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ORIGINAL ARTICLE

A five split-field three dimensional conformal technique versus an anterior-posterior on in postoperative radiotherapy for gastric carcinoma: a multicenter comparative study using quality of life measurements as well as clinical and dosimetric parameters

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Summary

Purpose: *Several adjuvant approaches are regarded as available options in the management of localized, resectable gastric cancer .The objective of our study was to evaluate multiple field and anteroposterior conformal technique.*

Methods: *Ninety-seven patients received three dimensional conformal (3DCRT) postoperative adjuvant radiation therapy for gastric carcinoma. Thirty-five patients received anteroposterior (AP/PA) fields (Group B), while 62 patients were irradiated with multifield technique (Group A). Their ages ranged between 29-85 years. The objective of the study was to evaluate the quality of life (QoL) for all patients after the completion of radiotherapy using the QLQ-C30 of the EORTC questionnaire (European Organization for Research and Treatment of Cancer) and to investigate any measurable differences between those two radiation techniques according to QUANTEC criteria and the radiotoxicity.*

Results: *In terms of QUANTEC criteria, the multifield technique was superior concerning the left kidney (p=0.025), right kidney (p<0.001), spinal cord (p<0.001) and planning target volume (PTV) coverage (p<0.001). According to EORTC/RTOG toxicity criteria, the rate of diarrhea was higher in AP/PA technique (p=0.028). In terms of QLQ-C30, the multifield technique was superior concerning appetite loss (p=0.022), diarrhea (p=0.046) and global QoL (p<0.001).*

Conclusion: *On the basis of QLQ-C30 questionnaire, EORTC/RTOG toxicity and dosimetric parameters, the present report has shown that the three dimensional multifield conformal radiotherapy is superior compared to AP-PA techniques.*

Key words: *conformal technique, dosimetry, gastric cancer, quality of life, radiotherapy*

Introduction

Gastric cancer is still the third most frequent reason for cancer mortality [1]. More prevalent in Asian countries, adenocarcinoma of the stomach remains a significant oncologic problem [2,3]. Al-

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though surgery still represents the cornerstone of management, adjuvant strategies have been seen to offer survival advantages in prospective randomized trials.

Several adjuvant approaches are regarded as available options in the management of localized, resectable gastric cancer [4]. In a study conducted by Cunningham et al. [5], the authors concluded that perioperative chemotherapy (epirubicin, cisplatin, and fluorouracil) improved the progression-free and overall survival rates among patients suffering from the disease. McDonald et al. [6], on the other hand, observed that postoperative chemoradiotherapy significantly improved the disease-free and overall survival rates among patients treated with resected adenocarcinoma of the stomach. The protocol of Intergroup Trial 0116 (INT 0116) involved two-dimensional radiation treatment planning, most typically a shaped anteroposterior-posteroanterior (AP-PA) beam arrangement. The 45 Gy of radiation was delivered in 25 fractions 5 days per week, to the tumor bed, to the regional lymph nodes and 2 cm beyond the proximal and distal margins of resection. The tumor bed was defined by preoperative computed tomographic imaging and in some cases by surgical clips. Perigastric, celiac, local paraortic, splenic, hepatoduodenal or hepatic-portal and pancreaticoduodenal lymph nodes were included in the radiation fields. Doses were limited so that less than 60% of the hepatic volume was exposed to more than 30 Gy of radiation. The equivalent of at least two thirds of one kidney was spared from the field of radiation and no portion of the heart representing 30% of the cardiac volume received more than 40 Gy of radiation [6].

However, this design augments the toxic effects and thus termination of the therapy in more than one-sixth of patients was necessitated. However, the findings from this study pointed out the important potential of radiotherapy and the need to overcome the problems that led to the toxic effects. With present-day three-dimensional (3D) planning systems, it is now possible to deliver radiation using multifield techniques that conform more accurately to the high-risk volume along with substantial sparing of critical normal tissues.

