

ORIGINAL ARTICLE

PROSPECTS OF NEOADJUVANT CHEMORADIOTHERAPY IN PATIENTS WITH STAGE III A NON-SMALL CELL LUNG CANCER AS A METHOD OF IMPROVING SURVIVAL

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ABSTRACT

The aim: To study the survival rate and count the number of complications in groups with NCRT, NCT and NCT + adjuvant radiotherapy.

Materials and methods: The studied patients were divided into three groups with a total number of 304 people, Patients who received neoadjuvant chemotherapy-149 people, who received neoadjuvant chemotherapy and adjuvant radiation therapy-90 people. Neoadjuvant chemoradiotherapy was performed in accordance with Cisplatin/Docetaxel or Carboplatin/Paclitaxel 4 Mg and simultaneous radiation therapy with a total radiation dose 30 gray with a single dose of 2 Mg. After neoadjuvant treatment, patients of all groups underwent radical surgery. It consisted of lobectomy, bilobectomy and pneumonectomy. Postoperative complications and the duration of stay in the clinic after surgery were studied. Survival was assessed on the Kaplan and Mayer scale.

Results: The study analyzed the main results of treatment, which showed that the 5 years survival in the main group was 28.1±5.9%, in the control groups-the first control group (neoadjuvant chemotherapy) - 10.4±3.8% and the second control group (neoadjuvant chemotherapy and adjuvant radiation therapy) - 5.8±2.0%, respectively.

Conclusions: 1. The overall survival rate of patients receiving NCT compared to patients receiving neoadjuvant chemotherapy is higher than in the neoadjuvant chemotherapy group and 13 months higher than in the adjuvant radiation therapy group. 2. Patients who had the phenomenon of a complete morphological response have a significantly higher survival rate (45 and 39 months, respectively).

KEY WORDS: non-small cell lung cancer, neoadjuvant therapy, chemoradiotherapy

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INTRODUCTION

Treatment of stage III A non-small cell lung cancer (NSCLC) is a controversial issue, despite combined and complex treatment, survival remains low - 58% of patients live no more than a year after diagnosis [1, 2]. At the moment, there is no convincing data on the advantages of surgical treatment with neoadjuvant chemotherapy, surgical treatment with neoadjuvant radiation therapy, targeted therapy and chemoradiotherapy according to a radical program [2 -8]. In neoadjuvant treatment, comparative studies of various radiation therapy regimens and courses of chemotherapy cycles are continuing, and there is also no standard approved in clinical protocols. In this regard, there is an active search for new and improvement of existing treatment methods, the accumulation and processing of clinical data for the approval of clear standards for the treatment of stage III A NSCLC [4 - 5].

Based on the conducted studies, it was found that one of the promising methods of increasing survival is the method of neoadjuvant chemoradiotherapy followed by radical surgical intervention. The article discusses its principle of operation, advantages, difficulties and limitations.

In the treatment of NSCLC, NCRT is not included in

the Ukrainian clinical protocols and can be used as part of neoadjuvant therapy, if the doctor deems it necessary. In the NCCN clinical protocol, if radical surgery is performed at stage III A of NSCLC, the use of radiation therapy before or after radical surgery is mandatory (Fig 1) [2].

THE AIM

The aim of the work was to study the survival rate and count the number of complications in groups with NCRT, NCT and NCT + adjuvant radiotherapy.

MATERIALS AND METHODS

The studied patients were divided into three groups with a total number of 304 people, 1 group (main) was 65 people, 2 and 3 – control 149 and 90 people, respectively.

The effect of NCRT was studied in 65 patients with stage III A NSCLC in the Department of Lung and Mediastinal Tumors of the National Cancer Institute, Kiev. This method of treatment was prescribed to study the effect of NCRT, but was used for such indications as unresectability at the time of diagnosis of the tumor, proximity and growth of the

