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Original Article

Influence of advanced age on postoperative outcomes and total loss following breast reconstruction: a critical assessment of 560 cases.

Influência da idade avançada sobre a evolução pós-operatória e a perda total da reconstrução mamária: análise crítica de 560 reconstruções.

Walter Koiti Matsumoto[1]; Alexandre Mendonça Munhoz[1,2,3]; Alberto Okada[3,4]; Eduardo Montag[3,4]; Eduardo Gustavo Arruda[3,4]; Alexandre Fonseca[3,4]; Orlando Ferrari[4]; José Augusto Brasil[1]; Lia Pretti[4]; José Roberto Filassi[2,3,5]; Rolf Gemperli, TCBC-SP[4].

1. Sírio-Libanês Hospital, Plastic Surgery, São Paulo, SP, Brazil.
2. Faculty of Medicine, University of São Paulo, Mammary Reconstruction Group, São Paulo, SP, Brazil.
3. University of São Paulo, Cancer Institute of the State of São Paulo, São Paulo, SP, Brazil.
4. Faculty of Medicine, University of São Paulo, Division of Plastic Surgery, São Paulo, SP, Brazil.
5. Sírio-Libanês Hospital, Mastology, São Paulo, SP, Brazil.

ABSTRACT

Objective: to evaluate the role of age in the risk of postoperative complications in patients submitted to unilateral breast reconstruction after mastectomy, with emphasis on total reconstruction loss. **Methods**: we conducted a retrospective study of patients submitted to breast reconstruction, whose variables included: oncological and reconstruction data, postoperative complications, including loss of reconstruction and complications of surgical wound. We divided the patients into two groups, according to the classification of the Brazilian National Elderly Policy and the Statute of the Elderly: young (age <60 years) and elderly (60 years or more). We also grouped them according to the World Health Organization classification: young people (age <44 years), middle age (45-59 years); elderly (age 60-89 years) and extreme advanced age (90 years or older). We applied the surgical risk classification of the American Society of Anesthesiologists to investigate the

role of the preoperative physical state as a possible predictor of complications. **Results**: of the 560 patients operated on, 94 (16.8%) were 60 years of age or older. We observed a local complication rate of 49.8%, the majority being self-limited. The incidences of necrosis, infection and dehiscence were 15.5%, 10.9% and 9.3%, respectively. Patients older than 60 years presented a chance of complication 1.606 times greater than the younger ones. Forty-five (8%) patients had loss of the reconstruction; there was no statistically significant difference in the mean age of the patients who presented this result or not (p=0.321). **Conclusion**: in selected patients, breast reconstruction can be considered safe; most documented complications were limited and could be treated conservatively.

Keywords: Reconstructive Surgical Procedures. Mastectomy. Age groups. Postoperative complications. Breast neoplasms

INTRODUCTION

Breast reconstruction is a well established procedure and is considered the standard treatment for patients with breast cancer who wish to repair the oncologic defect[1]. The choice of the reconstruction technique depends on the individual characteristics of each patient and is also influenced by the analysis of the surgical risk profile by the plastic surgeon[2,3]. Data from the Brazilian Institute of Geography and Statistics (IBGE) show that the elderly population is the one with the highest growth rates in Brazil, and similar demographic patterns can be found in other countries[4,5]. At the same time, the incidence of breast cancer increases with age, with 50% of cases occurring in women over 65 years of age[6]. The technological advances in medical treatment, among other factors, led to an increase in life expectancy, suggesting that the elderly population will require an increasing number of surgical procedures[7]. With advancing age, the decrease in the efficiency of the healing process and the reduction of cardiovascular function may represent an increase in the perioperative risk of this subgroup of cancer patients[7-9]. In addition, advanced age is often referred to as an independent risk factor for complications in general surgery patients[9,10]. However, few studies have evaluated the influence of age on the complications rates and on the disadvantages and benefits of breast reconstruction[7,8,11-13]. Some clinical series that evaluated the impact of age on complications in specific reconstruction techniques demonstrated greater clinical and surgical morbidity[11-13].

Considering that data on breast reconstruction in the Brazilian elderly population are limited, this study sought to investigate the postoperative complications in this specific

patients' group. The main objective of the study was to globally quantify the effect of age on postoperative complications. We also sought to investigate the relationship between age and total loss of the breast reconstruction.