The objective of the study was to evaluate among the two groups, the dosimetric differences in terms of dose volume histograms (DVHs) as well as the differences regarding the toxicity and the

Table 1. Patient characteristics

Characteristics	*Group A (n=62)* *n (%)*	*Group B (n=35)* *n (%)*	*p value*
Sex			0.216*
Male	51 (82)	27 (77)	
Female	11 (18)	8 (23)	
Age, years, median (range)	62.3 (40-85)	63.1 (29-84)	0.747**
Stage			0.324**
T2N1M0	5 (8)	4 (11)	
T2N2M0	19 (30)	9 (26)	
T3N1M0	18 (29)	10 (29)	
T3N2M0	8 (13)	5 (14)	
T3N3M0	9 (15)	6 (17)	
T4N1M0	-	1 (3)	
T4N2M0	3 (5)	-	0.795**
Surgery			
Partial	32 (52)	18 (51)	
Total	30 (48)	17 (49)	
Technique			0.683**
D1	22 (35)	13 (37)	
D2	40 (65)	22 (63)	
Tumor localization			0.112**
Stomach body	28 (45)	12 (34)	
Cardiac-esophagus junction	20 (32)	8 (23)	
Lesser curvature	9 (15)	10 (29)	
Major curvature	5 (8)	5 (14)	

*x^2 test; **Mann-Whitney U test

QoL for all patients after completion of the radiotherapy using the QLQ-C30 of the EORTC questionnaire (European Organization for Research and Treatment of Cancer) [7]. The study was defined as retrospective, in terms of feasibility, QoL, dosimetric (DVHs) and clinical (toxicity and overall survival) evaluations.

Methods

Patients

Ninety seven patients with gastric cancer received postoperative adjuvant chemo-radiotherapy, with the objective to evaluate the toxicity and feasibility of the conformal radiotherapy between January 2005 and February 2014. The first 35 patients received irradiation with anterior-posterior technique, while in 2008 in all centers we changed into mulltifield technique. Thus 62 patients received three dimensional conformal multifield radiotherapy technique (Group A) and 35 patients were treated by antero-posterior three-dimensional conformal technique (Group B). The aim of our retrospective study was to evaluate the feasibility as well as the differences in toxicity, dosimetry and QoL between the two groups. The study was approved from the local ethical committee.

The eligibility criteria included the following: histologically confirmed adenocarcinoma of the gastroesophageal junction or the stomach; complete resection of the neoplasm; stage II/III; ECOG performance status of 2 or lower; creatinine concentration no more than 25% higher than the upper limit of normal; hemogram, serum aspartate aminotransferase, alkaline phosphatase concentration and bilirubin within the normal limits. The follow-up was up to 60 months post irradiation. In Table 1, data are shown, regarding the demographics of patients in terms of age, gender, localization of disease, staging, type of surgical treatment, and the kind of the applied radiotherapy technique.

Toxicity and Quality of life evaluation

During radiation treatment, once per week, the evaluation of toxicity was assessed with the EORTC/RTOG toxicity grading scale in terms of nausea-vomitting and diarrhea. The maximum score monitored every week was taken as the final score for each patient. At the completion of treatment, assessment was carried out regarding the QoL of irradiated patients using QLQ-C30 questionnaire the EORTC [7]. The EORTC QLQ-C30 is a questionnaire developed to assess the QoL of cancer patients. It includes a series of 30 questions classified into 3 categories:

- The first category includes questions 29,30 for assessing the general condition of the patient (Global health status).
- The second category of questions relates to the patient's level of functioning such as physical activity, role functioning, emotional functioning, cognitive function and social activities.
- The third category covers the patient's symptoms such as fatigue, nausea and vomiting, pain, dyspnea, insomnia, loss of appetite, constipation, diarrhea and financial difficulties.

Chemotherapy

Patients received one cycle of fluororacil (5-FU) 425 mg/m^2/day + leucovorin 20 mg/m^2 for 5 days, followed by concomitant 5-FU and leucovorin with radiation. An additional two cycles of 5-FU and leucovorin were given following completion of chemoradiation [4-6,8,9]. All patients started their chemotherapy schedule within 40 days after surgery.

