

Fighting against thymic cancer: conventional treating options and advances

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Abstract: The passage mainly talks about the treatment of thymic cancer. The chemotherapy uses doxorubicin, cisplatin, and carboplatin for the drugs of thymic cancer, and the side effects of those drugs. Doxorubicin, cisplatin, and carboplatin need to be injected through veins. Doxorubicin has side effects like hair loss, cisplatin has disadvantages like damage to the kidney, carboplatin such as severe allergy. The chemotherapy that using Hyperthermic Intrathoracic Chemotherapy (HITHOC) that use high temperature to kill cancer cell and remove residual cancer cells inside the body. And the introduction of adjuvant treatment and neoadjuvant therapy, the information of a combination of chemo radiotherapy. Adjuvant treatment that helps decrease the ability of cancer cells that come back to patients' body. Neoadjuvant treatments include chemotherapy, radiation therapy, and hormone therapy to reduce the size of a tumor. Differences between adjuvant therapy and neoadjuvant treatment are that adjuvant is usually after the surgery that makes sure the chances of getting cancer again is smaller, and neoadjuvant usually before the surgery that decreases the size of the tumor. Chemoradiotherapy uses both drugs and radiation to kill cancer cells. Also, the radiotherapy involved in External Beam Radiation Therapy (EBRT) that helps to shrink tumors.

1. Introduction (heading 1)

Thymic cancer is the type of cancer that happens in the epithelial cells of the thymus. Table 1 shows that the patient characteristic of getting thymic cancer usually happens in males that have an average of 40-50 years old. The incidence of getting this disease is higher in males than females. [1] Among the people who have thymic carcinoma, lymphoid epithelioid carcinoma often appears in children, basal cell carcinoma mostly appears in middle-aged men, mucoepidermoid carcinoma and adenosquamous carcinoma appeared most often in elderly women. The symptoms of thymic carcinoma vary from person to person, the majority of the people have pectoralgia, or chest pain. Other patients may have cough, hard to breathe, or emaciation. The examination of thymic carcinoma can present lesion size, density, and edge, further indicating the relationship between the lesions and surrounding organs of the thoracic cavity, including great vessels, lungs, pericardium, heart, and pleura. The X-Ray can display the mediastinal conditions and anterior mediastinal mass image, to further acknowledge whether the heart is enlarged and whether the tumor is invading the lung tissue.[2] Different types of carcinoma like squamous cell carcinoma, lymphoepitheliomatoid carcinoma, basal cell carcinoma, mucoepidermoid carcinoma, sarcomatoid carcinoma, small cell undifferentiated mixed carcinoma, clear cell carcinoma, and undifferentiated carcinoma.

Table 1. Characteristics of thymic cancer.

	No.	%
Gender		
Male	88	65.2%
Female	47	34.8%
Age		
<=60	92	68.1%
>60	43	31.9%

2. Drug usage for thymic cancer

2.1 Doxorubicin

Doxorubicin is the type of medicine used in the treatment of thymic carcinoma. It is usually used in the treatment of acute leukemia. [3] This type of medicine is not taken orally like other pills, it can only inject through the human body by intravenous injection (IV). Doxorubicin can stop the division of cells to cause damage to cancer cells, but it can also impair the immune system of the human body. Adults usually take 50-60 mg once per 3 to 4 weeks, children is taken half of the dosage of adults. Doxorubicin can be used with other drugs to cure other types of cancer like cyclophosphamide, doxorubicin, and fluorouracil to treat breast carcinoma. The side effects of doxorubicin cause hair loss for 90% of the patient, anorexia, and the severe one is a cardiac failure which increases the heart rate or heart rate becomes abnormal. [4] Especially for the people excess 550m/m^2 , the incidence rate of cardiac failure of the usage of doxorubicin increases. It is prohibited for people that have an allergy to doxorubicin, or leukocytes less than $3500/\mu\text{L}$ or thrombocytes less than $50,000/\mu\text{L}$ to use this type of drug.