METHODS

We carried out a retrospective cohort that identified all patients submitted to unilateral breast reconstruction at the Cancer Institute of the State of São Paulo (ICESP) and at the Sírio-Libanês Hospital (HSL). We conducted this study in accordance with the ethical guidelines of the Declaration of Helsinki, and it was approved by the Ethics and Research Committees of the respective institutions (approval protocols 474/13 and 714.543).

We analyzed the database of each institution (ICESP/HSL) for information on clinical complications associated with breast reconstruction. We excluded patients with incomplete information. The variables included were: oncological data, reconstruction data (technique), postoperative complications, including loss of reconstruction, surgical wound complications (reconstruction site and donor area), early infection (during hospitalization for reconstruction), late infection, seroma, dehiscence, hematoma. We divided the patients according to the classification of the Brazilian National Elderly Policy and the Statute of the Elderly (NEP)[14] in two groups: young people (age <60 years) and elderly (60 years or more). We also divided them into groups according to the World Health Organization (WHO) classification[15]: group I, young people (age <44 years); group II, middle age (age 45-59 years); group III, elderly (age 60-89 years), and group IV, extreme old age (90 years or more). We applied the American Society of Anesthesiologists (ASA) classification to investigate the role of preoperative physical status as a possible predictor of complications: Class 1 (healthy patient), Class 2 (mild or moderate systemic disease), Class 3 (severe systemic disease), Class 4 (severe systemic disease with constant risk of life), and Class 5 (patient to die within 24 hours despite surgical treatment).

We compared demographic and comorbidity data between age groups based on the NEP and WHO classifications. As the oldest patient in the sample was 88 years old, we grouped all patients older than 60 years for statistical analysis. To compare the continuous variables for the occurrence of complications (yes or no) or by any other categorical variable with two categories, we used the Student's t-test. To compare the continuous variables with more than two categories, we used the analysis of variance (ANOVA) model. To compare the categorical variables for the occurrence of complications (yes or no) or by any other categorical variable with two or more categories, we used the

chi-square test. We used the Fisher's exact test or the Likelihood Ratio when necessary. We also used the simple logistic regression model to verify which variables, individually, related to the occurrence of complications, to obtain the Odds Ratio (OR) for the occurrence of the mentioned outcomes for each variable. After the logistic regression analysis for each clinical risk factor and for the complications, we conducted a multivariate logistic regression analysis. However, some of the variables were significantly correlated with the others, and it was not possible to include all variables in the same model. Therefore, we chose to construct new variables with the combination of variables considered as risk factors. The new variables, combined two to two, were part of a simple logistic regression model. The value of p=0.05 was considered statistically significant. We used the SPSS software for Windows 7.0 (SPSS Inc. Chicago, Illinois) for all statistical analysis.

RESULTS

We analyzed the medical records of 560 consecutive patients (ages between 23 and 88 years) treated between October 2010 and May 2016. The minimum postoperative follow-up time was nine months, with an average of 35.6 months (range of nine to 66). According to the WHO classification, 153 patients (27.3%) were in group I, and 94 (16.8%), in group III. According to the NEP classification, 466 (83.2%) were young and 94 (16.8%) were elderly. Both in young patients (50.6%, 236 of 466 cases) and in the elderly ones (38.3%, 36 of 94), reconstruction with alloplastic materials was the most common reconstruction modality. Table 1 shows the distribution of reconstruction techniques in the different age groups.

Table 1. Distribution of reconstruction techniques by age groups.

Age	Breast reconstruction technique		
	Autogenic (%)	Alloplastic (%)	Autogenic + Alloplastic (%)
Age Groups (NEP)			
<60 years	119 (25.6)	236 (50.6)	111 (23.8)
≥60 years	35 (37.2)	36 (38.3)	23 (24.5)
p-value		0.042	
Age Groups (WHO)			
Young	36 (23.5)	79 (50.6)	38 (24.8)
Middle-age	83 (26.5)	157 (50.6)	73 (23.3)
Elderly/Extremely old	35 (37.2)	36 (38.2)	23 (24.4)
Total	154 (27.5)	272 (48.6)	134 (23.9)
p-value		0.145	

NEP: National Policy for the Elderly and the Elderly Statute; WHO: World Health Organization.

