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RADIOTHERAPY IN GASTRIC CANCER IN QUITO-ECUADOR

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ABSTRACT

OBJECTIVE: To analyze the general survival of the patients with gastric cancer who received adjuvant chemoradiotherapy treatment in stages IB-IIIC according to the dose of Radiotherapy received.
METHODS: Retrospective analysis of patients diagnosed with gastric adenocarcinoma or gastroesophageal junction by Kaplan Meier curves.
RESULTS: Radiation therapy can be seen as there is no difference between 45Gys and 50Gys with a p = 0.001. Likewise, it can be seen that survival decreases in those patients who have not fulfilled the standard fractionation filing
CONCLUSION: Although 50.4 Grays (Gy) was administered in the intergroup 0116 study, subsequent studies demonstrated similar effectiveness when applying 45 Gy, data that are corroborated by our research, with no differences in this amount of radiation.

INTRODUCTION

The curative treatment of stomach cancer has been described as surgery, however it has been possible to appreciate since Macdonald's work that gastrectomy alone does not constitute a definitive curative treatment. (1)

The high frequency of relapse of this disease has led to consider the benefits of adjuvant treatment, however more current studies have opted for neoadjuvant treatment as a better option seeking to increase the overall survival of patients with Locally advanced gastric.

In Ecuador, according to the data reported in the National Tumor Registry 2014, gastric cancer ranks second in incidence in men and fourth in women. (2)

For the year 1965 Lauren makes a pathological determination of gastric cancer by dividing it into adenocarcinoma of the intestinal and diffuse type that to date is still well accepted for its ease, in which the diffuse type is of worse prognosis; it was observed that the type of diffuse adenocarcinoma was seen in younger people, while the intestinal type was preceded by chronic gastritis and metaplasia; It is true that a molecular classification is currently available in view of the fact that it can be seen in both a surgical piece and a diffuse intestinal component, determining as chromosomal instability, somatic mutation, Epstein Bar infection and DNA methylation.

The primary objective of this research is to analyze the overall survival of patients with gastric cancer who received adjuvant chemoradiotherapy treatment in stages IB-IIIC according to the dose of radiation therapy received.

MATERIALS AND METHODS

Data from electronic medical records were collected from 01/27/2011 to 11/10/2015 of those patients with confirmed diagnosis of gastric cancer clinical stage IB to IIIC over 18 years old who received surgical treatment and subsequently adjuvant with Radiotherapy plus Fluorouracil according to the INT 0116 study, in an Oncology Hospital of Quito, of those patients over 18 years of age with a confirmed diagnosis of gastric adenocarcinoma or clinical stage gastroesophageal junction adenocarcinoma IB to IIIC in whom type D2 gastrectomy was performed.

The patients received adjuvance with 3D radiation therapy, covering gastric bed and lymphatic chains in cases of total gastrectomy. In the case of subtotal gastrectomy, gastric residual and ganglion regions were treated, defining them according to international recommendations for the contouring of volumes in this pathology. The dose used was 45-50 Gy in fractions of 1.8 Gy / day.

A descriptive analysis was carried out with the collected variables and a statistical analysis with the SPSS and EXCEL program, the survival by means of Kaplan Meyer curves until 08/30/2018.

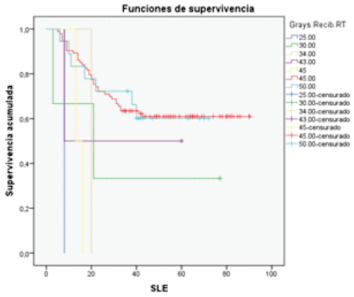
RESULTS

A sample of 197 individuals was obtained, of which 115 were men (58.4%) and 82 women (41.6%); with ages between 18 and 89 years, distributed in clinical stages IB to IIIC according to the AJCC seventh edition, also the histopathological type was determined by the Lauren classification as shown in Table 1.