2.2 Cisplatin

Cisplatin is the type of Medicine that causes severe side effects such as nephrotoxicity, digestive tract reaction, ototoxicity, neurotoxicity. Cisplatin is one of the medicines that is widely used for the treatment of cancer. Because cisplatin is metabolism from the kidney, it caused damage to the kidney. Patients from 4%-23% still have acute kidney injury although the method hydration diuresis is used during the clinic. [5]. Cisplatin is a type of cell cycle nonspecific drug, it can cure sarcoma, malignant epithelial tumor, or lymphoma. This drug needs to inject from the vein once a week, in 5-7 weeks. Also, radiotherapy is combined to cure the patients with cisplatin. Cisplatin may have reactions with other antibiotics like tobramycin, or vancomycin. Patients should beware of the medicine they are using with cisplatin.

2.3 Carboplatin

Carboplatin is injected through veins just like cisplatin and doxorubicin. [6] This drug usually treats lung cancer, ovarian cancer, neuroblastoma, and head and neck cancer. The side effects of this drug would be a severe allergy or an increase in the rate of incidence for the future of getting cancer. [7] It causes damage for the infants during women's gestation. It's used to interfere with the duplicate of DNA to resist the cancer cells. Studies show that the combination of carboplatin and Taxol can treat thymic cancer. And Taxol is one of the effective medicine for anti-cancer in 20 years. [8] But there are still several side effects of the treatment with both carboplatin and taxol which decrease leukopenia, alopecia, diarrhea, or loss of appetite. The typical side effect is the myelosuppression and allergy. Patients should examine before taking the carboplatin.

3. Surgery of thymic carcinoma

3.1 TNM classification

The TNM classification is helped the doctors for the surgery of thymic carcinoma. T represents tumor, N means nodes, and M stands for metastasis. The classification of thymic cancer for Type A is medullary or spindle cell thymoma; Type B1 is lymphocyte-rich thymoma; Type B2 is cortical thymoma; Type B3 is epithelial plastic or atypical or well-differentiated thymic carcinoma; Type AB is mixed thymoma; Type C is thymic carcinoma. Before the surgery, doctors need an image examination to determine whether or not the cancer cell can be eliminated. The majority of the situation is using median sternotomy, which is a mid-chest incision that was made to separate the sternum and remove the entire thymus and the tumor, also called thymectomy. Sometimes the thymic cancer is growing on the nearby tissues such as the pleura, pericardium, precava, nerve, or other partial lung tissue. Surgeons trying to eliminate those thymic carcinomas as well that already spread to other tissues. Majority of the patients that in stage III thymoma and stage IV thymoma that tumor

has spread to the periphery or other organs, surgeons use tumor reduction and treatment with radiotherapy or chemotherapy afterward. Doctors will treat thymic carcinoma first with radiotherapy or chemotherapy, and then surgery is needed to remove the carcinoma after the tumor has shrunk. There are also some side effects of the surgery that excessive bleeding, wound infection, or pneumonia. The patients have to wait for 1-2 months after the surgery and restore the incision to eliminate thymic carcinoma.