Radiotherapy

Radiotherapy generally followed the recommendations outlined in INT0116 [6]. A radiation therapy of 45 Gy was delivered in 25 fractions, 5 days per week for 5 weeks. The clinical target volume (CTV) included the tumor bed defined by preoperative CT scan, the area of resected perigastric local tumor extension, anastomosis, distal duodenum limb and the following draining nodes: gastric, gastroepiploic, celiac, porta hepatis, subpyloric, gastroduodenal, splenic, suprapancreatic and retropancreaticoduodenal. For proximal T3-T4 lesions, the medial two thirds to three fourths of the left hemidiaphragm were included in the CTV. For proximal lesions involving the cardia or gastroesophageal junction with any positive nodes, the lower paraesophageal nodes were included in the CTV. Dose variation in the PTV was kept according to the International Commission on Radiation Units and Measurements (ICRU) 50-62 recommendations [8-13]. The PTV was defined by the physician and typically included the CTV with a 0.5-1 cm margin for set up variation and organ motion. At the discretion of the physician, PTV margin of up to 2 cm were sometimes used superiorly because of marked diaphragmatic breathing motion as assessed of fluoroscopy. The mean value of PTV volume using this technique was approximately 1,360 cm^3 (range, 522-2,126).

Normal tissue dose limitations included the following: dose to 10% of the spinal cord volume within the treatment region should not exceed 45Gy and no part of the spinal cord should receive > 50Gy; 30% of one kidney should not receive >20Gy (if possible, the dose to the second kidney should be kept to this limit, but could be up to 45 Gy); 20% of liver should not receive >40Gy. The isocenter was placed at the tumor bed. For "split-field" technique, the fields were split with two posterior-anterior ones above the isocenter and three fields (anterior-posterior and left) below the isocenter. The intention was to spare the kidneys as much as possible. Radiation was delivered using linear accelerator with photon energy of 6 MV or 15MV. Either an ECLIPSE-Varian, or PLATO Nucletron, or ONCETRA Nucletron treatment planning system was used for CTV contouring and planning, depending on the radiotherapy center. Treatment was delivered with either aVarian 2100C 15MV linear accelerator, or Siemens 6MV, or Electa 6MV, with multileaf collimator (MLC), depending on the radiotherapy center. DVH were recorded for the kidneys, liver and spinal cord and PTV in all patients. The evaluation of the irradiation dose in

organs at risk (right kidney, left kidney, liver, spinal cord, healthy part of the esophagus and heart) when using conformal three-dimensional - multiple fields compared with anteroposterior technique, included dose decreasing to surrounding tissues as well as QUANTEC criteria (Quantitative Analysis of Normal Tissue Effects in the Clinic) [8-20]. In all cases, the QUANTEC should be met. In detail:

- 46% of the volume effect of the heart<30 Gy
- 55% of the volume of the kidney <12 Gy
- Esophagus dose < 32 Gy
- Mean dose to the liver < 32 Gy
- Spinal cord doses <45 Gy

The patients were treated either in "Attikon" University Hospital, or in "Aretaieion" University Hospital, or in Larisa University Hospital. A typical treatment planning using the multi-field technique is shown in Figure 1.

Statistics

In order to statistically analyze the two groups of patients regarding the DVH analysis for the PTV, the spinal cord, the kidneys and the liver, x^2 test was used. The optimal within patient's error covariance structure was specified by means of non-parametric tests [21]. Differences in percentage were evaluated with the x^2 test. Due to the small number of patients, the comparison was performed with the Mann-Whitney non-parametric test. The evaluation of differences in overall survival between the two groups was performed with the log-rank test regarding Kaplan-Meier curves. The level of significance was set at 5%, while calculations were performed using SPSS v.10 (Chicago, IL, USA).

