Original Article

Evaluation of acute skin toxicity during radiotherapy for breast cancer in elderly patients

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Background: For women with early stage breast cancer, the hypofractionation is the standard of care, whereas for women in other situations the standard dose is still recommended. Although the hypofractionation studies included elderly patients (>70 years), many studies excluded this population. The goals of this study are to demonstrate our results in terms of acute skin toxicity in elderly patients, and to show that they can receive the same treatment as young patients.

Methods: We conducted a retrospective study searching our database for patients at least 70 years old at the beginning of the treatment for breast cancer. The treatment planning and the medical records were reviewed to check not only the details of the treatment but also the skin reactions developed. The RTOG (Radiation Therapy Oncology Group) was used to take note of the skin toxicity.

Results: Two hundred and seventy-six patients treated from June 2015 to May 2019 were included in the final analysis. The vast majority of patients (72.99%) developed only a RTOG grade 1 reaction, the only two patients which presented with RTOG 4 had ulceration of skin, achieving full recovery. Regarding the volume of treatment, the percentages for RTOG 1 were similar for "Breast" and "Breast plus Drainage" (~75%). Patients receiving treatment aiming breast, drainage and boost had the higher percentage of RTOG 4 (6.2%). Patients that received the hypofractionation showed slightly better results than the standard fractionation, with no patient with RTOG 4 and lesser patients with RTOG 2 and 3, RTOG 1 was predominant for all sub-groups analyzed. Mild erythema and dry desquamation are common reactions that usually do not greatly affect the quality of life of the patients. The volume of treatment has an important effect on skin reactions with the number of events increasing considerably at larger volumes. Overall, there is a benefit in favor of hypofractionation in terms of acute skin toxicity.

Conclusions: It can clearly be seen that elderly patients can tolerate the acute side effects of the radiotherapy and they should receive the same treatment as young patients. Larger volumes of treatment increased the toxicity, hence these patients should be more carefully evaluated during the treatment.

Keywords: Breast cancer; radiotherapy; skin toxicity

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Introduction

For women with early stage breast cancer, the hypofractionation is the standard of care based on the results of the Canadian and Start A and B trials (1-3), while for women in other situations the standard dose of 50 Gy in 25 fractions is still recommended (4-6).

Table 1 RTOG grade and No. of patients

RTOG	N (%)
0	39 (14.23)
1	200 (72.99)
2	25 (9.12)
3	8 (2.92)
4	2 (0.73)
5	0 (0)

RTOG, Radiation Therapy Oncology Group.

Although the hypofractionation studies included elderly patients (>70 years), many of the most important studies in the last decades excluded this population (7-9), preventing us from having the results regarding toxicities. Moreover, the vast majority of the studies focus on late toxicities (8,10), neglecting the harmful effect of acute skin reactions on patient's quality of life.

The goals of this retrospective study are to demonstrate our results in terms of acute skin toxicity when treating elderly patients. Therefore, to show that, regarding skin toxicity, elderly patients can receive the same treatment as young patients.

Methods

We conducted a retrospective study in our oncology center (Americas Centro de Oncologia Integrado - Botafogo) searching the Aria® database to find patients that meet our criteria. The inclusion criterion was patients at least 70 years old at the beginning of the treatment for breast cancer. We did not take into consideration the technique used or the side of the breast, thus, right and left breast, 3D, IMRT, RapidArc® and Calypso® were allowed. The treatment planning was reviewed to check the volume of treatment (breast or breast and local drainage), fractionation (standard of hypofractionation), total dose and number of fractions. For volume of treatment, either chest wall or breast were noted only as "breast", since our objective is to evaluate only skin reaction.

We also conducted a medical record review to check the grade of skin reaction noted by the radiation oncologist during the treatment. Patients in our clinic are evaluated weekly and the RTOG (Radiation Therapy Oncology Group) scale (11,12) is used to describe the skin reaction. If the RTOG grade was not presented in the medical records, we looked for the description of the level of skin reaction in order to allocate it to the correct position on the scale as following: RTOG 0, no change; RTOG 1, faint erythema, dry desquamation, epilation, decreased sweating; RTOG 2, tender or bright erythema, moderate edema, patchy moist desquamation; RTOG 3, moist desquamation in areas other than in skin folds, pitting edema; RTOG 4, ulceration, hemorrhage, necrosis; RTOG 5, death. This research was approved by the ethics committee of our institution.

Results

After the research, we found a total of 300 patients treated from June 2015 to May 2019. Twenty-six patients were excluded from the evaluation for different reasons. Twelve (patients) because they had had palliative treatments, thirteen patients did not have mention of skin reaction on their records, and one was a male patient. Therefore, a total of 274 patients were included in the final analysis, with an average age of 77 years, ranging from 70 to 97 years of age.

