate for preserving operation and another for post-mastectomy reconstructive procedure. Factors that are already known are age, economical status, race, education, geographical background and surgeon's attitude^{27–30}.

Many studies show that breast amputation causes psycho-social disorders and difficulties in perception of one's body, so called »body image«. Losing a breast can lead to severe depression, loss of femininity, serious marital problems and sexual dysfunction. Besides, amputated breast is a constant reminder of cancer³¹. Patients' experiences with external breast prostheses are poor because they are uncomfortable to wear. Besides the prosthesis being uncomfortable, it is hard to keep it in place, especially in warm water. It also requires a certain dress code and interferes with normal physical activity^{2,32}. Breast reconstruction corrects this handicap and offers patients better psychological and psychosocial sensation. Besides, reconstructive methods correct body asymmetry and set patients free from wearing uncomfortable external breast prosthesis³³. Primary breast reconstruction allows women to avoid even temporary body deformity, which is the case when delayed reconstruction is planned.

We questioned 102 women who were about to undergo surgical treatment for breast cancer. Only 2 women denied our interview and would not complete the questionnaire. This suggests a strong interest (>98%) in this issue and women's active attitude in the process of healing.

Patients were divided into 3 groups in regard to their attitude toward post-mastectomy immediate breast reconstruction: those who were against the procedure, those who were for it and those who felt that they were uninformed and had no particular attitude toward this problem. Out of 100 women, 46 accepted immediate breast reconstruction. Numbers are similar in other studies worldwide (49.6%)³⁴.

Statistical analysis between the groups was performed, in respect to demographical and clinical variables.

Median age of patients was 49 for women who want immediate breast reconstruction and 58 for those who do not want immediate reconstruction. Most studies state that age is approximately from 45 to 49 for the group that is pro reconstruction, and from 55 to 61 for the group that is against it $^{34-36}$.

Age, out of all demographic variables, has the most significant influence on the decision for accepting immediate breast reconstruction^{35–37}.

Most of the patients who undergo surgical treatment, in respect to age, are in the range 40-59 years of age (70%), which coincides with the biggest incidence of breast cancer in this age group. Patient's age is significant predictor of reconstruction. Younger women aged 30-54 are more likely to accept the possibility of immediate breast reconstruction than women aged 55-79 (59% and 23% respectively) (Figures 1-5). The willingness for this procedure decreases by 20% in average per decade. World references site yearly decrease by 5%38. According to the results of the present study, breast reconstruction for women aged from 70 to 79 is completely eliminated. The reason for this is unknown. It is assumed that older women are more passive and less fond of surgical treatment, while also more liable to trust doctor's advice not to have the operation. On the other hand, older women have other priorities and different perception of death, which can be of great influence on their attitude towards primary breast reconstruction³⁹.

When asked what kind of reconstructive method they would like to undergo, 25 out of 46 women chose silicone implant reconstruction, while 21 of them wanted autologous tissue reconstruction. Therefore, there is practically no difference in the method choice. Also, in comparison to world references, there is almost equal number of silicone implant reconstructions as there is of autologous tissue. In the last few years there is a trend that favors the autologous tissue reconstructive method, which can be explained by negative propaganda and fear of silicone implants, after the FDA disapproval^{38,40}.

There are also some attitudes that silicone implants are not recommended in patients in whom irradiation therapy is necessary due to capsular contraction and consequently poorer aesthetic results. However, if patient desires implants then it is better to perform the procedure prior irradiation due to post-irradiative complications. However, the number of complications is less after immediate breast reconstruction following mastectomy prior irradiation than after irradiation⁴⁰.

By analyzing patients in respect to age, it can still be concluded that women aged 35–50 are more likely to accept silicone implant reconstruction than women over 65 years of age. Other similar studies have shown that women younger than 40 years and older than 65 years are more willing to undergo silicone implant reconstruction. This can be explained by the fact that younger women wish to have better breast image then before the operation, while for older women muscle flap reconstruction is more demanding and also requires longer hospitalization^{41–43}.

Conclusion is that younger women are better informed about immediate breast reconstruction possibilities. Regarding the way of reconstruction the choice between silicone implant reconstruction and autologous tissue breast reconstruction is almost equal. Women aged 40–49 years prefer silicone implants, while younger and older women prefer autologous tissue breast reconstruction.