Results

There was no significant difference in the homogeneity between the two groups, as shown in Table 1. The toxicity according to EORTC/RTOG criteria is shown in Table 2. It seems that there was a significant difference concerning the diarrhea (p=0.028), while no difference was noted in terms of nausea-vomiting. Concerning the QoL scoring between the two groups, there was a significant difference only for global QoL, appetite loss (p=0.022) and diarrhea (p=0.046), as shown in Table 3. With 3D conformal multifield radiotherapy, Group A was

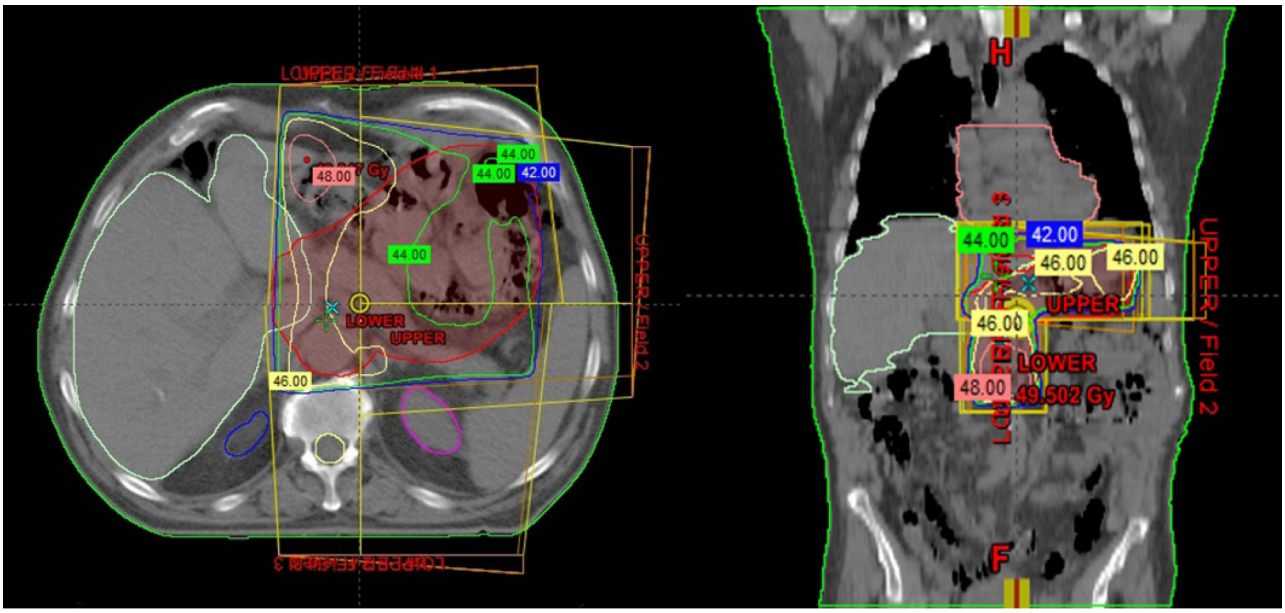

Figure 1. Typical 5-field technique treatment planning. Left: sagittal section. Right: coronal section.

Table 2. EORTC/RTOG toxicity score for nausea-vomitting and diarhoea between group A and B

	Nausea - vomiting			*Diarrhea*		
Grade	*Group A n (%)*	*Group B n (%)*	*p*	*Group A n (%)*	*Group B n (%)*	*p*
0	24 (38.7)	17 (48.5)	0.49	36 (58.1)	13 (37.1)	0.028*
1	16 (25.8)	8 (22.9)		24 (38.8)	15 (42.9)	
2	15 (24.2)	4 (11.4)		2 (3.2)	6 (17.1)	
3	6 (9.7)	5 (14.3)		-	1 (2.9)	
4	1 (1.6)	1 (2.9)		-		

*x^2 test

measured to be nearly twice as better concerning the overall QoL (global QoL) with respect to the 3D conformal radiotherapy two fields (p <0.001). A trend was noted for superiority for nausea-vomiting in favor of multifield technique but without statistical significance.