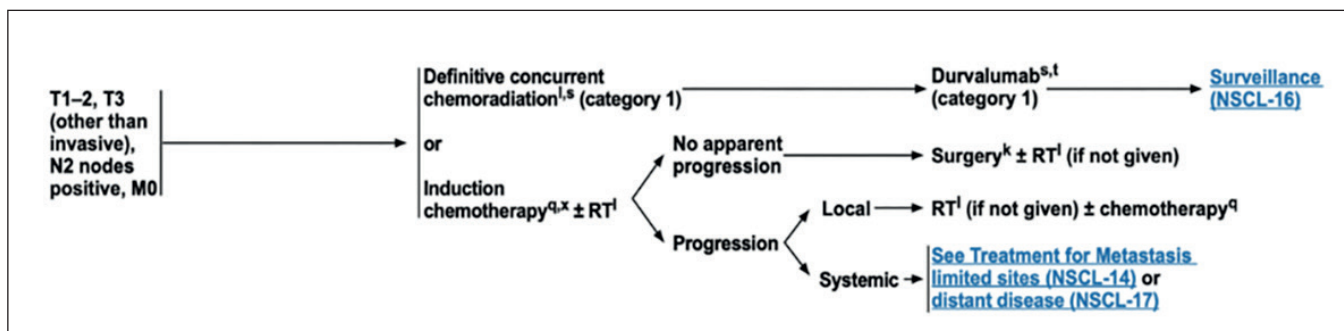


Fig. 1. NCCN standard for the treatment of resectable lung cancer III A

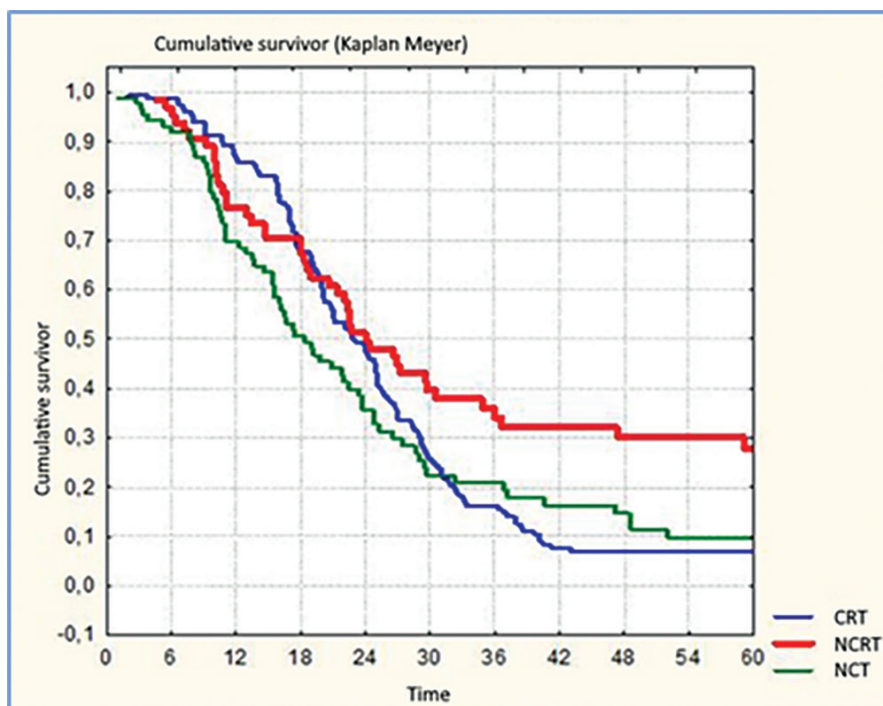


Fig. 2. Survival in the first control group (NCT)

tumor in the main vessels, tumor growth in the chest wall, superior vena cava syndrome and severe pain syndrome. For comparison, 2 and 3 groups were identified: patients who received neoadjuvant chemotherapy-149 people, who received neoadjuvant chemotherapy and adjuvant radiation therapy-90 people. Neoadjuvant chemoradiotherapy was performed in accordance with Cisplatin/Docetaxel or Carboplatin/Paclitaxel 4 Mg and simultaneous radiation therapy with a total radiation dose 30 gray with a single dose of 2 Mg.

The increase in the effectiveness of chemoradiotherapy compared to the use of separate chemotherapy and radiation therapy is due to the fact that both methods cause a rupture of the double-stranded DNA of the tumor, and when used simultaneously, they potentiate each other, enhancing the clinical effect. When using this method, it is mandatory to include platinum preparations in the chemotherapy regimen and use radiation therapy in the classical fractionation mode with a single dose of 2 Mg [9 - 12].

All patients were examined in the same way: histological verification of the tumor before treatment, computed tomography of the chest, abdomen and pelvis with intra-

venous contrast before and after neoadjuvant treatment, general blood analysis, general urine analysis, blood biochemistry, coagulogram and ECG before each course of chemotherapy and before radical surgery. Both the main and control groups received neoadjuvant chemotherapy with Cisplatin/Carboplatin and Docetaxel/Paclitaxel in the amount of 3 or 4 courses. In addition to chemotherapy, the main group received radiation therapy for the tumor area and mediastinal lymph nodes at a dosage of 30 Gray before surgery, and the second control group received radiation therapy for the tumor area and mediastinal lymph nodes in an adjuvant mode.

After neoadjuvant treatment, patients of all groups underwent radical surgery. It consisted of lobectomy, bilobectomy and pneumonectomy, depending on the degree of the tumor process, and all patients underwent radical operations with dissection of mediastinal lymph nodes during which the edges of resection of each histological preparation were examined and morphological studies of removed tumors, lymph nodes N1 and N2 were performed.