With respect to the oncological characteristics, 141 (25%) patients were classified as T1, 186 (33.2%), as T2, 95 (17%), as T3, 36 (4%), as T4, 63 (11.3 %), as a tumor in situ, and 26 (4.6%), as T0. In this sample, 215 (38.4%) patients underwent neoadjuvant chemotherapy, 249 (44.5%), adjuvant chemotherapy, three (0.7%) received neoadjuvant radiotherapy, and 335 (59.9%), adjuvant radiotherapy. The local recurrence rate was 6.6% and the incidence of distant metastases was 4.1%.

The comparison of the different age groups (NEP and WHO classifications) showed no relation between age and Body Mass Index (BMI, p=0.217). Patients with diabetes mellitus (DM) had a significantly higher mean age (58 years) than non-diabetic ones (49.4 years, p<0.001). Advanced age was an independent risk factor for DM (OR 4.57, p<0.001). Similarly, we found a significant relationship between age and systemic arterial hypertension (SAH, p<0.001). The comparison between non-hypertensive and hypertensive patients showed a significant increase in the proportion of elderly patients in the second group (p<0.001). Among the elderly patients, 71 (75.5%) were non-smokers, 14 (14.9%) were former smokers and nine (9.6%) were smokers. In relation to smoking, the groups of young and old (NEP classification) were statistically similar (p=0.408). However, considering the WHO classification, there was a significant difference (p=0.007), with a higher percentage of young patients in the nonsmoking contingent compared to smokers and former smokers. ASA 1 patients represented 30.7% (172/560) of the sample, while those ASA 2 and 3 accounted for 69.3%. No patient had an ASA 4 or 5 status (Table 2).

Table 2. Distribution of Comorbidities by age groups

Age	Comorbidities				
	Mean BMI (SD)	SAH (%)	DM (%)	Smoking (%)	ASA 2 and 3 (%)
Age Groups (NEP)					
<60 years	27.2 (4.8)	113 (24.2)	26 (5.6)	65 (13.9)	302 (64.8)
≥60 years	27.1 (4.9)	55 (58.5)	20 (21.3)	9 (9.6)	88 (93.6)
p-value	0.905	< 0.001	< 0.001	0.408	< 0.001
Age Groups (WHO)					
Young	26.6 (4.4)	15 (9.8)	1 (0.6)	14 (9.1)	83 (54.2)
Middle-age	27.5 (5)	98 (31.3)	25 (8)	51 (16.3)	219 (70)
Elderly/Extremely old	27.1 (4.9)	55 (58.5)	20 (21.3)	9 (9.6)	88 (93.6)
Total	27.2 (4.8)	168 (30)	46 (8.2)	74 (13.2)	389 (69.3)
p-value	0.146	< 0.001	< 0.001	0.007	< 0.001

SD: standard deviation; SAH: Systemic Arterial Hypertension; DM: Diabetes Mellitus; NEP: National Policy for the Elderly and the Elderly Statute; WHO: World Health Organization; BMI: body mass index.

Of the 560 patients, 279 (49.8%) developed local complications, most of them minor complications that did not require reoperation and could be treated on an outpatient basis. Seroma was the most frequent complication, with a total incidence of 22.1% (124/560), representing almost 45% of all complications. The incidences of necrosis, infection, dehiscence and hematoma were 15.5%, 10.9%, 9.3%, and 2.7%, respectively. Seroma occurred in 101 of the 466 (21.7%) young patients, and in 23 of the 94 (24.5%) elderly patients. There was no significant difference in the mean age between groups with or without seroma (p=0.333), infection (p=0.471), dehiscence (p=0.918) or necrosis (p=0.411). Patients with hematoma had a mean age of 58.8 years, while patients who did not evolve with it were 50.9 years old on average (p=0.004). After statistical analysis, we found a significant relationship between total reconstruction loss (8% of the whole sample) and the variables BMI, seroma, infection and necrosis. Patients who presented a loss of reconstruction had significantly higher mean BMI (30.2kg/m^2) than those without it (27.8kg/m^2, p=0.002). The ASA score did not show a significant correlation with the incidence of complications (p=0.139).