Furthermore, the evaluation of the percentage for the volume of normal tissues (heart, kidney, esophagus, liver and spinal cord) receiving radiation compared with QUANTEC criteria is shown in Table 4. Specifically, the average rate in percentage of the total volume of the OAR in all patients was:

- Heart: In group A, the mean volume of the organ irradiated with 30 Gy was 15.79%. However, 12.5% of the patients have been irradiated over the QUANTEC criteria. In group B the mean volume was 17.54% and only one patient has been irradiated over the QUANTEC criteria.
- Left kidney: The mean volume of the organ irradiated with 12 Gy was 39.04% and 47.61%, in group A and B respectively. Nevertheless, 15.38% of group A cases and 20% of group B cases have been irradiated over the QUANTEC criteria.
- Right kidney: In group A, the mean volume of the organ irradiated with 12 Gy was 24.51%, while 15.22% of cases have been irradiated over the QUANTEC criteria. In group B, the mean volume was 34.29% and only one patient was treated over the QUANTEC criteria.
- Esophagus: In group A, the average irradiation value of the organ was 22.02 % with a rate of only 2.13% irradiated above the QUANTEC criteria. In group B, 6 patients (17.1%) were treated over the QUANTEC criteria.
- Liver: In group A, the average irradiation value of the organ was 22.24 Gy with a rate of 2.27% over the QUANTEC criteria. In group B the mean dose was 23.74 Gy with 3 patients irradiated over the QUANTEC criteria.
- Spinal cord: In group A and B, the average irradiation rate of the organ was 19.86 Gy and 33.48Gy, respectively. None of the patients was irradiated over the QUANTEC criteria in both groups.

Table 3. EORTC QLQ-30 scoring between group A (n=62) and group B (n=35)

EORTC QLQ-30	*Group A (±SD)*	*Group B (±SD)*	*p value**
Physical functioning	68.06 (27.02)	73.52 (17.22)	0.776
Emotional functioning	57.39 (27.29)	64.52 (21.04)	0.263
Cognitive functioning	76.61 (23.66)	75.7 (21.14)	0.661
Social functioning	57.26 (31.45)	61.43 (29.09)	0.59
Role functioning	54.57 (35.98)	68.10 (20.36)	0.124
Fatigue	51.08 (27.69)	49.21 (21.94)	0.743
Pain	31.45 (26.67)	30.95 (21.06)	0.846
Dyspnoea	30.11 (30.60)	24.76 (26.00)	0.50
Insomnia	34.41 (32.49)	34.29 (30.77)	0.948
Constipation	22.04 (30.74)	27.62 (33.81)	0.439
Diarrhoea	16.44 (21.11)	20.95 (31.40)	**0.046**
Financial difficulties	45.16 (33.66)	39.05 (32.83)	0.433
Nausea-vomiting	22.85 (24.19)	17.14 (20.80)	0.077
Appetite loss	41.44 (37.34)	45.71 (36.23)	**0.022**
QoL (global)	53.90 (21.16)	27.14 (10.37)	**<0.001**

SD: standard deviation, *Mann-Whitney U test. Bold numbers denote statistical significance

Table 4. Report of each organ at risk (OAR) regarding the criteria QUANTEC

Dosimetry	*Group A (±SD)*	*Group B (±SD)*	*p value*
Heart: V30<46%	15.79 (±18.45) %	17.54 (±12.14) %	0.063*
Esophagus: mean < 34 Gy	22.02 (±11.31) Gy	22.29 (±9.33) Gy	0.941*
Kidney left: V12 <55%	39.04 (±18.52) %	47.61 (±8.94) %	**0.025***
Kidney right: V12 <55%	24.51 (±14.55) %	34.29 (±13.43) %	**<0.001***
Liver: mean < 32Gy	22.24 (±6.20) Gy	23.74 (±6.19) Gy	0.051*
Spinal cord: Mean (Gy)	19.86 (±5.40) Gy	33.48 (±5.93) Gy	**<0.001***
PTV coverage for 98% of dose	95% (CI: 93%-99%)	71% (CI: 69%-97%)	**<0.001****

