Neoadjuvant Radiotherapy for Breast Cancer Exploring New Pathways for Treatment

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DOI: 10.32629/jcmr.v5i4.3300

Abstract: Breast cancer is one of the most prevalent malignancies affecting the female population, and the role of adjuvant radiotherapy is crucial in the treatment of breast cancer. With the continuous advancement of radiotherapy techniques, neoadjuvant radiotherapy has received renewed attention. In this paper, we will review the application of neoadjuvant radiotherapy in patients with early breast-conservation, breast reconstruction and LABC, and synthesize and analyze the results of existing research, with the expectation that it can provide a more comprehensive and in-depth understanding of the treatment of breast cancer, as well as look forward to its future trajectory and prospects.
***Keywords*:** locally advanced breast cancer; neoadjuvant radiotherapy; preoperative radiotherapy

1. Effectiveness of neoadjuvant radiotherapy for early breast cancer

Neoadjuvant radiotherapy has been shown to be safe and effective in colorectal, breast and various other types of malignant tumors, showing potential advantages in reducing metastatic stem cell activity, providing clinical staging and reducing potential intraoperative risks[1].In the field of breast cancer research in recent years, there is a paucity of literature on the use of neoadjuvant radiotherapy techniques for the treatment of early stage breast cancer, thus further research on neoadjuvant radiotherapy for breast cancer is of significant interest. Neoadjuvant radiotherapy is an emerging therapeutic sequence that has been systematically evaluated, and preliminary results have demonstrated the technical and oncologic safety of this treatment, but these studies still need to be evaluated with longer follow-up and larger prospective controlled clinical trials[2].

Poleszczuk et al. studied the long-term survival of patients with early-stage cancer who received neoadjuvant radiotherapy versus adjuvant radiotherapy. The study found that neoadjuvant radiotherapy had a lower risk of second primary tumors in estrogen receptor-positive women compared to adjuvant radiotherapy. Overall survival was independent of the order of radiotherapy. Neoadjuvant radiotherapy significantly improved disease-free survival without decreasing overall survival, especially in estrogen receptor-positive patients. These findings provide a basis for future studies of the potential benefits of neoadjuvant radiotherapy in the treatment of early-stage cancer[3].

From the above studies, it is easy to see that neoadjuvant radiotherapy can significantly improve disease-free survival in estrogen receptor-positive patients with early-stage cancers without decreasing the overall survival rate, and although the preliminary results have demonstrated the technical and oncological safety of this treatment, there are not many relevant studies, and there is still a need for longer follow-up evaluation and larger prospective controlled clinical trials of these studies, all of which have yielded more reliable experimental data and results.

2. Therapeutic efficacy of neoadjuvant radiotherapy for locally advanced breast cancer (LABC)

LABC usually includes stage IIB (T3NOMO) and stage IIIA (T3N1M0) breast cancers that are feasible for radical surgery, and stage IIIB and IIIC breast cancers that are difficult to undergo radical surgery with skin, chest wall or regional lymph node involvement[4].LABC has traditionally been treated with a multimodal approach of chemotherapy, surgery and post-mastectomy radiotherapy[5].

In the study by C. Sousa et al, about 4% of European patients were diagnosed with locally advanced breast cancer (LABC), and systemic therapy was identified as the treatment of choice, while radiation therapy was also considered to be an effective means of reducing tumor stage. The aim of this study was to evaluate the therapeutic efficacy of neoadjuvant radiation therapy in patients with locally advanced breast cancer that cannot be treated surgically. The results of the study showed that 18% of patients achieved complete breast remission. 5-year OS reached 54% and PFS was 61%. Further subgroup analysis revealed that pR>90% was significantly associated with better OS (p=0.004). The basal-like intrinsic

subtype was associated with poorer OS and PFS ($p<0.05$). The study confirms that neoadjuvant radiotherapy is an effective downsizing treatment for inoperable locally advanced breast cancer with or without systemic therapy. To improve patient selection and treatment optimization, prospective studies are necessary to explore predictive response biomarkers[6].

In patients with locally advanced breast cancer (LABC), the pathological response rate to preoperative paclitaxel-synchronized radiotherapy is high, with half of the patients with HR-negative tumors obtaining a pathological response that translates into superior DFS and OS[7]. In contrast, preoperative 5-fluorouracil combination radiotherapy for patients with locally advanced breast cancer is well tolerated by radiotherapy and is effective in shrinking the majority of patients, converting inoperable breast cancer into easily resectable disease[8]. In a study by Alvarado-Miranda, A. et al. it was mentioned that the unconventional multimodal treatment of neoadjuvant chemotherapy followed by simultaneous radiotherapy had good locoregional control of LABC[9].