Patients who did not present complications had a mean age of 48.8 years, while the mean age of those who presented them was 51.4 years (Table 3). Considering only those who developed complications, 20.1% (56/279) were elderly. Patients 60 years of age or older presented a 1.606-fold greater risk of complications than did patients younger than 60. Obese patients had a 2,276-fold greater risk of complications when compared to non-obese patients (Table 4). Patients both elderly and obese presented a 3.16-fold higher risk of complications than did patients without any of these risk factors (p=0.005), as shown in Table 4. Patients with diabetes presented a risk of complications 2.471 times the risk of complications without DM. Elderly and diabetic patients presented a 2.67-fold greater risk of complication than non-diabetic young women (p=0.048). We observed a significant increase in complication rates in the advanced age groups (p=0.015) (Table 3); each one-

year increment corresponded to a 2.4% increase in the risk of complications, as demonstrated by the logistic regression analysis. The same analysis showed that the elderly/extremely old patients presented a complication chance 2.1 times higher when compared to the younger age groups.

Table 3. Distribution of age groups with averages, standard deviations, medians and range in the groups with and without complications and with or without total loss of reconstruction

Age (years)	Groups		p-value
	Without complications	With complications	
Average (SD)	48.8 (10.5)	51.4 (10.2)	0.003
Median (range)	48 (23-83)	51 (23-88)	
Age Group (NEP)			
<60 years – n (%)	243 (86.5)	223 (79.9)	0.05
≥60 years – n (%)	38 (13.5)	56 (20.1)	
Age Group (WHO)			
Young – n (%)	90 (32)	63 (22.6)	0.015
Middle-age – n (%)	153 (54.4)	160 (57.3)	
Elderly/Extremely old – n (%)	38 (13.5)	56 (20.1)	
Age (years)	Without total loss of reconstruction	With total loss of reconstruction	p-value
Average (SD)	51.4 (10.2)	49.7 (9.8)	0.321
Median (range)	51 (23-88)	50 (23-70)	

SD = standard deviation; NEP: National Policy for the Elderly and the Elderly Statute; WHO: World Health Organization.

Forty-five patients (8%) had total loss of reconstruction, 37 of the 466 young women (7.9%) and eight of the 94 elderly women (8.5%). We found no significant difference in the mean age between the patients who presented this outcome and those who did not (p=0.331), as shown in Table 3. Comparison of the young and old patients showed that the total loss of reconstruction was statistically equivalent in both groups (p=0.974). Likewise, there was no significant difference in the incidence of this complication among the young, middle-aged and elderly/extremely old age groups (p=0.405).

Table 4. Correlation of risk factors versus age groups and complications (singly, one by one, and two by two). Results of the logistic regression analysis.

Isolated Risk Factor	OR	95% CI	p-value
Age group (≥60 *vs*. <60)	1.606	(1.024-2.519)	0.039
BMI (obese *vs*. non-obese)	2.276	(1.548-3.346)	0.001
DM (Yes *vs*. No)	2.471	(1.288-4.74)	0.006
Hypertension (Yes *vs*. No)	1.945	(1.345-2.812)	0.001
Smoking (Yes *vs*. No)	1.671	(1.014-2.754)	0.044
Risk factor	OR	95% CI	p-value
Age group and BMI			
Any of the two *vs*. none	2.053	(1.427-2.951)	0.001
Both simultaneously *vs*. none	3.164	(1.408-7.11)	0.005
Age group and DM			
Any of the two *vs*. none	1.720	(1.105-2.675)	0.016
Both simultaneously *vs*. none	2.675	(1.009-7.088)	0.048
Age group and Hypertension			
Any of the two *vs*. none	1.392	(0.951-2.038)	0.089
Both simultaneously *vs*. none	2.974	(1.602-5.52)	0.001
Age group and Smoking			
Any of the two *vs*. none	1.837	(1.254-2.692)	0.002
Both simultaneously *vs*. none	1.489	(0.394-5.627)	0.557

BMI: body mass index; DM: Diabetes Mellitus; OR: *odds ratio*; CI: confidence interval.