*Mann-Whitney U test, **x^2 test, CI: confidence interval. Bold numbers denote statistical significance

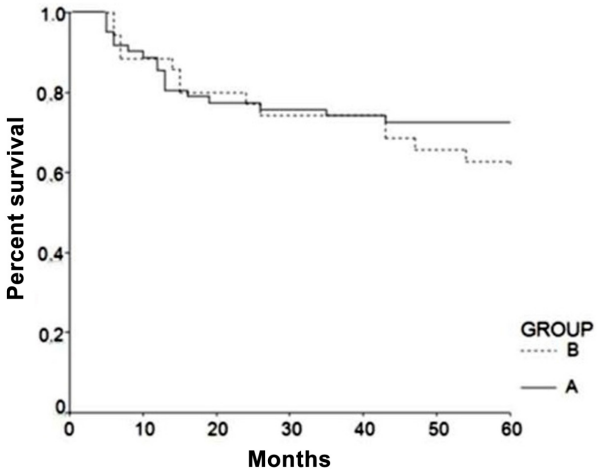

Figure 2. Kaplan Meier curve for overall survival in group A vs B (Log-rank, p=0.44).

Regarding overall survival, 73% of the patients irradiated with multifield technique were alive 5 years after the therapeutic intervention. Although there was a trend for better overall survival in favor of the multiple fields technique, no significant difference was noted (log-rank, p=0.44), as shown in Figure 2.

The DVH comparisons have shown that the conformal multifield technique provides better coverage of the target volume with 99% of the volume of the PTV receiving 95% of the prescribed dose, compared to 96% when using AP-PA technique (p<0.001). The percentage of the PTV receiving 98% of the prescribed dose was 95% for the conformal multifield technique and only 71% for the AP-PA technique (p<0.001). The radiation dose to the spinal cord was considerably and statistically significantly lower with conformal technique (p<0.001).

Discussion

The prognosis of gastric cancer remains dismal, especially in western countries where the incidence of early gastric cancer is very rare [1]. High relapse rates (stage-dependent up to 80%) indicate the need for adjuvant therapy after surgery. The postoperative chemoradiation improved the survival in patients with resectable gastric cancer according to the INT0116 trial [6]. However the local relapse rates in our study were really lower than the reported in the INT trial (4% vs 19%, respectively). This fact may be explained by the radiotherapy technique in terms of the high conformity to the target, while the irradiation of the normal tissues was minimal. It should be mentioned that in the INT trial, a conventional anterior-posterior radiotherapy technique was used and not a 5-field one. However, the low number of patients included in the present study should not be underestimated. Cunningan et al. demonstrated a survival benefit of a neoadjuvant-adjuvant chemotherapy regimen alone for the first time [5], followed by a second randomized trial from Japan [22]. The extent of surgery and absolute survival numbers, however, differed significantly between these studies. It is therefore unclear if chemotherapy alone or radiochemotherapy is the most beneficial approach for locoregionally advanced gastric cancer in a perioperative setting [23]. Moreover, the best chemotherapy schedule is still under consideration [5,6]. Radiotherapy for gastric carcinoma is currently under a major revision as perioperative chemotherapy and D2 lymphadenectomy [24]. The CLASSIC trial investigated the combination of chemotherapy and surgery with D2 technique, and showed a 3-year disease-free survival rate up to 74% [25]. Moreover, the ACTS-GC trial showed a 5-year relapse free survival rate up to 65.4%, when S-1 molecular targeted agent was associated with D2 gastrectomy [26]. However, in European centers, the D2 lymphadenectomy is not a common practice. In an editorial by McDonald, it seems that there is definitely a different surgical technique in the Western hemisphere in comparison with Japan (where D2 technique is mandatory). Thus the results related to D2 surgery are difficult to be applied for patients in Europe and US [27].