4. Chemotherapy for thymic carcinoma

Hyperthermia Intrathoracic Chemotherapy uses Intrapleural perfusion hyperthermia (IHP) to heat the infusion fluid or the fluid containing chemotherapy drugs to a certain temperature and continuously circulates at a constant temperature into the patient's chest cavity for a certain time. [9]The purpose is to kill and remove residual cancer cells and tiny lesions in the body cavity through the synergistic sensitization, and mechanical scouring effect of thermochemotherapy. The first mechanism of HITHOC is to use the thermal effect to directly kill tumor cells and induce apoptosis. [10]The structure and function of the microenvironment and blood vessels in the tumor are different from that in the normal tissue, which makes the heat dissipation of the tumor more difficult. The normal tissue can withstand the tumor cell apoptosis at 47 Celsius for 1 hour and 43 Celsius for 1 hour. The second mechanism uses intrathoracic medication to increase local drug concentration. The intracavitary anti-cancer drug concentration is much higher than the systemic circulating concentration but does not increase systemic toxicity. The third is the synergistic sensitization of thermochemotherapy. The anticancer effect of chemotherapeutic drugs was enhanced under the condition of heating. Heating enhances the permeability of anticancer drugs, the penetration depth from 1-2mm to 5mm. The fourth mechanism is mechanical scouring which causes the removal of cancer cells and small metastasis in the thorax. The fluidity of the water ensures that the infusion with chemotherapy can fill every corner of the chest as much as possible, reducing dead cavities. Fifth, to promote visceral parietal pleural adhesion and pleural atresia. This mechanism causes intrathoracic anti-fibrinolysis and promotes cellulose condensation, accelerates pleural fibrosis, promotes visceral parietal pleural adhesion and pleural atresia. Improve pleural blood circulation, promote the clearance of small pleural veins and lymphatic blockage, and facilitate the absorption of the pleural effusion. The last one is enhanced immune function and anti-tumor effect. This mechanism is to mobilize various biological immune activities molecules, enhance immune function, and anti-tumor effect. High fever can directly lead to the release of heat shock protein, induce specific immunity of the body, activate NK cells, increase DC cells, promote the role of antigen delivery, and inhibit tumor metastasis. This method has several contraindications like four weeks after radiotherapy or chemotherapy or within two weeks after chemotherapy, tuberculosis at the tumor site, metal objects implanted in the body such as steel plates, and nails, pregnant women, leukemia patients, and patients with an advanced malignant tumor that can only survive for less than 2 months.

Adjuvant treatment reassures the patients that have fewer chances of cancer coming back by removing the residual cancers. Adjuvant treatment usually occurs to patients after surgery. The treatment depends on the integrity of the surgical excision. It includes chemotherapy, radiation therapy, hormone therapy, targeted therapy, and biological therapy. Chemotherapy such as the drugs above destroys thymic cancer. Radiation therapy uses X, Y rays to eliminate thymic cancer. Hormone therapy such as octreotide that use to decrease the number of growing cancer. Targeted therapy used octreotide, Everolimus, or Sunitinib to destroy certain types of cancer cells. Biological therapy includes helping the patients that restore the immune system. The side effects of adjuvant therapy may include vomiting, fatigue and weakness, damage to surrounding tissues, and hair loss. Neoadjuvant therapy such as chemotherapy, radiation therapy, and hormone therapy. It helps to reduce the size of a tumor. But the side effects occur in neoadjuvant chemotherapy such as extreme fatigue, loss of appetite, sores in the mouth, hair loss, or even increased risk of infection. The advantage of neoadjuvant therapy is the overall survival and recurrence-free survival rate are the same as post-operative chemotherapy, serve as an in vivo sensitivity test, increase the rate of breast-

conserving therapy, and facilitate the study of cancer biology. Neoadjuvant is before the surgery whereas adjuvant therapy is after the surgery because neoadjuvant is a process of treatment that helps to decrease the size of cancer cell, adjuvant therapy is reassured and make the chances of reoccurring cancer cells decrease.

Chemoradiotherapy is a combination of chemotherapy and radiotherapy that uses both drugs and radiation to decrease the number of cancer cells and eliminate those cancer cells. The radiotherapy also destroys other normal cells that may cause side effects such as hair loss, vomiting, fatigue, or rubefaction. The difference between those two therapies is that chemotherapy has a stronger effect basically on systemic effects, but it's weaker on the local effects, radiotherapy cannot do systemic effects, but it only can do on the local effects. The current discussion on the relative advantages of preoperative and postoperative radiotherapy continues over time. Both have their advantages and disadvantages. The effect depends on the individual characteristics of the tumor and the patient. In theory, cancer cells grow faster before they are disturbed by surgery. At this time, they should be more susceptible to radiation than after surgery. However, each patient's condition must be individually evaluated to determine the best treatment. Preoperative radiotherapy that to kill tumor cells, reduce the size of the tumor, and reduce the risk of metastasis. Reducing the size of tumors through radiation allows doctors to remove previously inoperable tumors. The advantage is to reduce the risk of local recurrence and remote metastasis. The disadvantages are the border of the tumor may be blurred due to the shrinkage and destruction of the edge of the tumor, this may affect the operation, and also the postponement of the operation may cause anxiety for some patients, and increase the risk of postoperative complications. Postoperative radiotherapy has been shown to eliminate tumor cells that still exist after surgery, and it can also reduce tumors that may occur in the surgical site or nearby lymph nodes. Postoperative radiotherapy is usually performed after the wound has healed, 4-6 weeks after the operation.

