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Current landscape of gastrointestinal radiation oncology in Spain: a multicenter real-life survey and comparison with key clinical guidelines

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ABSTRACT

Background: The GI Tumors Workgroup, a division of the Spanish Society of Radiation Therapy, conducted a survey in December 2020 to assess the adherence of radiation oncologists in Spain to international guidelines for gastrointestinal tumors.

Materials and methods: Using Google Forms, we designed a survey covering treatments for esophageal, gastric, pancreatic, and rectal cancers.

Results: In esophageal cancer treatment, neoadjuvant chemoradiation was the standard in 76.7% of institutions. Radiation doses range from 41.1 to 50.4 Gy in conventional fractionation. Planning positron emission tomography-computed tomography (PET-CT) was performed in 83.3% of centers, and intensity-modulated radiation therapy/volumetric-arc radiation therapy (IMRT/VMAT) was the preferred technique in 86.7% of institutions. For gastric cancer, 71.4% followed perioperative chemotherapy guidelines. In the case of adjuvant radiotherapy, the majority prescribed 45–50.4 Gy, and 82.1% used IMRT/VMAT for treatment. For pancreas cancer, neoadjuvant chemotherapy followed by surgery in borderline resectable tumors and induction chemotherapy followed by radical radiotherapy for non-resectable tumors were the most frequent approaches. IMRT/VMAT was the primary technique. Locally advanced rectal cancer treatment is mainly based on neoadjuvant radiotherapy in all institutions. The preferred radiation doses typically range from 45 to 50 Gy in conventional fractionation. IMRT/VMAT was standard in most Institutions.

Conclusions: Spain's radiotherapy practices among respondents generally align with international guidelines for GI tumors highlighting Spain´s commitment to evidence-based medical practice.

Key words: gastrointestinal; survey; esophageal cancer; gastric cancer; pancreas cancer; rectal cancer

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Introduction

As a division of the Spanish Society of Radiation Therapy (SEOR), the GI (Gastrointestinal) Tumors Workgroup plays a crucial role in developing recommendations, guidelines, and research projects pertaining to the treatment of gastrointestinal tumors. In December 2020, the members of this workgroup decided to conduct a comprehensive survey aimed at analyzing the real-life practices of radiation oncologists in Spain. The primary objective was to assess the level of adherence to international guidelines for GI tumors.

The survey encompasses various aspects of radiation treatment, including treatment schemes and other technical considerations specific to esophageal, gastric, pancreatic, and rectal cancer.

By comparing the survey results with the existing clinical guidelines, we anticipate obtaining an accurate and realistic portrayal of the current state of GI radiotherapy in Spain. This evaluation will provide valuable insights into the alignment of real-life practices with international standards and identify potential areas for improvement. Ultimately, this endeavor aims to enhance the quality of care and optimize outcomes for patients undergoing GI tumor treatments in Spain.

Materials and methods

In December 2020, a survey was created on Google Forms to gather data from the members of the gastrointestinal tumors workgroup. The survey was distributed twice to enhance participation and collect responses, with an interval of one month between each distribution, ensuring sufficient time for participants to respond. Clear instructions were provided, emphasizing that respondents should complete the survey only if they had not done so previously and limiting responses to one per institution. Subsequently, we verified that there were no duplications in responses from the same institution included in the survey results.

To maintain objectivity and minimize potential biases, only one response per center was allowed in cases where multiple members from the same institution were part of the workgroup. This approach aimed to standardize the responses and present a comprehensive overview of the standard protocols approved within each institution. According to data from the Sociedad Española de Oncología Radioterápica (SEOR), there were a total of 105 radiation oncology facilities operational at the time of the survey.

For accessibility and convenience, an English translation of the survey was made available as Supplementary File 1, enabling non-Spanish-speaking participants to read and understand it.

Once the predetermined time limit for the survey was reached, it was closed, and the gathered data was analyzed using the descriptive statistics tools provided by Google Forms.

The survey results were compared with the primary international guidelines for each specific gastrointestinal tumor in order to assess the level of concordance between them. The guidelines predominantly employed include those from the National Comprehensive Cancer Network (NCCN), the European Society for Medical Oncology (ESMO), and the American Society for Radiation Oncology (ASTRO), along with key pivotal studies relevant to each pathology.

Results

A total of 28 radiation oncologists responsible for GI tumors in different centers among 16 Spanish provinces (Fig. 1) fulfilled the survey. This constitutes 27% of the total radiation oncology facilities, spanning across 32% of the provinces in Spain.