DISCUSSION

Advanced age is recognized as a risk factor for cancer, and 60% of new cases are diagnosed in patients over 60 years[16,17]. Moreover, the increase in life expectancy has increased the number of elderly patients who require surgeries for oncologic resections and reconstructions[18]. Despite the evolution of breast cancer treatment and the aging process of the female population, treatment protocols in the elderly population are still based on studies with limited levels of evidence[19]. Due to the scarcity of studies with sufficient evidence to define the risks and benefits for this population segment, elderly patients tend to receive incomplete treatment for breast cancer[19,20]. In fact, some studies have shown discrepancies in relation to breast reconstruction rates in the different age groups, and only a minority of the elderly patients with breast neoplasia choose to undergo reconstruction[21].

Another important point is the controversy in establishing the age limits between the different age groups and the lack of uniformity in the definition of the term elderly. Some studies used the age of 50 as a reference[22], while others used 55 years[23], 60[24], or 65 years[25]. In the present study, we defined the age of 60 years as the limit between young and old, as recommended by the Brazilian National Elderly Policy[14]. This classification

proved useful and clinically relevant, since the great reduction in breast reconstruction rates is observed after the fifth and sixth decades of life. We also used the WHO classification to include an international categorization usually employed in public health worldwide[15].

In breast reconstruction, it is essential to determine the anthropometric and clinical factors associated with higher complication rates[25-27]. Age[13,23], smoking[22,25,28], obesity[22,23,25,27,28], SAH[24,25,27] and DM[24] are frequently mentioned as potential risk factors. In this scenario, there is no consensus regarding the role of age on complications in patients with breast neoplasms undergoing reconstruction[13-17]. In this sample, patients with DM had a significantly higher mean age than non-diabetics, and there was also a significant relationship between age and SAH. Similarly, the mean age for ASA 1 patients was significantly lower than for patients classified as ASA 2 or 3. We found no significant relationship between smoking and obesity in elderly patients. Despite this, considering the WHO classification, we observed a greater percentage of young patients in the non-smokers group in relation to smokers and former smokers.

Regarding breast reconstruction, some studies have compared the rates of complications among young and old patients[7,8,11-13]. In this study, the comparison of complication rates among age groups according to NEP classification showed a higher incidence of complications in the advanced age group, although this difference occurred at the limit of significance (p=0.05). When we used WHO classification, we observed a significantly higher incidence of complications in the elderly/extremely old. Moreover, the overall rate of surgical complications in young and old patients was 47.8% and 59.6%, respectively, higher than those reported in other published series[7,8,11-13,29]. This is due to the inclusion of minor complications, such as mild to moderate seromas, which exhibited a total incidence of 22% and accounted for almost 45% of all complications. In spite of the high incidence of seromas when compared to other studies, we must be emphasize some points. Some studies with large samples are based on the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP), which does not include some adverse events (such as seroma) in the list of complications[22,23]. Thus, if the seroma were excluded from the list of complications in this study, the results would become comparable to previously published clinical series[7,8,11-13].

Considering all types of adverse events, there was no significant difference in the mean age among patients who presented complications. In addition, the comparison of young and elderly patients did not show a significant difference in the isolated incidence of each type of complication, with the exception of hematoma. And although there is no

consensus to characterize age as a risk factor for breast reconstruction, some studies have demonstrated ASA classification as a predictor for perioperative complications[7,30]. In this series, patients classified as ASA 2 or 3 accounted for almost 70% of the entire sample. In contrast to observations from other studies[7,30], the ASA classification did not demonstrate a significant correlation with the incidence of complications. At this point, we believe that this aspect should not contraindicate reconstruction, although one should take additional care in patients with a higher surgical risk.

Despite the higher rates of complications in the present study, the total loss of reconstruction was less frequent than in other series with lower global rates of adverse events[12,29]. Furthermore, it is important to note that, although the complication rate was higher in elderly patients, this difference did not result in a higher incidence of total reconstruction loss. On the other hand, other studies have observed that age greater than 50[22] and 55 years[23] were independent predictive factors for reconstruction loss. In a paradoxal way, the incidence of reconstruction loss was lower in patients who had presented seroma and necrosis than in patients who did not present such outcomes. One hypothesis to explain this finding is that the diagnosis of these two events motivated a rapid treatment by the medical team with intensive follow-up, re-hospitalization, drainage of collections, debridement of devitalized tissues and antibiotic therapy, which resulted, in the end, in lower reconstruction loss rates when compared to patients with subclinical infections.