5. Radiotherapy for thymic carcinoma

Radiotherapy is using high-energy waves such as X, Y rays to eliminate cancer cells. High doses of radiation can slow the growth of cancer by damaging their DNA. It can halt the dividing of the cells, or they will die and remove through the metabolism of the body. The radiation does not kill cancer cells immediately, but it takes time to do treatment that causes damage to DNA. The cancer cells will continue to die in the next few weeks or months.

Table 2. Treatment summary for thymic cancer.

	No.	%
R0 resection	4	3.0%
Plus radiotherapy	19	14.1%
Plus chemoradiotherapy	8	5.9%
Plus chemotherapy	4	3.0%
Debunking resection plus		
Chemoradiotherapy	18	13.3%
Radiotherapy	14	10.4%
Chemotherapy	2	1.5%
Radiotherapy	38	28.1%
Chemoradiotherapy	24	17.8%
Chemotherapy	4	3.0%

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The studies show that a higher percentage of patients have the treatment of radiotherapy. The types of radiation such as external beam radiation (EBRT), the patient is lying on the treatment table. The external radiation source acts on the volume established during the planning period while minimizing the amount of radiation received by the surrounding structures. Patients stay awake during the treatment, and they cannot feel the radiation, also they can resume all activities immediately after delivery of treatment. The common types of external radiation are intensity-modulated radiation therapy (IMRT), and three-dimensional conformal radiation therapy (3D-CRT). [11] Three-dimensional conformal radiation is using the computer to present the graph of the tumor to let doctors give the doses of radiation to the patient. Intensity Modulated Radiotherapy is an external radiation radiotherapy method that uses a multi-leaf collimator (MLC). Each leaf of the multi-leaf collimator is made of materials with high atomic numbers. These materials can move in and out of the path of the particle beam independently to adjust its shape and contour to the shape of the tumor. This is an advanced treatment planning and calculation algorithm that allows repeated optimization of the positioning of the MLC complex does delivery. The dose distribution of IMRT is characterized in that it delivers less dose to nearby normal tissues. According to the conventional dose division of EBRT, patients receive a single small dose, 15 minutes a day, 5 days a week, for about 2 to 8 weeks. On the other hand, through low-resolution techniques, large doses of radiation can be delivered to tumors in 5 doses or less. The type of dose division used in treatment depends on many factors. Photon radiation uses high-energy rays composed of photons. And it helps by destroying the target cell's molecules and interfering with normal cell functions. The types of photon radiation are gamma rays and X-rays. Gamma rays are produced by the decomposition of radioactive isotopes of elements such as cobalt-60 and radium. X-rays have come from a machine that excites electrons through a cathode ray tube or linear accelerator. Particle radiation uses subatomic particles to destroy cells. Due to the need for complex and expensive equipment, in clinical practice, the use of particle radiation therapy is very limited, but there are some advantages to using this method. It can deliver higher doses of radiation to the target area while causing less damage to surrounding tissues. This makes the difference of treatment smaller, the effect is more obvious, and there are fewer side effects. Another type of radiotherapy is called Brachytherapy. Brachytherapy is a form of radiotherapy in which a radiation source is placed in or near the area to be treated. Depending on the specific conditions of cancer, brachytherapy usually comes in the form of high dose rate (HDR) or low dose rate (LDR). During any type of brachytherapy surgery, the patient usually needs to receive general anesthesia. Patients can resume all normal activities after a few days of brachytherapy. In high-dose-rate brachytherapy, the machine automatically mobilizes and retracts a single small radioactive source along a needle implanted at a specific location, delivering high-dose radiation within 1-10 days. Each delivery is divided into 1-5 divided irradiation, and each divided irradiation lasts a few minutes. The high-dose brachytherapy machine allows doctors to control the radioactive source to stay at a predetermined location for a stay time to form a 3D dose cloud in the tumor or cavity. It can be used alone or as "enhanced treatment". Low-dose-rate brachytherapy is the permanent placement of a sealed radiation source that provides gradually decreasing low-dose radiation within a few months. Similar to high-dose-rate brachytherapy, low-dose-rate brachytherapy can be used alone, or it can be used as "enhanced therapy, that is as an adjunct to external beam radiation therapy (EBRT).