Zinzindohoué, C. et al. mentioned in their study that breast-conserving mastectomy and immediate breast reconstruction are increasingly being used in invasive breast cancer, which suggests that breast-conserving mastectomy and immediate breast reconstruction after radiochemotherapy is safe and acceptable for its local recurrence rate, but long-term data are still needed to assess the recurrence rate [10]. This treatment is within acceptable safety limits for oncologic therapy, while maintaining the aesthetics of the breast and protecting the patient's self-esteem This treatment sequence does not appear to increase the incidence of IBR, nor does it alter disease-free survival or overall survival Neoadjuvant radiotherapy combined with chemotherapy is significantly higher than chemotherapy alone in terms of remission rates in breast cancer. Compared with radiotherapy alone, patients with operable breast cancer who were given a combination of chemotherapy and radiotherapy prior to mastectomy followed by mastectomy had significantly improved outcomes.

3. Problems of neoadjuvant radiotherapy that still need to be solved

In recent years, the relevant literature reports on the toxic side effects of neoadjuvant radiotherapy/neoadjuvant radiochemotherapy mainly include the following research results. First, the postoperative complications of modified radical mastectomy after neoadjuvant radiotherapy, Riet and others found that the total incidence of postoperative complications of modified radical mastectomy in patients with breast cancer treated with neoadjuvant radiotherapy alone was 19%, of which grade 2 or higher surgical incision dehiscence accounted for 4%, grade 3 skin necrosis accounted for 4%, hematoma and infection led to secondary surgery accounted for 5%, lymphedema accounted for 5%, myocardial infarction accounted for 0.5%, and pulmonary embolism accounted for 0.5%. 0.5%, and pulmonary embolism accounted for 0.5%.In a study by Niamh et al, 16 patients with LABC who underwent breast reconstruction after neoadjuvant radiotherapy were compared to 32 patients with LABC who underwent breast reconstruction followed by adjuvant radiotherapy after previous breast reconstruction.In the neoadjuvant radiotherapy group, there were 3 cases of incision infection, 1 case of incision dehiscence, and 1 case of postoperative respiratory infection, whereas in the postoperative radiotherapy group, there were 2 cases of seroma, 1 case of hematoma and 1 case of parastomal effusion, the difference in postoperative complications in the neoadjuvant radiotherapy group compared with the postoperative radiotherapy group was not statistically significant ($P = 0.117$). In addition, in a study by Matuschek et al, 315 breast cancer patients were treated with neoadjuvant radiotherapy/ neoadjuvant radiochemotherapy, which showed that neoadjuvant radiotherapy/neoadjuvant radiochemotherapy did not result in side effects, such as grade 3 or 4 cutaneous fibrosis, and that neoadjuvant radiotherapy was associated with good cosmetic outcomes.

Neoadjuvant radiotherapy-induced vascular fibrosis can also increase the difficulty of intraoperative tumor tissue separation. Therefore, the irradiation time and intensity of neoadjuvant radiotherapy should be strictly controlled to reduce the impact of neoadjuvant radiotherapy on surgery. In addition, neoadjuvant radiotherapy in LABC patients often changes the anatomical relationship between normal tissues and tumor tissues, which makes separation difficult during surgery and increases the difficulty of surgery. Therefore, when radiotherapy is performed before surgery, the target area should be accurately outlined, and the time and dose of radiotherapy should be strictly controlled. Under normal circumstances, the decision of whether to carry out surgical treatment should be made after 6 weeks of neoadjuvant radiotherapy, and this period of time is conducive to the establishment of tumor antigen and antibody system, which is effective in preventing the recurrence of breast cancer. When patients undergo neoadjuvant radiotherapy, doctors need to assess the patient's condition according to the patient's specific situation to adopt an appropriate neoadjuvant radiotherapy plan for treatment and reduce the impact of neoadjuvant radiotherapy on patients.

4. Conclusion

Radiotherapy technology has made great progress in recent years, and preoperative radiotherapy has become a research

hotspot. The current number of cases of neoadjuvant radiotherapy for breast cancer is still small, and longer follow-up is needed. The potential benefits of neoadjuvant radiotherapy (with or without biologics) now warrant further exploration in prospective randomized controlled trials to assess its potential benefits. Prospective clinical trials have a high strength of argument in further clarifying the advantages of preoperative radiotherapy for breast cancer in different populations, and are more conducive to finding appropriate treatment options and safer treatment modalities for breast cancer patients, leading to longer survival rates.

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