Variable		n	%
SEX	Man	115	58,4
	Woman	82	41,6
	TOTAL	197	100
Age	>60 years	118	59,9
	<60 years	79	40,1
		197	100
Stage	IB	18	9,1
	IIA	32	16,2
	IIB	29	14,7
	IIIA	24	12,2
	IIIB	53	26,9
	IIIC	41	20,8
		197	100
Ethnic group	Latino	119	60,4
	Indigenous	32	16,2
	Latino 1	43	21,8
	Latino 2	2	1
	Afrodescendents	1	0,5
	Total	197	100
PATHOLOGY	Diffuse	66	33,5
	intestinal	130	66
	Scamous	1	0,5
DIFFUSE ADENOCAR CINOMA	Latino	41	62,1
	Indigenous	13	19,7
	Latino 1	12	18,2
	Latino 2	0	0
	Afrodescendents	0	0
	Total	66	100
INTESTINAL ADENOCAR CINOMA	Latino	77	59,2
	Indigenous	19	14,6
	Latino 1	31	23,8
	Latino 2	2	1,5
	Afrodescendents	1	0,8
	Total	130	100

Latino 1 = Latino America with indigenous parents
Latino 2 = Latino America with Caucasian parents

As for radiotherapy, it can be seen that there is no difference between 45Gys and 50Gys with a P = 0.001. Likewise, it can be seen that survival decreases in those patients who have not fulfilled the standard fractionation filing Figure 1.



DISCUSSION

More than 15 years have passed since the study by Macdonald et al; on which the adjuvant chemotherapy radio treatment is based describing an average survival of 36 months over those who only received surgery and observation, with all discussions regarding the surgical technique, surgical fields that have been discussed for a long time in the fact that the main limitation for the global acceptance of the INT-0116 regimen as an adjuvant treatment modality in gastric cancer has been the limited lymph node dissection (D0 or D1) performed in 90% of the patients included in the test. Although the superiority of D2 lymph node dissection in reducing locoregional relapse has not been consistently demonstrated compared to D1 dissection (13–17). In the present study in the context of Gastrectomy D2, we can see that the average survival reaches 51.5 months. It is important to mention that there are patients who find a total overall survival of 90 months and that from this subgroup subsequent analyzes should be performed.

Despite these results, we must also discuss the ARTIST study described by Lee J et al, as well as the ARTIST II study, in which it was proposed to elucidate whether after chemotherapy D2 gastrectomy was sufficient or required chemoradiotherapy, with the conclusion that concurrent chemoradiotherapy did not reduce the recurrence rate compared to chemotherapy alone, however, to the subgroup of patients with metastatic nodules after gastrectomy, reporting that for the adjuvant chemoradiotherapy group the estimated rates of disease-free period at 3 years were 78.2%, while in our institution at a time of 7 years we reached an approximate survival of 50%. (18–20) For Fabio Grosso et al, who analyzes the adjuvant treatment of Gastric Adenocarcinoma in Colombia demonstrates that a 2-year follow-up of patients treated with the Intergroup 0116 scheme in 96.8% of patients has disease-free survival at this time of 77.4%, that if we extrapolate our data to 2 years our survival is lower reaching almost 50%. (22)

For Chung et al; It is important to note that, as published in the analysis of the intergroup 0116 study, one of the main criticisms of the comparison that was made was the divergence in the techniques used to administer two-dimensional and three-dimensional radiation therapy as well as the lack of unification in the criteria for the contour of volumes applied to patients treated with 3D technique (22), in this study it is important to note that all patients were treated with the same radiotherapeutic technique and applying uniform criteria for the definition of volumes.