Regarding reconstruction techniques, almost 50% of the patients underwent reconstruction with alloplastic materials, 27% with autogenous tissues and 24% with a combination of alloplastics and autogenous tissues. Both young and elderly patients underwent alloplastic reconstruction more frequently. Like other authors, we did not find a correlation between age and the incidence of complications when performing the analysis of the alloplastic, autogenous and alloplastic / autogenous groups separately[7,13,22,23,25,31]. One of the obvious limitations of this study is the relatively small sample size in each subgroup of reconstruction technique. Future studies with a larger number of patients may reveal whether current findings are due to inadequate sample size or are a valid consideration.

Other limitations of the present study require attention. First, we collected the data prospectively but evaluated them retrospectively. In addition, the study was observational and non-randomized. There is, therefore, a selection bias that cannot be excluded. Although the sample size of this series is significant, the notable low incidence of some types of complication and some reconstruction modalities may have prevented the

analysis from achieving the desired statistical power. In addition, we could not perform comparisons of the results in patients with extreme old age, smoking and diabetics, as well as subgroups of different surgical techniques, so that the clinical relevance of the type of breast reconstruction in these groups remains controversial. Prospective studies will be needed to clarify this issue and to define which operative techniques are most appropriate for elderly patients. Second, questions about quality of life and the analysis of treatment costs were not part of the objectives of this study, but will be relevant to future research. Finally, although the postoperative complications reported by the medical team may be criticized for possible underreporting, the data in the present study reflect the unique experience of a single team in a tertiary hospital dedicated to the Brazilian population.

We conclude that breast reconstruction is a valid option for adequately selected patients. This study showed that age is an independent risk factor for surgical complications, although the vast majority of these complications have been limited and could be treated conservatively. However, patients who are candidates for immediate reconstruction should be advised that age will not necessarily imply a greater risk of loss of reconstruction. Thus, it is appropriate to indicate breast reconstruction in elderly patients and this procedure should be considered in counseling patients under treatment for breast cancer.

RESUMO

Objetivo: avaliar o papel da idade no risco de complicações pós-operatórias de pacientes submetidas à reconstrução mamária unilateral pós-mastectomia, com ênfase na perda total da reconstrução. **Métodos**: estudo retrospectivo de pacientes submetidas à reconstrução mamária, cujas variáveis incluídas foram: dados oncológicos e da técnica de reconstrução, complicações pós-operatórias, incluindo perda da reconstrução e complicações da ferida operatória. As pacientes foram divididas de acordo com a classificação da Política Nacional do Idoso e Estatuto do Idoso em dois grupos: jovens (idade <60 anos) e idosas (60 anos ou mais). Também foram agrupadas de acordo com a classificação da Organização Mundial da Saúde: jovens (idade <44 anos); meia-idade (idade 45-59 anos); idosas (idade 60-89 anos) e velhice extrema (90 anos ou mais). A classificação do risco cirúrgico da Sociedade Americana de Anestesiologistas foi aplicada para investigar o papel do estado físico pré-operatório como possível preditor de complicações. **Resultados:** das 560 pacientes operadas, 94 (16,8%) apresentavam 60 anos ou mais. Observou-se taxa de complicações locais de 49,8%, a maioria, limitadas. As incidências de necrose, infecção e deiscência foram de 15,5%, 10,9% e 9,3%,

respectivamente. Pacientes com 60 anos ou mais apresentaram chance de complicação 1,606 vezes maior do que as jovens. Quarenta e cinco (8%) pacientes apresentaram perda da reconstrução e não houve diferença estatisticamente significante na média de idade das pacientes que apresentaram ou não esse desfecho (p=0,321). **Conclusão:** em pacientes selecionadas, a reconstrução mamária pode ser considerada segura; a maioria das complicações documentadas foi limitada e pode ser tratada conservadoramente.
Descritores: Procedimentos Cirúrgicos Reconstrutivos. Mastectomia. Grupos Etários. Complicações Pós-Operatórias. Neoplasias da Mama.

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Mailing address:

Alexandre Mendonça Munhoz

E-mail: munhozalex@uol.com.br / walterkm3@gmail.com