In addition, patients of all groups were analyzed for hematological parameters and ECG data at all stages of

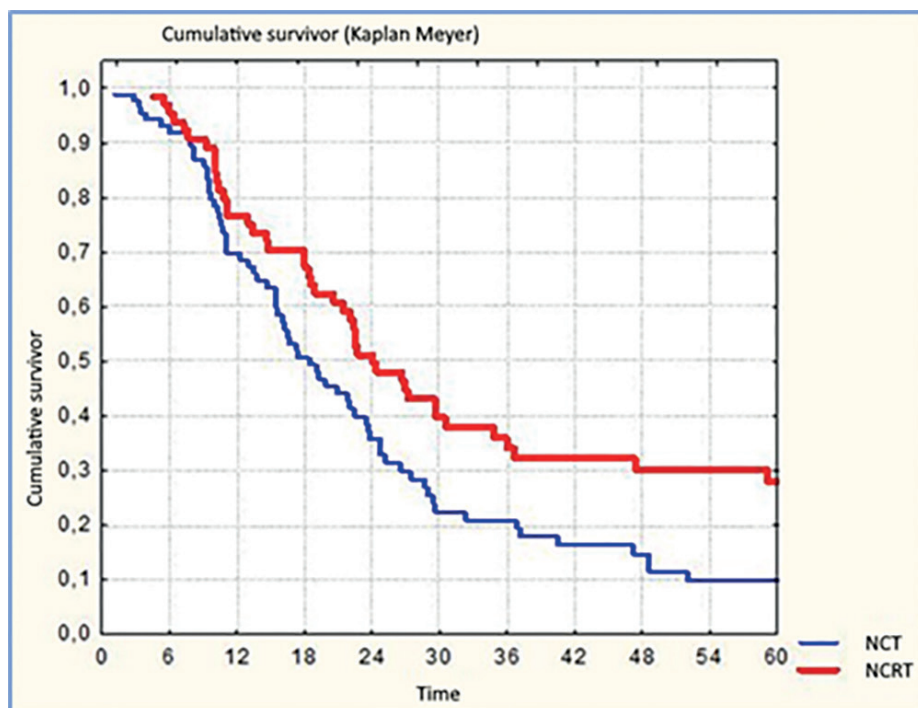


Fig. 3. Survival in the main group (NCRT)

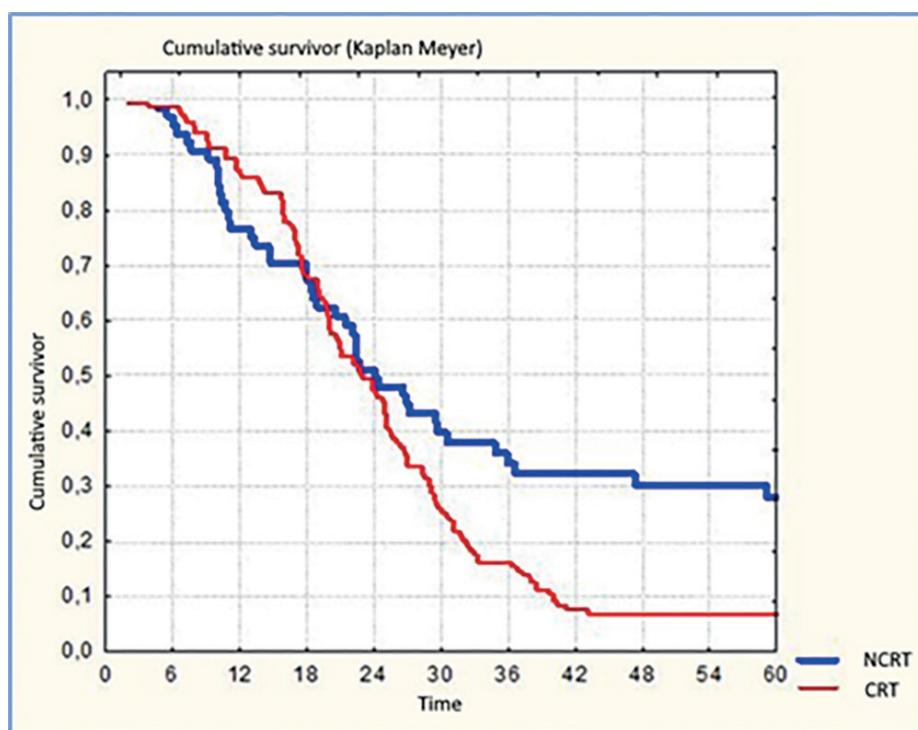


Fig. 4. Survival in the second control group (NCT + adjuvant radiation therapy)

treatment. Postoperative complications and the duration of stay in the clinic after surgery were studied. During the treatment, the patients were registered at the dispensary, underwent computed tomography of the chest, abdominal cavity and pelvis in the first year 1 time in three months, in the second year 1 time in 6 months and in the following 1 time a year. Patients who experienced the progression of the disease (subsequently) received further adjuvant and symptomatic treatment [13 - 17].