Regarding the dose used, although intergroup 0116, administered 50.4 Gy, subsequent studies demonstrated similar effectiveness when applying 45 Gy, data that are corroborated with our research, having no differences in this amount of radiation. (2.3)

INTEREST CONFLICT

None

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REFERENCES

1. Macdonald JS, Smalley SR, Benedetti J, Hundahl SA, Estes NC, Stemmermann GN, et al. Chemoradiotherapy after Surgery Compared with Surgery Alone for Adenocarcinoma of the Stomach or Gastroesophageal Junction. N Engl J Med [Internet]. 2001 Sep 6;345(10):725–30. Available from: http://www.nejm.org/doi/abs/10.1056/NEJMoa010187
2. SOLCA. EPIDEMIOLOGÍA DEL CÁNCER EN QUITO 2006-2010 [Internet]. 15th ed. Cueva P, editor. Quito; 2014. Available from: http://www.estadisticas.med.ec/Publicaciones/PUBLICACION-QU-2006-2010.pdf
3. MA J, SHEN H, KAPESA L, ZENG S. Lauren classification and individualized chemotherapy in gastric cancer. Oncol Lett [Internet]. 2016 May;11(5):2959–64. Available from: https://www.spandidos-publications.com/10.3892/ol.2016.4337
4. Chen Y-C, Fang W-L, Wang R-F, Liu C-A, Yang M-H, Lo S-S, et al. Clinicopathological Variation of Lauren Classification in Gastric Cancer. Pathol Oncol Res [Internet]. 2016 Jan 27;22(1):197–202. Available from: http://link.springer.com/10.1007/s12253-015-9996-6
5. Qiu M, Cai M, Zhang D, Wang Z, Wang D, Li Y, et al. Clinicopathological characteristics and prognostic analysis of Lauren classification in gastric adenocarcinoma in China. J Transl Med [Internet]. 2013;11(1):58. Available