In the current study all patients had an excellent compliance to the treatment. In the INT trial, up to 64% of patients did not complete the treatment protocol due to toxicity. However in our study all patients completed the radiotherapy schedule. This might be related to the lower irradiation to the normal tissues achieved by our 5-field technique, confirming the potential superiority of our technique in terms of toxicity as well as to treatment compliance.

Many radiation oncologists are unwilling to use anteroposterior-posteroanterior (AP-PA) field arrangements when treating gastric cancer with adjuvant postoperative radiotherapy due to concerns about normal tissue toxicity, particularly in relation to the kidneys and spinal cord. Moreover, with a variety of techniques using 3-field and 4-field arrangement it soon became apparent that it was not possible to consistently cover the target volume in all patients while respecting normal tissue tolerance [24]. The use of split field technique allows different field arrangements. That's why we used a mono-isocentric asymmetric jaws technique to achieve an effective transverse match plane between the upper and lower sections of the PTV. The level in which we split the PTV varies between

patients and it depends on the individual patient anatomy following surgery. In the majority of patients the split is placed near the upper level of the kidneys. Splitting the field at this level allows treatment of the lower section with a technique that will spare most of the renal tissue. This is also the level in which the PTV often changes shape and position as different nodal groups are treated. However, in our study we used more conservative dose constraints adopted that volume of the organ irradiated with 20 Gy (V_{20}) for both kidneys be less than 30% and V_{40} for liver be less than 20%. Our results reveal that this multiple field conformal radiation therapy produces superior dose distributions compared to AP-PA techniques. However, apart from providing superior dose distributions, the major advantage of this conformal technique is the reduction of the radiation dose to the kidneys and spinal cord. The use of multiple fields has allowed considerable sparing of these organs from the high dose volume as illustrated by comparative DVH data [20,28,29].

The radiation technique that we applied should be compared with intensity modulated radiation treatment (IMRT) technique that is the more accurate and modern. Reports of the feasibility of IMRT planning and its implementation have been already published [25-27]. In most cases, the adoption of IMRT for the treatment of gastric cancer was advised. In those studies, IMRT plans were compared to CRT plans that usually consisted of coplanar 3-field beam arrangements or, at most, 4-field box techniques. We should be cautious regarding the theoretical sequelae of IMRT. For example, the integral dose is likely to be higher for IMRT than for 3D CRT. Additionally, if the beam energy exceeds 10 MV, the photoneutron dose becomes more relevant. For this reason, the risk of second malignant neoplasm is probably greater for IMRT than for 3D CRT. Although these sequelae are unlikely in patients with advanced gastric cancer, patients should be informed of the potential limitations and advantages of IMRT. Some investigators have gone so far as to say that the clinical gains yielded by IMRT are not enough to guarantee the efforts required to generate IMRT plans in this patient population. Specifically, the addition of IMRT neither improved the coverage of the PTV nor excluded larger volumes of adjacent critical structures in a clinically relevant way [30,31].

Although we have no doubt that IMRT can be delivered safely and effectively in patients with adenocarcinoma of the stomach, we cannot categorically recommend its use in the adjuvant treatment of this cancer. Nevertheless, the incremental benefits conferred by IMRT approaches are probably worth pursuing in those patients in whom renal reserve is a special consideration (e.g., those with brittle forms of diabetes or hypertension and those with risk factors for kidney disease or a preexisting nephropathy). It is reassuring to know that complex 3D CRT techniques can deliver radiation dose distributions that are equal with distributions delivered by IMRT techniques. Nonetheless, we believe that further study of IMRT in this setting is warranted, as many questions about its use and potential are unanswered and the superiority of IMRT against 3D CRT is still unclear [3,30-35].