Survival was assessed on the Kaplan and Mayer scale.

RESULTS

The study analyzed the main results of treatment, which showed that the 5 years survival in the main group was $28.1 \pm 5.9\%$ (fig 2) 0, in the control groups-the first control group (neoadjuvant chemotherapy) - $10.4 \pm 3.8\%$ (Fig 3) and the second control group (neoadjuvant chemotherapy and adjuvant radiation therapy) - $5.8 \pm 2.0\%$ (Fig 4), respectively.

Of great importance was the phenomenon of a complete morphological response of the tumor-a clinical situation when

the tumor and enlarged lymph nodes were not detected on repeated CT, and tumor cells were not detected in the histological preparation. In addition to the complete morphological response, a morphological response of a highly differentiated tumor was detected (residual viability of the tumor tissues up to 12 + - 5%). In the main group, 5 patients had a complete morphological response of the tumor and a morphological response of the residual viability of the tumor tissue, the correlation with survival was as follows: the average survival in patients with a complete morphological response of the tumor was 45 months, with a morphological response of the residual viability of the tumor tissue was 39 months. The patients of both control groups did not have a morphological response of the tumor of such a high degree as in the main one.

DISCUSSION

NCRT has entered the standards for the treatment of such oncological diseases as rectal cancer, cervical cancer, glioblastoma and has significantly improved their survival rate [18 - 21].

There is currently no consensus on the effectiveness of NCRT in non-small cell lung cancer. Some meta-analyses [22, 23] prove the lack of advantages of this method of treatment compared to neoadjuvant chemotherapy. Other studies [24 - 26] have proved an improvement in survival and a decrease in the number of postoperative complications in the group of patients receiving neoadjuvant chemoradiotherapy. There are also meta-analyses and systematic reviews that show the effectiveness of NCRT compared to neoadjuvant chemotherapy for stage III A non-small cell lung cancer, however, statistical differences are not reliable.

Most likely, this situation is explained by the small number of studies on this topic and, as a result, the inability to standardize clinical data on the number of chemotherapy courses, chemotherapy regimens and the number of Grays.

The experience gained in our study shows that chemotherapy with platinum preparations and drugs from the taxane group in combination with simultaneous radiation therapy with a single dose of 2 Gy and a total dosage of 30 Gy increases survival by 9 months compared to the results after NCT and reduces the number of bilobectomies and pneumonectomies in favor of lobectomies, which is a sufficient reason to continue research in this direction. The study used 3 courses of chemotherapy and 30 Gy during radiation therapy. It is possible that an increase in the number of Gy and 4 courses of chemotherapy will improve the result without significantly increasing the toxicity of treatment [20 - 24].

Another important aspect associated with NCRT is the complete morphological response of the tumor. In our work, it occurred in 10% of patients and correlates with an increase in the average survival value, which coincides with the literature data [3, 7, 8, 13, 16]. In our work, it was revealed that a high degree of morphological response—a 10 - 15% of the residual viability of the tumor tissues also correlates with an increase in survival. There is no information about such a concept as a high degree of morphological response in the literature data. At the moment, no predictors of increasing the probability of

a complete morphological response of the tumor have been identified, and this should be the topic of further scientific research. However, from the results obtained, it can be concluded that neoadjuvant chemoradiotherapy is also promising from the point of view of the potential inclusion of the patient in the group of a complete morphological response of a tumor or a morphological response of a high degree of tumor and, accordingly, an increase in survival.

The results of treatment in the group of NCT and adjuvant radiation therapy were worse than in the other groups. This phenomenon can probably be explained by the fact that adjuvant radiation therapy was prescribed in cases of potentially non-radical surgery.

CONCLUSIONS

Based on the conducted research and analysis data, conclusions are made:

1. The overall survival rate of patients receiving NCT compared to patients receiving neoadjuvant chemotherapy is higher than in the neoadjuvant chemotherapy group and 13 months higher than in the adjuvant radiation therapy group.
2. Patients who had the phenomenon of a complete morphological response have a significantly higher survival rate (45 and 39 months, respectively). This phenomenon was not observed in patients who received adjuvant radiation therapy or neoadjuvant chemotherapy. Thus, this therapeutic tactic can be considered potentially more promising than neoadjuvant chemotherapy with significantly non-increasing risks.
3. Of the three regimens recommended for the treatment of stage III A non-small cell lung cancer (neoadjuvant chemoradiotherapy and neoadjuvant chemotherapy, and adjuvant radiation therapy), the treatment regimen with neoadjuvant chemoradiotherapy is more promising from the point of view of patient survival.

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Conflict of interest:

The Authors declare no conflict of interest.

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