Overall, the vast majority of patients (72.99%) developed only a grade 1 reaction (*Table 1*). For the RTOG 0, 2, 3 and 4, the figures were 14.23%, 9.12%, 2.92% and 0.73%, respectively. The only two patients which presented with RTOG 4 had ulceration of skin, achieving full recovery after approximately one month. There were no patients with RTOG 5.

The volume of treatment was also important, and the results showed consistency among the categories. As we can see in *Table 2*, the percentages were similar for "Breast" and "Breast plus Drainage" regarding RTOG 1 (approximately 75%). Still looking at the RTOG 1, the percentage decreases in the next two groups "Breast plus Boost" and "Breast plus Drainage plus Boost", the former mainly because of an increase in grade 0 and the latter because of an increase in the grade 2 reactions.

The last group, despite being the least in terms of absolute number of patients, was the group with the higher percentage of RTOG 4. From all the patients that received this treatment aiming the breast, drainage and boost, 6.2% developed the grade 4 reaction.

Moving on to the fractionation (*Table 3*), the total number of patients was equal with 137 patients receiving the standard fractionation and another 137 patients receiving the hypofractionation. The dose used in the standard treatment was 50 Gy in 25 fractions, whereas in the hypofractionation group a wider range of doses were used. The main dose was 42.4 Gy in 16 fractions, followed by 40 Gy in 15 fractions.

Table 2 Volume of treatment and RTOG grade

Volume	RTOG 0, n (%)	RTOG 1, n (%)	RTOG 2, n (%)	RTOG 3, n (%)	RTOG 4, n (%)	RTOG 5, n (%)	Total
B	25 (14.2)	133 (75.6)	15 (8.5)	3 (1.7)	0 (0)	0 (0)	176
B + D	4 (7.3)	42 (76.4)	6 (10.9)	2 (3.6)	1 (1.8)	0 (0)	55
B + BO	8 (29.6)	16 (59.3)	1 (3.7)	2 (7.4)	0 (0)	0 (0)	27
B + D + BO	2 (12.5)	9 (56.3)	3 (18.8)	1 (6.3)	1 (6.3)	0 (0)	16

RTOG, Radiation Therapy Oncology Group; B, Breast/Chest Wall; D, Drainage; BO, Boost.

Table 3 Fractionation schedules

Fractionation	RTOG 0, n (%)	RTOG 1, n (%)	RTOG 2, n (%)	RTOG 3, n (%)	RTOG 4, n (%)	RTOG 5, n (%)	Total
Standard	13 (9.5)	99 (72.3)	18 (13.1)	5 (3.6)	2 (1.5)	0 (0)	137
Hypofractionation	26 (19.0)	101 (73.7)	7 (5.1)	3 (2.2)	0 (0)	0 (0)	137

RTOG, Radiation Therapy Oncology Group.

The figures for the standard fractionation were 9.5%, 72.3%, 13.1%, 3.6% and 1.5%, for the RTOG 0, 1, 2, 3 and 4, respectively. The patients that received the hypofractionation showed slightly better results, with no patient with RTOG 4 and less patients with RTOG 2 and 3. The final numbers for this schedule were in the sequence from RTOG 0 to 3: 19.0%, 73.7%, 5.1% and 2.2%.

Discussion

The first thing to consider before beginning the analysis is that the level of skin reactions was low and acceptable, and that these numbers may be even better. This happens because the patients excluded for lack of information regarding skin reaction were probably RTOG 0; it is common for the physician not to take note when the patient does not show any reaction.

The RTOG 1 was predominant in absolute (n=200) and relative numbers (72.99%), and we can see similar number for all sub-groups analyzed. Mild erythema and dry desquamation are common and easy to handle reactions that usually do not greatly affect the quality of life of the patients. Therefore, this would not be a problem, even when it comes to elderly patients.

The volume of treatment has an important effect on the development of acute skin reactions, and this can be clearly seen by the results. The number of events grade 2, 3 and 4 increases considerably when we add more volume to the treatment, especially if the drainage is included. In the treatments where this region is included the percentage of the aforementioned toxicities may be up to six times higher than the treatments without the drainage.

Lastly, the table for the fractionation shows a clear benefit in favor of hypofractionation. Despite having more patients with RTOG 0, the percentage for RTOG 2 in the hypofractionation schedule was almost 3 times lower than the standard fractionation (13.1%×5.1%). For the RTOG 1 there was no significant difference between the schedules (70.8%×73.7%).

Conclusions

In conclusion, it can clearly be seen that elderly patients can tolerate the acute side effects of the radiotherapy treatment for breast cancer and they should receive the same treatment as young patients. The grades of reaction were mild and expected for this kind of treatment, without major consequences for the quality of life of the patients. Furthermore, larger volumes of treatment increased the level of acute skin toxicity, hence these patients should be more carefully evaluated during the treatment.

In addition, the vast majority of studies focus only on late skin side effects. However, the acute side effects can be even more harmful for the quality of life of the patients and should be paid more attention in future trials.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This research was approved by the ethics committee of our institution. Informed consent was waived.

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