6. Conclusion

Nowadays, there are more opportunities for patients to cure thymic cancer in different ways through chemotherapy and radiotherapy. But the side effects are still a problem for the chemotherapy and radiotherapy to the patients. The drugs like doxorubicin that cause hair loss, anorexia, and cardiac failure that increase the heart rate or cause abnormal heart rate. Cisplatin that metabolism from the kidney can cause certain damage. And Carboplatin causes severe allergy or increases the possibility of the future of getting cancer. The side effects of radiotherapy that cause fatigue, shortness of breath,

hair loss, nausea, and shoulder stiffness. The challenge of chemotherapy is that patients who have difficulty swallowing need to have rehabilitation training. They need to choose the food that has a good consistency, a proper position, or swallow food. [12]The challenge of patients to radiotherapy is that they may suffer from pleural and pericardial effusion. It leads the patient to have difficulty to breathing. They are difficulties for the patients that suffer from side effects of chemotherapy and radiotherapy. Scientists still need to develop a new method of treating cancer and decrease the side effects of those drugs and therapies. The patients' haven cancer suffer from those side effects and want to have a healthy life. The development of science on the treatment of cancer cells is improved from day to day use. And it will reach the goal of treating the cancer cell let the patients suffer less from it.

References

- [1] Wang, Jinghui, and Shucui Zhang. Zhongguo fei ai za zhi = Chinese journal of lung cancer vol. 13, 10 (2010): 985-91. doi:10.3779/j.issn.1009-3419.2010.10.10J. Clerk Maxwell, a Treatise on Electricity and Magnetism, 3rd ed., vol. 2. Oxford: Clarendon, 1892, pp.68-73.
- [2] Information from: <https://zhiliao.chujingyi.cn/xiongxianai>.
- [3] Information from: <https://www.cancer.org/cancer/thymus-cancer/treating/chemotherapy.html>.
- [4] Information from: <https://medlineplus.gov/druginfo/meds/a682221.html>.
- [5] Information from: <https://www.macmillan.org.uk/cancer-information-and-support/treatments-and-drugs/cisplatin>.
- [6] Information from: <https://zh.wikipedia.org/wiki/%E5%8D%A1%E9%93%82>. Wang, Jinghui, and Shucui Zhang. Zhongguo fei ai za zhi = Chinese journal of lung cancer vol. 13, 10 (2010): 985-91. doi:10.3779/j.issn.1009-3419.2010.10.10J. Clerk Maxwell, a Treatise on Electricity and Magnetism, 3rd ed., vol. 2. Oxford: Clarendon, 1892, pp.68-73.
- [7] Information from: <https://www.webmd.com/drugs/2/drug-4551/carboplatin-intravenous/details>.
- [8] Information from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5999718>
- [9] Girard, Nicolas et al. Zhongguo fei ai za zhi = Chinese journal of lung cancer vol. 17, 2 (2014): 116-21. doi:10.3779/j.issn.1009-3419.2014.02.09
- [10] Information from: <http://sxyy.cqu.edu.cn/info/2291/3222.htm>
- [11] Information from: <http://www.mzjhkepu.com/cancer/article/51575>.
- [12] Information from: https://m.sohu.com/n/491462518/?wscrid=95360_6