One aim of the study by Wieland et al. was the demonstration of some benefits of using the Mimic system of arc treatment [30]. With the advent of new delivery methods, such as those developed by Varian (Rapid Arc; Walnut Creek, CA) and Elekta (VMAT), further examining IMRT might be worth trying. The use of newer technologies, especially the ones regarding high-resolution multileaf collimation, might be particularly effective in improving results. IMRT appears to offer only limited advantages compared to sophisticated 3D CRT planning in this setting, so we believe that 3D CRT represents "the most practical arrangement for the overwhelming majority of postoperative adjuvant radiotherapy cases".

We recognize that the kidneys are particularly vulnerable to injury during the radiation treatment of gastric cancer and understand the apprehension regarding the late manifestation of nephrotoxicity that has been expressed [30,32]. Obviously, it is reasonable to evaluate treatment plans that deposit the dose within the kidney in the context of the V12. In our study, the V12<55% was lower in both kidneys in favor of multifield technique. However, the maximum doses in some cases regarding the right kidney were higher in group A, which might be related to anatomical variations among patients. In such cases, IMRT technique or more than 5 fields might be the solution for optimal dose distribution [20,30,31].

The mean dose to the spinal cord also favored the multifield technique. The consequences of radiation-related myelopathy have urged physicians to be especially vigilant regarding this critical structure. The mean dose to the liver was subcritical with all modalities but it was the lowest with the multifield technique. Because liver tolerance was never exceeded, physicians enjoyed more latitude with regard to this normal organ when exploring complex plans for the irradiation of the CTV among gastric cancer patients. According to the study by Leong et al. [20], the radiation dose to the liver was higher with their conformal, 6-field

technique. Our study demonstrated slightly lower liver radiation doses. Moreover, the maximum doses that were delivered to the organ were lower in the conformal technique when it was compared with AP-PA technique. Esophagus did not demonstrate any difference between the two techniques, obviously related to the delineation of PTV which was similar in group A and B. In the same context, nausea and vomiting, in both scales of QLQ-C30 and EORTC/RTOG, was not significantly different due obviously to the same delineation of PTV for both groups. However, loss of appetite was lower in group A, probably related to the inhomogeneities (overdosed) delivered in AP/PA technique. In a previous study, Koukourakis et al. have also compared the DVHs between AP-PA and multifield technique, showing that there was a better coverage of the PTV and lower doses at OARs. The conformal technique provides more adequate coverage of the target volume with 99% of the PTV receiving 95% of the prescribed dose compared to 96% using AP-PA fields [36]. Nevertheless, it should be mentioned that 3D-conformal techniques are superior to 2D-techniues based on bone structures but not to computerized tomography images [37].

It is unclear whether more advanced treatment techniques will improve the therapeutic ratio in this clinical setting [5,20]. Also, it does not immediately imply that improving the dose-volume histogram for an OAR will mean less clinically relevant toxicity. At the moment biological outcome data requires a long time to accumulate, which is at odds with the pace of technological development. There is relatively little data on late toxicity associated with the use of adjuvant chemoradiation in gastric cancer with modern techniques. A detailed summary is precluded, but several groups have started to evaluate this further; late effects can take many years to develop after irradiation, thus prolonged patient follow-up is required to ascertain the true rate of toxicity [30,39].

Last but not least, in any case, the final decision for either the technique or the potential toxicity from combined treatment should be taken under a multidisciplinary approach which is definitely a local tumor board in the hospital [40,41].

Conclusions

On the basis of QLQ-C30 of the EORTC questionnaire and the treatment planning comparison, the present report has shown that the 3D multifield conformal radiotherapy produces superior dose distributions and reduced radiation doses to the OARs compared to AP-PA techniques, with the exception of the right kidney, with the potential to reduce treatment toxicity. Thus any clinical advantage or disadvantage of 3D CRT and IMRT remains to be confirmed and technological developments in radiation oncology must be included in multicenter trials with adequate follow-up to assess late toxicity. In practice, however, clinical resources and the availability of technology will govern what is possible in individual treatment centers. Finally, there is room to develop the methodology of planning studies and to take the opportunity to develop interactive tools that would allow inter-institutional benchmarking.

Conflict of interests

The authors declare no conflict of interests.

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