REFERENCES

1. MCGUIRE KP. SANTILLAN AA. KAUR P. MEADE T. PARBHO J. MATHIAS M, SHAMENDI C, DAVIS M, RAMOS D, COX CE, Ann Surg Oncol, 10 (2009) 2862. DOI: 10.1245/s10434-009-0635-x. — 2. KORVE-NOJA M L, SMITTEN K, ASKO-SELJAVAARA S, Ann Chir Gynaecol, 87 - 3. ELKOWITZ A, COLEN S, SLAVIN S, SEIBERT J, WEIN-STEIN M, SHAW W, Plast Reconstr Surg, 92 (1993) 92. DOI: 10.1097/ 00006534-199307000-00011. — 4. STYBLO TM, LEWIS MM, CARLSON GW. MURRAY DR, WOOD WC, LAWSON D, LANDRY J, HUGHES L, NAHAI F, BOSTWICK J, Ann Surg Oncol, 3 (1996) 375. DOI: 10.1007/ BF02305667. — 5. GERSHENWALD JE, HUNT KK, KROLL SS, ROSS MI, BALDWIN BJ, FEIG BW, AMES FC, SCHUSTERMAN MA, SIN-GLETARY SE, Ann Surg Oncol, 5 (1998) 529. DOI: 10.1007/BF02303646. - 6. GABKA CJ, MAIWALD G, BOHMERT H, Plast Reconstr Surg, 5 (1998) 1228. DOI: 10.1097/00006534-199804050-00009. — 7. KHOO A, KROLL SS, REECE GP, MILLER MJ, EVANS GRD, ROBB GL, BALD-WIN BJ, WANG B, SCHUSTERMAN MA, Plast Reconstr Surg, 4 (1998) 964. DOI: 10.1055/s-2007-1000179. — 8. PETIT JY, RIETJENS M, CON-TESSO G, BERTIN F, GILLES R, Ann Surg Oncol, 4 (1997) 511. DOI: 10.1007/BF02303678. — 9. KRAEMER O, ANDERSEN M, SIIM E, SCAND J Plast Reconstr Surg Hand Surg, 30 (1996) 201. DOI: 10.3109/ 02844319609062815. — 10. FORMAN DL, CHIU J, RESTIFO RJ, WARD BA, HAFFTY B, ARIYAN S, Ann Plast Surg, 40 (1998) 360. DOI: 10.1097/ 00000637-199804000-00007. — 11. KURUL S, DINCER M, KIZIR A, UZUNISMAIL A, DARENDELILER E, Eur J Surg Oncol, 23 (1997) 48. 12. CHEVRAY PM, Cancer J, 4 (2008) 223. DOI: 10.1097/PPO. 0b013e3181824e37. — 13. CHATTERJEE JS, LEE A, ANDERSON W, BAKER L, STEVENSON JH, DEWAR JA, THOMPSON AM, Br J Surg, 10 (2009) 1135. DOI: 10.1002/bjs.6693. — 14. STEVENS LA, MCGRATH MH, DRUSS GD, DRUSS RG, KISTER SJ, GUMP FE, FORDE KA, Plast Reconstr Surg, 73 (1984) 619. DOI: 10.1097/00006534-198404000-00018. - 15. WELLISCH DK, SCHAIN WS, NOONE RB, LITTLE JW III, Plast Reconstr Surg, 76 (1985) 713. DOI: 10.1097/00006534-198511000-00010. 16. VANDEWEYER E, HERTENS D, NOGARET J-M, DERAEMAE- CKER R. Plast Reconstr Surg. 107 (2001) 1409. DOI: 10.1097/00006534-200105000-00013. — 17. SPIEGEL AJ, BUTLER CE, Plast Reconstr Surg. 111 (2003) 706. DOI: 10.1097/01.PRS.0000041440. 12442.05. — 18. SLAVIN SA, LOVE SM, GOLDWYN RM, Plast Reconstr Surg, 93 (1994) 1191. DOI: 10.1097/00006534-199405000-00013. — 19. NOONE RB, FRAZIER TG, NOONE GC, BLANCHET NP, MURPHY JB, ROSE D, Plast Reconstr Surg. 93 (1994) 96. DOI: 10.1097/00006534-199401000-00015. — 20. MURPHY RX, WAHHAB S, ROVITO PF, HARPER G, KIM-MEL SR, KLEINMAN LC, YOUNG MJ, Ann Plast Surg, 50 (2003) 333. DOI: 10.1097/01.SAP.0000041488.88950.A2. — 21. LANGSTEIN HN, CHENG MH, SINGLETARY SE, ROBB GL, HOY E, SMITH TL, KROLL SS, Plast Reconstr Surg, 111 (2003) 712. DOI: 10.1097/01.PRS. 0000041441.42563.95. — 22. MC CARTHY CM, PUSIC AL, SCLAFANI L, BUCHANAN C, FEY JV, DISA JJ, MEHRARA BJ, CORDIERO PG, Plast Reconstr Surg, 2 (2008) 381. — 23. ROSEN WM, ASHTON MW, TAYLOR GI, Clin Breast Cancer, 2 (2008) 134. — 24. LEWIS RS, KONTOS M, Int J Pract, 11 (2009) 1642. DOI: 10.1111/j.1742-1241.2009. 02199.x. — 25. HELVIE MA, BAILEY JE, ROUBIDOUX MA, PASSHA, CHANG AE, PIERCE LJ, WILKINS EG, Radiology, 224 (2002) 211. DOI: 10.1148/radiol.2241010061. — 26. PADUBIDRI AN. YETMAN R. BROWN WE, LUCAS A, PAPAY F, LARIVE B, ZINS JE, Plast Reconstr Surg, 107 (2001) 342. DOI: 10.1097/00006534-200102000-00007. POLEDNAK AP, Plast Reconstr Surg, 106 (2000) 298. DOI: 10.1097/ 00006534-200008000-00008. — 28. POLEDNAK AP, Plast Reconstr Surg, 104 (1999) 669. DOI: 10.1097/00006534-199909030-00008. — 29. PUSIC THOMPSON TA, KERRIGAN CL, SARGEANT R, SLEZAK S, CHANG BW, KELZLSOUER KJ, MANSON PN, Plast Reconstr Surg, 104 (1999) 1325. DOI: 10.1097/00006534-199910000-00013. — 30. FINLAY-SON CA, MACDERMOTT TA, ARYA J, Am J Surg, 182 (2001) 649. DOI: 10.1016/S0002-9610(01)00788-7. — 31. REABY L, Plast Reconstr Surg, 101 (1998) 1810. DOI: 10.1097/00006534-199806000-00006. — 32. ROW-LAND JH, DIOSO J, HOLLAND JC, CHAGLASSIAN T, KINNE D, Plast Reconstr Surg, 5 (1995) 812. DOI: 10.1097/00006534-199504001-00008.

