

Treatment of abdominal tumors using radiotherapy

TRATAMENTO DE TUMORES ABDOMINAIS COM RADIOTERAPIA

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The Guidelines Project, an initiative of the Brazilian Medical Association, aims to combine information from the medical field in order to standardize procedures to assist the reasoning and decision-making of doctors.

The information provided through this project must be assessed and criticized by the physician responsible for the conduct that will be adopted, depending on the conditions and the clinical status of each patient.

DESCRIPTION OF THE EVIDENCE COLLECTION METHOD

Through the development of three relevant clinical questions related with the proposed subject, we tried to present the main evidence for the safety, toxicity and effectiveness of the radiotherapy techniques in question. The study population consisted of male and female patients of all ages with abdominal tumors (stomach, pancreas, biliary tract and sarcomas) regardless of histological type, staging, treatment context (neoadjuvant, radical or adjuvant) of the disease, or the presence of comorbidities. For this, a systematic review of the literature was performed in primary scientific research databases (Medline - Pubmed; Embase - Elsevier; Lilacs - Bireme; Cochrane Library - Central Register of Controlled Trials). All articles available until November 30, 2012, were included. The keywords used in the search were: ("Retroperitoneal Neoplasms" OR "Sarcoma" OR "Abdomen" OR "intra-abdominal sarcoma" OR "abdominal neoplasms" OR "intra-abdominal neoplasms" OR "abdominal pelvic" OR "stomach" OR "gastrointestinal" OR "gastric"), ("Radiotherapy, Conformal" OR "3D radiotherapy" OR "tridimensional radiotherapy" OR "3D RT" OR "3DCRT" OR "CRT"), ("Conventional radiotherapy" OR "2D radiotherapy" OR "2D RT" OR "standard radiotherapy"). The articles were selected based on critical evaluation using the instruments (scores) proposed by Jadad and Oxford; references with greater strength of evidence were used. Recommendations were prepared from discussion with the writing group, composed of 14 members of the Brazilian Society of Radiotherapy. The guideline was reviewed by an independent group specializing in evidence-based clinical guidelines. After completion, the guideline was made available for public consultation for 15 days and the suggestions for-

warded to the writers for evaluation and consideration (possible incorporation) into the final text.

GRADE OF RECOMMENDATION AND STRENGTH OF EVIDENCE

- A. Experimental or observational studies of higher consistency.
- B. Experimental or observational studies of lower consistency.
- C. Case reports (non-controlled studies).
- D. Opinions without critical evaluation, based on consensus, physiological studies, or animal models.

OBJECTIVE

To assess the most appropriate method of radiation therapy for the treatment of patients with abdominal tumors.

CONFLICT OF INTEREST

No conflict of interest informed.

INTRODUCTION

Radiotherapy is used in at least one phase of treatment in the main abdominal malignant tumors, including the stomach, pancreas, biliary tract and soft tissue sarcomas.

In stomach cancer, radiotherapy is performed after surgery (adjuvant) in tumors staged as locally advanced (A)¹(B)^{2,3} in patients with positive margins and, as a palliative treatment, in inoperable tumors and in patients with high surgical risk (B).^{4,5}

In pancreatic cancer, radiotherapy is indicated after surgery (adjuvant) to prevent recurrence of locoregional disease (B).⁶⁻⁸ Another application is for unresectable tumors in order to make them surgically resectable, preferably associated with chemotherapy (B).^{9,10}

For malignant tumors of the biliary tract, radiotherapy has the function of controlling microscopic *foci* of residual disease after surgical resection (B)^{11,12} or palliative treatment for inoperable tumors, including the use of high doses of radiation (B).¹³

Sarcomas of the abdominal area generally originate in the retroperitoneal space. Radiotherapy has a primary role in these tumors in order to decrease local recurrence rates after surgery (B).¹⁴⁻¹⁶

Radiotherapy has evolved in recent decades thanks to the advances of computer systems that allow the recognition of internal body structures. Such recognition is performed by imaging tests on the patient, generally using computed tomography. The most accurate dose distribution, reaching the region to be treated while sparing the normal organs, is obtained thanks to the information passed onto the radiotherapy device by the computerized planning system developed. This form of dose delivery is known as the conformal technique. In addition to the computer program showing the radiation dose distribution within the patient's body, it creates dose intensity charts for each organ or target volume. This allows obtaining information on the potential toxicity of these organs and whether the tumor is being treated appropriately (D).¹⁷

In the abdominal area, where there are several organs sensitive to radiation, such as the liver, pancreas, small intestine, spinal cord, spleen and kidneys, the use of conformal radiotherapy becomes the minimally recommended technique for patient safety (D).¹⁷

Based on clinical experience with complications related to radiotherapy, a standard dose limit per volume of the normal tissue was created, called Quantec (Quantitative Analysis of Normal Tissue Effects in the Clinic) (D).¹⁸ This standardization is recommended worldwide and currently as a practice guide for conducting radiotherapy on all parts of the body. It is only possible to know the dose quantification using the conformal technique.