Esophageal cancer

In most participating institutions (76.7%), neoadjuvant chemoradiation (CRT) was the standard treatment for esophageal cancer. Another approach, used in 16.7% of the institutions, involved induction chemotherapy (CT) followed by CRT. In 3% of the institutions, the treatment choice between neoadjuvant CRT and induction CT followed by CRT depended on patient characteristics. One center offered radical chemoradiation (CRT) as the primary treatment option.

When it comes to the prescribed radiation dose, 90% of the participating institutions varied their dose prescription between 41.1–50.4 Gy in conventional fractionation.

In terms of adjuvant radiotherapy, none of the institutions performed it in any case, except

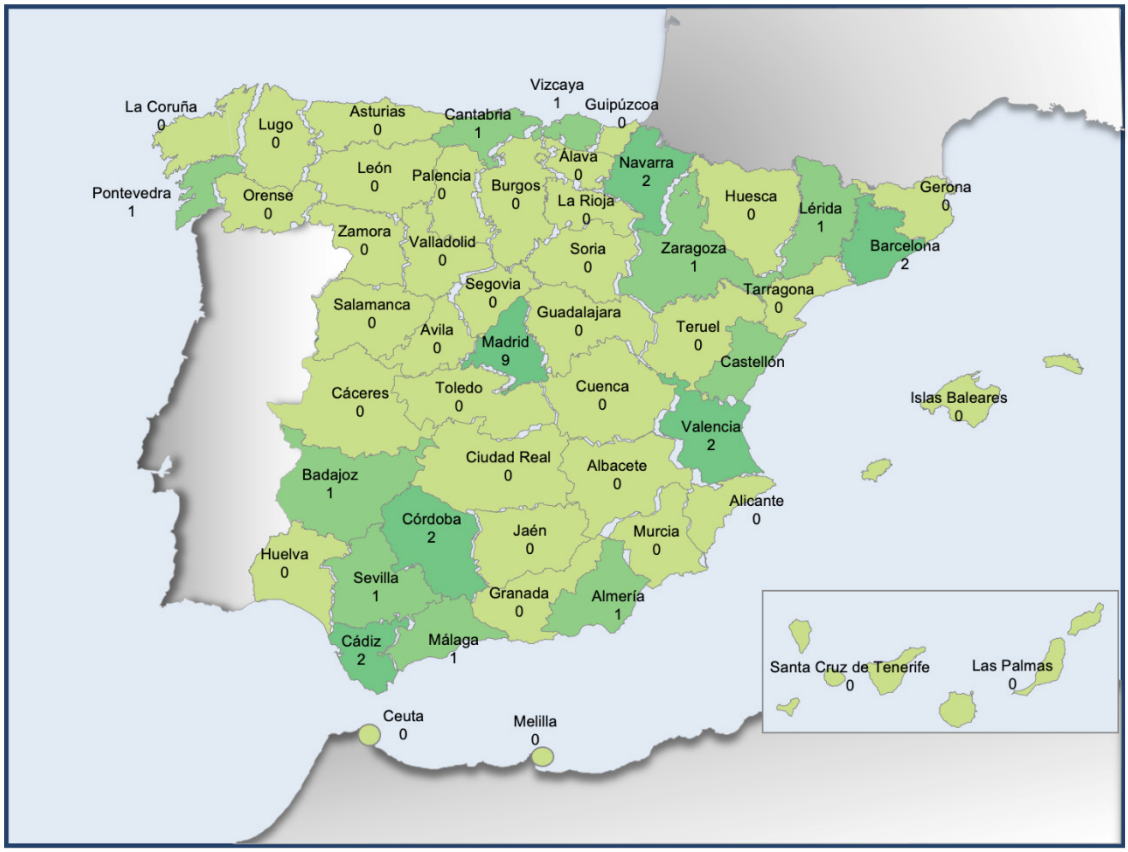

Figure 1. Distribution of survey responders

for one center that indicated its use in cases of R1 surgery. The administered dose for adjuvant radiotherapy ranged between 45–50 Gy in conventional fractionation.

For treatment planning techniques, positron emission tomography-computed tomography (PET-CT) was utilized in 83.3% of the centers to aid in the planning process. The standard techniques employed for radiation delivery were intensity-modulated radiation therapy (IMRT)/volumetric-arc radiation therapy (VMAT) in 86.7% of the institutions. Additionally, all the centers utilized image-guided radiotherapy (IGRT) based on cone beam computed tomography (CBCT) for precise treatment guidance.