from: http://translational-medicine.biomedcentral.com/ articles/ 10.1186/ 1479-5876-11-58
6. Turner ES, Turner JR. Expanding the Lauren Classification: A New Gastric Cancer Subtype? Gastroenterology [Internet]. 2013 Sep;145(3):505–8. Available from: https://linkinghub. elsevier.com/ retrieve/pii/ S0016508513010706
7. LAURÉN P. THE TWO HISTOLOGICAL MAIN TYPES OF GASTRIC CARCINOMA: DIFFUSE AND SO-CALLED INTESTINAL-TYPE CARCINOMA. Acta Pathol Microbiol Scand [Internet]. 1965 Sep;64(1):31–49. Available from: http://doi.wiley.com/10.1111/apm.1965.64.1.31
8. Lin X, Zhao Y, Song W, Zhang B. Molecular classification and prediction in gastric cancer. Comput Struct Biotechnol J [Internet]. 2015;13:448–58. Available from: https://linkinghub.elsevier.com/ retrieve/ pii/ S2001037015000367
9. Lee KE. Prognostic Significance of p53, nm23, PCNA and c-erbB-2 in Gastric Cancer. Jpn J Clin Oncol [Internet]. 2003 Apr 1;33(4):173–9. Available from: https://academic.oup.com/jjco/article-lookup/doi/10.1093/jjco/hyg039
10. Polkowski W, van Sandick JW, Offerhaus GJA, ten Kate FJW, Mulder J, Obertop H, et al. Prognostic Value of Laurén Classification and c-erbB-2 Oncogene Overexpression in Adenocarcinoma of the Esophagus and Gastroes ophageal Junction. Ann Surg Oncol [Internet]. 1999 Apr;6(3):290–7. Available from: http://link.springer.com/10.1007/s10434-999-0290-2
11. Liu S, Guan W, Wang H, Pan L, Zhou Z, Yu H, et al. Apparent diffusion coefficient value of gastric cancer by diffusion-weighted imaging: Correlations with the histological differentiation and Lauren classification. Eur J Radiol [Internet]. 2014 Dec;83(12):2122–8. Available from: https://linkinghub.elsevier.com/ retrieve/pii/S0720048X14004653
12. Flucke, Stefan P. Mönig, St U. Differences between Biopsy- or Specimen-related Laurén andWorld Health Organization Classification in Gastric Cancer. World J Surg [Internet]. 2002 Mar 15;26(2):137–40. Available from: http://link.springer.com/10.1007/s00268-001-0195-0
13. Macdonald JS, Smalley SR, Benedetti J, Hundahl SA, Estes NC, Stemmermann GN, et al. Chemoradiotherapy after Surgery Compared with Surgery Alone for Adenocarcinoma of the Stomach or Gastroesophageal Junction. N Engl J Med [Internet]. 2001 Sep 6;345(10):725–30. Available from: http:// www.nejm.org/doi/abs/10.1056/NEJMoa010187
14. Debets-Ossenkopp YJ, Reyes G, Mulder J, aan de Stegge BM, Peters JTAM, Savelkoul PHM, et al. Characteristics of clinical Helicobacter pylori strains from Ecuador. J Antimicrob Chemother [Internet]. 2003 Jan;51(1):141–5. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12493799
15. Viúdez-Berral A, Miranda-Murua C, Arias-de-la-Vega F, Hernández-García I, Artajona-Rosino A, Díaz-de-Liaño Á, et al. Current management of gastric cancer. Rev Española Enfermedades Dig [Internet]. 2012 Mar;104(3):134–41. Available from: http://scielo.isciii.es/scielo.php? script=sci_ar ttext&pid= S1130-01082012000300006&lng=en&nrm=iso&tlng=en
16. Sastre J, Garcia-Saenz, Diaz-Rubio. Chemotherapy for gastric cancer [Internet]. World Journal of Gastroenterology. 2006. p. 204–13. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4066028/
17. Lim L, Michael M, Mann GB, Leong T. Adjuvant Therapy in Gastric Cancer. J Clin Oncol [Internet]. 2005 Sep;23(25):6220–32. Available from: http://ascopubs.org/doi/10.1200/JCO.2005.11.593
18. Lee J, Lim DH, Kim S, Park SH, Park JO, Park YS, et al. Phase III Trial Comparing Capecitabine Plus Cisplatin Versus Capecitabine Plus Cisplatin With Concurrent Capecitabine Radiotherapy in Completely Resected Gastric Cancer With D2 Lymph Node Dissection: The ARTIST Trial. J Clin Oncol [Internet]. 2012 Jan 20;30(3):268–73. Available from: http://ascopubs.org/ doi/10.1200/JCO.2011.39.1953
19. Park SH, Sohn TS, Lee J, Lim DH, Hong ME, Kim K-M, et al. Phase III Trial to Compare Adjuvant Chemotherapy With Capecitabine and Cisplatin Versus Concurrent Chemoradiotherapy in Gastric Cancer: Final Report of the Adjuvant Chemoradiotherapy in Stomach Tumors Trial, Including Survival and Subset Analyses. J Clin Oncol [Internet]. 2015 Oct;33(28):3130–6. Available from: http://ascopubs.org/doi/10.1200/JCO.2014.58.3930
20. Park SH, Lee SJ, Kim ST, Lee J, Park JO, Park YS, et al. Multicenter phase III trial of adjuvant chemoradiotherapy in stomach tumors 2 (ARTIST 2). J Clin Oncol. 2015;
21. Fabio G. Supervivencia en adenocarcinoma gástrico posterior a tratamiento adyuvante tratados en el Instituto Nacional de Cancerología de Colombia durante el 2009. Rev Colomb Cancerol [Internet]. 2013;17(0123-9015):55–61. Available from: http://www.elsevier.es/es-revista-revista-colombiana-cancerologia-361-articulo-supervivencia-adenocarcinoma-gastrico-posterior-tratamiento-X0123901513239230
22. Chung HT, Shakespeare TP, Wynne CJ, Lu JJ, Mukherjee RK, Back MF. Evaluation of a radiotherapy protocol based on INT0116 for completely resected gastric adenocarcinoma. Int J Radiat Oncol [Internet]. 2004 Aug;59(5):1446–53. Available from: http://linkinghub.elsevier.com/ retrieve/pii/S0360301604001002
23. McMillan MT, Ojerholm E, Roses RE, Plastaras JP, Metz JM, Mamtani R, et al. Adjuvant Radiation Therapy Treatment Time Impacts Overall Survival in Gastric Cancer. Int J Radiat Oncol [Internet]. Elsevier Ltd; 2015 Oct;93(2):326–36. Available from: http://dx.doi.org/ 10.1016/ j.ijrobp. 2015.05.025