For the reasons above, conventional radiotherapy should be dismissed if the area to be treated includes organs that are sensitive to radiation, such as the abdominal area, given that this technique does not provide information about the distribution of the dose to these organs.

IS THE IRRADIATION OF THE ABDOMINAL AREA USING CONFORMAL RADIOTHERAPY SUPERIOR WHEN COMPARED TO CONVENTIONAL RADIOTHERAPY?

Stomach tumors

Dosimetric studies show the superiority of conformal radiotherapy over conventional radiotherapy consider-

ing some criteria, such as lower irradiation to the kidneys and spinal cord with a smaller volume in these organs receiving higher doses of radiation (B)¹⁹⁻²⁵ and better irradiation of targets of interest such as stomach bed and lymphonodular drainage regions (A)¹ (B),^{20,23} clearly showing the superiority of conformal radiotherapy compared to conventional, in terms of safety and dose distribution.

Pancreatic and biliary tract tumors

Retrospective studies with dosimetric analysis have shown the advantages of the conformal technique (B).²⁶ Non-comparative prospective studies show the importance of correct identification of the site to be irradiated and organs at risk (B)^{27,28}(C)²⁹ and the importance of determining the dose in partially irradiated organs and its association with late onset toxicity (D).³⁰⁻³²

Studies evaluating the planning of conformal radiotherapy with radiation field entry at different angles showed better clinical outcomes, making conformal radiotherapy superior to conventional radiotherapy in the planning of radiotherapy for tumors in the pancreas and biliary tract (B)^{23,25,33-36}(D).^{37,38}

Soft tissue sarcomas

Dosimetric studies have shown better dose distribution in areas of the abdomen where sarcomas usually originate both in adults (B)^{35,39} (D)⁴⁰ and children (B),⁴¹ when the conformal technique was used.

All studies used computerized planning systems that allowed the recognition of target volumes and organs at risk by creating charts with dose distribution by volume (dose/volume histograms) enabling a suitable analysis of the dose distribution in normal tissues and the choice the best technique.

In addition, the conformal technique allows the selection of the treatment plan that best fits each case, respecting individual peculiarities and increasing multidisciplinary integration.

Recommendation

Conformal radiotherapy is superior for irradiation of the abdominal area compared to conventional radiotherapy, demonstrating superiority in terms of safety and dose distribution in stomach tumors. Conformal radiotherapy with the entry of radiation fields at different angles has shown better clinical outcomes for pancreas and biliary duct tumors. In soft tissue sarcomas, the use of a computerized planning system that allows dose/volume histograms to be produced is recommended.

IS THERE LESS TOXICITY IN THE USE OF CONFORMAL RADIOTHERAPY COMPARED TO CONVENTIONAL RADIOTHERAPY FOR ABDOMINAL TUMORS?

Stomach tumors

The complications occurring most often in the irradiation of stomach bed and/or upper abdomen are enteropathy, nephropathy, liver disease, heart disease and lung disease associated with radiation (A)^{1,2}(B)^{19,21,24,25,33,43,45,47-50}(C)⁴⁴(D).⁴⁶

Within the scope of gastric cancer treatment, significant rates of toxicity associated with the conventional technique of irradiation were observed in a prospective cohort study, with 33% of gastrointestinal complications at grade III or higher, and 17% of patients disqualified for ending the proposed treatment, with radiotherapy and chemotherapy as adjuvants to radical surgical treatment (A).^{1,42}

Institutional series with prospective cohort studies in which patients received conformal radiotherapy showed lower rates of treatment-related complications, compared to rates observed with conventional radiotherapy, as well as a lower incidence of treatment discontinuation (B)^{43,45}(C).⁴⁴ Other series with conformal radiotherapy reported varying levels of grade III or higher gastrointestinal complications, from zero to about 57%, which can also be credited to more toxic chemotherapy regimens, although still lower than the historical rates with conventional radiotherapy (B)^{24,33,50-52}(D).⁴⁶