Gastric cancer

Regarding gastric cancer, the standard treatment approach in 71.4% of the participating centers involves induction chemotherapy (CT) followed by surgery and adjuvant CT. For 21.4% of the institutions, the standard treatment consists of induction CT followed by surgery and adjuvant CRT. A smaller percentage, 7.1% of the institutions, opts for neoadjuvant radiochemotherapy (CRT) as the primary treatment modality.

The prescribed radiotherapy doses for gastric cancer treatment range from 45 to 50.4 Gy in conventional fractionation in 95% of the participating centers. This variation allows for tailored radiation dosing based on individual patient characteristics and clinical considerations.

In terms of treatment planning techniques, 25% of the institutions utilize PET-CT for planning and evaluation. The majority, 82.1% of the centers, employ IMRT or VMAT as the standard techniques for treatment delivery. Additionally, 96.4% of the institutions rely on IGRT based on CBCT for accurate treatment guidance.

Pancreas cancer

In the case of borderline resectable pancreas cancer, the standard of care in 53.6% of the institutions involves induction chemotherapy followed by surgery. For 42.9% of the centers, the standard treatment approach is induction CT followed by

CRT or stereotactic ablative radiotherapy (SABR), followed by surgery. A smaller percentage, 3.6% of the participant centers, opts for upfront surgery as the primary treatment option.

For non-resectable pancreas cancer, most institutions (86.7%) adopt induction CT followed by chemoradiation or SABR as the standard treatment approach. In 9.7% of the centers, induction CT is followed by an attempt at surgery, and 3.6% of the institutions employ CT alone as the primary treatment modality.

The prescribed radiotherapy doses for both borderline resectable and non-resectable pancreas tumors range from 45 to 55 Gy in conventional fractionation. For adjuvant treatments, the dose ranges from 45 to 50.4 Gy in conventional fractionation. In the case of SABR, the prescribed dose is 50 Gy delivered in 5 fractions.

In terms of treatment planning techniques, PET-CT is utilized for planning purposes in 36.7% of the centers. The preferred technique for treatment delivery is IMRT or VMAT in 89.7% of the institutions, including the 10.7% that utilize SABR techniques. IGRT based on CBCT is employed in all centers. Intraoperative radiotherapy (IORT) is implemented in 10.7% of the institutions.

Rectal cancer

As part of the standard care, all centers prescribe neoadjuvant radiotherapy-based treatment for rectal cancer. Among the surveyed institutions, 10.7% utilize a short course of 25 Gy delivered in 5 fractions, while the remaining centers employ chemoradiotherapy (CRT) with doses ranging from 45 to 50.4 Gy in conventional fractionation. Adjuvant treatments are performed in all centers, except for one, with doses ranging from 45 to 50 Gy in conventional fractionation.

During the treatment planning process for rectal cancer, PET-CT is utilized in 90.3% of the centers. The preferred techniques for delivering radiation therapy are IMRT/VMAT in 58.1% of the institutions, and 3D conformal radiotherapy (3DCR) in 41.9% of the institutions. CBCT is the primary technology employed for IGRT, utilized in 80.6% of the centers.

In 19.4% of the institutions, IORT is implemented as part of the comprehensive treatment approach for rectal cancer.

Discussion

Esophageal cancer

The main guidelines strongly recommend chemoradiotherapy (CRT) as the preferred treatment approach for locally advanced esophageal cancers, ranging from T2N0 to T4b stage [1–4]. CRT can be utilized in both neoadjuvant and radical settings. Other treatment options include neoadjuvant or perioperative chemotherapy [1, 2, 4]. However, neoadjuvant CRT is considered the preferred option, especially for larger tumors that carry a higher risk of incomplete resection (R1-2). Perioperative chemotherapy is more commonly employed for smaller tumors or those located in the esophagogastric junction, where surgical resection can be more easily achieved [3].

Our data demonstrate a high adherence to the clinical guideline recommendations, with 76.7% of the participants indicating neoadjuvant radiochemotherapy (RCT) as the standard treatment for locally advanced esophageal cancer patients.

The prescribed radiation dose in 90% of the participating institutions falls within the range of 41.1–50.4 Gy, which is supported by literature findings [5–7].

PET-CT, although not considered an essential requirement in the guidelines, is a promising concept in radiotherapy planning. It helps radiation oncologists localize the disease burden and assists in tumor contouring [8]. In our survey, 83.3% of the participating institutions routinely incorporate PET-CT in their contouring process.

Both 3DCR and IMRT/VMAT techniques are recommended in the clinical guidelines. IMRT/VMAT allows for more conformal delivery of the high dose and better adaptation of the high dose isodoses to organs at risk [9–11]. Some studies suggest that this may translate into improved survival outcomes [12]. This could explain that in the survey, 86.7% of the institutions prefer IMRT/VMAT as the planning technique for esophageal cancer treatments.