— 33. TYKKÄ E, ASKO-SELJAVAARA S, HIETANEA H, Ann Plast Surg, 49 (2002) 258. DOI: 10.1097/00000637-200209000-00004. — 34. KEITH DJW, WALKER MB, WALKER LG, HEYS SD, SARKAR TK, HUTCHEON AW, EREMIN O, Plast Reconstr Surg, 3 (2003) 1051. — 35. ALLWEIS TM, BOISVERT ME, OTERO SE, PERRY DJ, DUBIN NH, PRIEBAT DA, Am J Surg, 183 (2002) 218. — 36. NISSEN MJ, SWENSON KK, RITZ LJ, FARRELL JB, SLADEK ML, LALLY RM, Cancer, 7 (2001) 1238. DOI: 10.1002/1097-0142(20010401)91:7<1238::AID-CNCR 1124>3.0.CO;2-X. — 37. STARADUB VL, HSIEH Y, CLAUSON J, LANGERMAN A, RADEMAKER AW, MORROW M, Cancer, 6 (2002) 1185. — 38. ZWEIFLER M, RODRIGUEZ E, REILLY J, LEWIS T, GLASBERG SB, Ann Plast Surg, 1 (2001) 53. DOI: 10.1097/00000637-200107000-

00010. — 39. WOJCIK BE, SPINKS MK, OPTENBERG SA, Cancer, 82 (1998)1310. — 40. CONTANT, CME, van GEEL AN, van der HOLT B, GRIEP C, TJONG JOE WAI R, WIGGERS TH, Eur J Surg Oncol, 26 (2000) 344. DOI: 10.1053/ejso.1999.0896. — 41. ALDERMAN AK, MCMAHON L, WILKINS EG, Plast Reconstr Surg, 2 (2003) 695. DOI: 10.1097/01.PRS.0000041438.50018.02. — 42. DE LORENZI F, RIETJENS M, SORESINA M, ROSSETTO F, BOSCO R, VENTO AR, MONTI S, PETIT JY, J Plast Reconstr Aestet Surg, 23 (2008) 511. — 43. VEIR Z, DUJMOVIĆ A, DUDUKOVIĆ M, MIJATOVIĆ D, CVJETIČANIN B, VEIR M, Coll Antropol, 35 (2011) 1303.

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PRIMARNA REKONSTRUKCIJA DOJKE I DOB ŽENA

SAŽETAK

Suvremeni pristup u liječenju raka dojke nakon mastektomije je i primarna rekonstrukcija dojke (rekonstrukcija učinjena u istodobno s mastektomijom). Poznavanje čimbenika koji utječu na odluku žena i njihovo zadovoljstvo važno je kao i poznavanje medicinske efikasnosti odabranog načina liječenja. U monocentričnoj, prospektivnoj studiji (N=102) istraživan je utjecaj dobi o stavu prema primarnoj rekonstrukciji dojke u žena. Za metode rada korišten je upitnik, intervju i pregled medicinske dokumentacije. Žene se podjednako odlučuju za rekonstrukciju silikonskim implantatima i vlastitim tkivom. Analizom raspodjele po dobi ipak se može zaključiti da žene u dobnoj skupini 35–50 godina te starije od 65 godina radije prihvaćaju rekonstrukciju silikonskim implantatima. To se može objasniti time što mlađe žene očekuju nakon rekonstrukcije bolju dojku od vlastite prije operacije, a u starijih činjenicom da je rekonstrukcija režnjem mišića zahtjevnija za bolesnicu i traži dulju hospitalizaciju.