Pancreatic and biliary tract tumors

Prospective studies show the relationship between dose and volume to an organ at risk, such as the kidneys, liver, stomach and small intestine, and the complication rates of these organs (B).^{47,53} The main complication reported when there is an excess dose is decrease in renal function when the kidney's dose is greater than its tolerance (B).⁵⁴

Assessments of the dose received by irradiated organ volume show the tolerance thresholds below which there is no toxicity (B)⁵⁵⁻⁶¹(D).⁶² Several prospective studies associate dosimetric parameters and toxicity of the organs at risk, showing lower toxicity with conformal therapy compared to conventional radiotherapy (B)^{20,63,64}(C)⁶⁵(D).⁶⁶⁻⁷³

Sarcomas

Late complications that can occur with radiotherapy in abdominal sarcomas include enteritis, perforation, fistula, and bowel obstruction (D).⁷⁴ This may increase the number of hospital admissions and emergency laparotomy. Furthermore, the involvement of the kidneys by scattered radiation can cause dialytic kidney failure if the dose limits are not respected (D).⁷¹

The morbidity associated with conformal radiotherapy is lower than that of the conventional technique (D).^{75,76} There are reports of significant toxicity rates associated with the conventional technique, with need for hospital intervention or progress to bowel obstruction (B).¹⁶

Institutional series in which patients received conformal radiotherapy showed low rates of treatment-related complications, such as bleeding, intestinal obstruction and nephropathy (B)^{77,78}(D).^{79,80}

Recommendation

The use of conformal radiotherapy compared to conventional radiotherapy for gastric tumors shows less complications and discontinuation of treatment. In pancreatic and biliary duct tumors, there is less toxicity with conformal radiotherapy compared to the conventional technique. There is a lower morbidity rate associated with conformal radiotherapy in abdominal sarcomas.

IS THERE A DIFFERENCE IN THE EFFECTIVENESS OF CONFORMAL AND CONVENTIONAL RADIOTHERAPY?

Stomach tumors

In a retrospective study that assessed two consecutive historical cohort studies, there was better relapse-free survival and distant metastasis-free survival for patients with gastric cancer surgery undergoing adjuvant treatment with conformal radiotherapy compared to conventional radiotherapy. In this study, in addition to the statistically significant difference in favor of conformal radiotherapy in terms of relapse-free survival ($p=0.03$) and distant metastasis-free survival ($p=0.05$) at 5 years, the authors found, in a multivariate analysis, that the use of planning techniques with computed tomography was predictive for improved loco-regional control, relapse-free survival, distant metastasis-free survival and overall survival (hazard ratio: 0.41, $p=0.005$) (B).⁴⁵

Prospective series data that used conformal radiotherapy technique demonstrate overall survival rates ranging from 70 to 88% and recurrence-free survival ranging from 64 to 70% at two years (B),^{47,49} suggesting better rates than those obtained in a prospective cohort study with conventional radiotherapy, with an overall survival of 58% and relapse-free survival of 55% at two years (A).^{1,42}

Pancreatic and biliary tract tumors

Prospective cohort studies with conformal radiotherapy show local control rates comparable or superior to those achieved with conventional radiotherapy (B)⁸¹⁻⁸³(D).⁸⁴ There is no clear difference in the effectiveness of mea-

surable tumor control between conformal and conventional techniques at the present time, according to prospective and randomized studies.

Sarcomas

Retrospective study data demonstrate disease-free survival rates at five years of 28-60% in patients treated with conventional radiotherapy (B)⁸⁵(D).⁷⁹ Similarly, the series of patients treated with conformal radiotherapy have shown local control rates varying from 20 to 69% (B)^{78,86}(D),⁷⁹ with no difference between the effectiveness of conformal or conventional radiotherapy treatments.

Conformal radiotherapy is considered the minimum standard technique for the abdominal area and serves as a basis for comparison in studies that assess more modern techniques such as intensity modulated radiation therapy (IMRT) and image-guided radiation therapy (IGRT) (B)¹⁹(B).⁸⁷⁻⁹⁰

Recommendation

There is no evidence of higher curability with conformal radiotherapy compared to conventional radiotherapy. The need to assess the dose distributed to the organs at risk and prospective data with lower toxicity are important enough to justify the recommendation of conformal radiotherapy as the minimally acceptable technique for radiotherapy in abdominal tumors.

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ERRATUM

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In the article “Treatment of abdominal tumors using radiotherapy”, published in the journal *Rev Assoc Med Bras*, vol. 61, n. 02: p.108-113, on page 108, where it reads:

“Authorship: Brazilian Society for Radiation”

It should read:

“Authorship: Brazilian Society for Radiation Oncology”