All centers (100%) employ three-dimensional IGRT based on CBCT.

The majority of Spanish institutions participating in the survey demonstrate adherence to international guideline recommendations for the treatment of esophageal cancer. The sole deviation from the recommended guidelines involves the incorpo-

ration of PET-CT in the contouring process. This variation can be elucidated by the pioneering initiatives of certain active institutions that have championed the use of PET-CT in planning for gastrointestinal tumors. This subject has been extensively deliberated in courses and symposia throughout Spain over the past decade.

Gastric cancer

Clinical guidelines recommend a perioperative approach based on neoadjuvant chemotherapy for locally advanced tumors, although there is a lack of randomized studies demonstrating superior benefits over adjuvant CRT. However, a meta-analysis of neoadjuvant chemotherapy has shown improved overall survival, progression-free survival, and a higher rate of negative margins without increased toxicity or surgical complications (13). Our survey data indicate a high adherence of 71.4% to these clinical recommendations.

The CRITICS study aimed to evaluate the role of radiotherapy after perioperative chemotherapy but did not show significant differences in survival due to limited treatment compliance. As a result, clinical adherence to this approach is low in our setting, with only 21.4% of centers adopting it [14].

Currently, meta-analyses do not support the use of preoperative CRT, as it does not provide benefits in terms of overall survival, pathological responses, or achieving complete tumor resection (R0) [15]. Consequently, its clinical utilization remains limited, with only 7.1% of centers implementing it.

Adjuvant treatment, on the other hand, has shown significant improvement in progression-free survival and reduction in local recurrences, although it does not confer a survival benefit [16].

Most international guidelines recommend a radiotherapy dose of 45–50.4 Gy (1.8 Gy per day), with higher doses as a boost in selected cases, such as patients with incomplete resections (R1-R2) [17]. Our survey data demonstrate that 95% of institutions adhere to this dose range.

The incorporation of PET-CT in treatment planning lacks robust evidence [18, 19], which explains why 75% of Spanish centers do not utilize it routinely. However, some data suggest its potential usefulness in defining the gross tumor volume (GTV) [20].

The use of modern radiotherapy techniques, such as IMRT and VMAT versus 3DCRT, is strongly supported in the literature [21]. IGRT with volumetric imaging, specifically CBCT, improves treatment accuracy and reduces geometric errors caused by patient movement between treatment sessions [22]. Our survey reflects this trend, with 96.4% of participating centers utilizing both IMRT/VMAT and IGRT techniques.

Pancreas cancer

According to international guidelines, the use of radiotherapy in pancreas cancer remains a topic of debate [23, 24]. There are three main treatment scenarios for the primary tumor: neoadjuvant, adjuvant, and radical treatments, where radiotherapy can be considered.

Surgery is the primary curative treatment for pancreas cancer and might be performed upfront before other oncologic treatments. Neoadjuvant treatment for pancreas cancer typically begins with chemotherapy (CT) to control potential microscopic metastatic disease [24, 25]. Radiotherapy may be added to shrink the primary tumor before surgery.

The heterogeneity of responses in the survey reflects the controversies surrounding pancreas cancer treatment. Clinical guidelines offer different options for each treatment scenario based on the varied results found in the literature [24, 26]. In 3.6% of the institutions, upfront surgery is the main treatment option for resectable and borderline resectable tumors, while the majority prefers a neoadjuvant approach, with 42.9% using induction CT followed by neoadjuvant radiation and 53.6% using induction CT alone.

The role of adjuvant radiotherapy is also debated. Clinical trials have not shown clear benefits in adding radiation to adjuvant chemotherapy, except in cases of R1 resection and lymph node involvement, where radiation may play an important role in disease control [27, 28].

In the management of locally advanced, non-resectable pancreas cancer, there is a growing consensus both in the literature and among the participant institutions [23, 24]. In the survey, 86.7% of institutions agreed on using CT followed by radical CRT or radiotherapy.

Guidelines recommend a radiotherapy dose of 45–50.4 Gy, with the possibility of a boost up to 54–56 Gy for the primary tumor. Stereotactic ablative radiotherapy (SABR) is considered for pancreas cancer in specialized centers with the neces-

sary experience and technology to ensure precision [29]. The survey reflected a high adherence to the guidelines, with the majority of institutions using conventional fractionation (89.3%), while a small percentage of specialized centers employed SABR techniques with 5 fractions (10.7%).

The use of PET-CT in pancreas cancer treatment planning lacks strong evidence. However, some data support its use in delineating the gross tumor volume [26, 29]. In the survey, 63.3% of institutions did not incorporate PET-CT in pancreas cancer radiotherapy.

IMRT/VMAT is strongly recommended for pancreas cancer radiotherapy due to the location of the pancreas and its proximity to critical organs at risk [23, 26, 29]. In the survey, 89.7% of institutions used IMRT/VMAT for pancreatic cancer radiotherapy. IGRT is mandatory according to guidelines, and all surveyed centers reported routine use.

Intraoperative radiotherapy, as a means of delivering an intraoperative boost to the pancreas bed, is implemented in 10.7% of the institutions, and this possibility is also considered in international guidelines.

Rectal cancer

Locally advanced rectal cancer treatment typically involves neoadjuvant radiotherapy as a standard approach, as supported by previous literature and clinical guidelines [30–33]. There are two main strategies for neoadjuvant radiation in rectal cancer: fluoropyrimidine-based CRT with 45–50.4 Gy delivered in conventional fractionation, or short-course radiotherapy with 25 Gy administered in 5 fractions. The surveyed Spanish institutions demonstrate high adherence to these guidelines, with 61.29% utilizing either 25 Gy in 5 fractions or 45–50 Gy in conventional fractionation. Among the centers that choose CRT, radiotherapy is typically administered in 25–28 fractions in 77.4% of cases.

Adjuvant treatment for rectal cancer is not considered a standard of care, as it has demonstrated to be inferior to neoadjuvant treatments [34, 35]. However, discrepancies in the initial staging may lead to surgical specimens revealing advanced tumors that require additional adjuvant treatments. In this adjuvant setting, 80% of the surveyed institutions prescribe doses of 45–50.4 Gy in conventional fractionation, demonstrating a high level of adherence to guideline recommendations. Furthermore, 16.67% of the institutions increase the dose above 50.4 Gy, up to a maximum of 56 Gy. The number of fractions used in adjuvant treatments ranges from 25 to 28, in line with guideline recommendations. The fluctuation in the recommended dose in chemoradiotherapy (CRT) can be attributed to the involvement of certain centers in dose escalation trials for rectal cancer during the survey period.

While PET-CT may aid in tumor localization and identification of pathologic lymph nodes, it is not recommended for tumor delineation in guidelines. Only magnetic resonance imaging (MRI) is recommended for this purpose according to the NCCN guidelines [32]. However, in the survey, 9.7% of the centers use simulation PET-CT for neoadjuvant rectal cancer radiation planning, suggesting some deviation from the recommended practice.

The guidelines recommend using 3DCRT, IMRT or VMAT techniques for rectal cancer radiation treatment. IMRT/VMAT is particularly recommended when dose constraints in the small bowel are problematic or when inguinal lymph nodes need to be included [30, 32]. In the survey, 41.9% of the institutions utilize 3D technique, while 58.1% employ IMRT/VMAT, aligning with the guideline recommendations.

Intraoperative radiotherapy (IORT) is recommended in cases of advanced T4 tumors, positive circumferential margins, the potential for R1 resection, or for the treatment of local relapses. A single dose of 10–20 Gy is the standard practice for IORT. In the survey, 19.4% of the institutions reported prescribing IORT with the same indications and doses specified in the guidelines.

The authors are aware that the survey, despite being sent to all centers represented in SEOR GI, was only responded to by a portion of them, perhaps those showing greater interest. As a result, its findings may exhibit some deviation from reality.

In Spain, SEOR plays a pivotal role in overseeing the quality assurance in radiotherapy through initiatives such as clinical recommendations, guidelines, and educational efforts. Within the SEOR GI, our focus is on enhancing the quality of radiotherapy treatments for gastrointestinal tumors, ensuring adherence to clinical guidelines, and keeping all members updated. Surveys like the one con-

ducted serve as valuable tools, providing us with a comprehensive understanding of the current state of GI radiotherapy. This insight enables us to develop future programs aimed at aligning our practices with international recommendations.

We recognize the limited sample size and the absence of data from some provinces, which may introduce bias into the survey results, as only the most active centers might have participated. Moving forward, endeavors will be undertaken to facilitate a more comprehensive update with broader participation, aiming to sustain the evaluation of radiotherapy quality for gastrointestinal tumors in Spain.

Conclusion

The survey findings suggest that radiotherapy protocols among the respondents generally conform well to international guidelines. Nevertheless, certain areas, such as the treatment of pancreatic cancer and the use of PET-CT in simulation and planning, exhibit more varied results in both the survey and the literature, underscoring the diversity in clinical practices.

Conflict of interests

Authors declare no conflict of interests.

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