ECRONICON OPEN ACCESS

EC GASTROENTEROLOGY AND DIGESTIVE SYSTEM

Research Article

Non-Surgical Treatment Outcomes for Anal Cancer: Analysis of 120 Cases Over 08 Years in a Brazilian Cancer Center

Phillipe Abreu-Reis[1]*, Flavio Tomasich[2], Vinícius Basso Preti[2], Luiz Antonio N Dias[2], Henrique Takayoshi Ida Nakatani[2], Hygor Trombetta[2], Gabriela Romaniello[2], Gabriella Jacomel[2], Regina Goolkate[2], Ana Luisa Bettega[2], Raphaella de Paula Ferreira[2], Carlos Arai Filho[3] and Thatiane Litenski[3]

[1]Resident Fellow, Department of Surgery, Hospital Erasto Gaertner, Curitiba, Brazil

[2]Department of Surgery, Hospital Erasto Gaertner, Curitiba, Brazil

[3]Department of Surgery, Hospital Erasto Gaertner, Curitiba, Brazil

***Corresponding Author:** Phillipe Abreu-Reis, Resident Fellow, Department of Surgery, Hospital Erasto Gaertner, Curitiba, Brazil.

Received: November 27, 2017; **Published:** July 19, 2018

DOI: 10.31080/ecgds.2018.05.00239

Abstract

Background: Anal canal cancer is an uncommon cancer of the digestive system, which the most common histological type is squamous cell carcinoma. The gold-standard treatment is combination therapy (chemotherapy and radiotherapy) and surgery should be reserved for cases of recurrent disease, persistent disease after initial treatment or complications. The aim of this study was to present data regarding anal cancer collected from the Cancer Database of Hospital Erasto Gaertner, a referred cancer center, from the period of 2005 to 2013 and to analyze the treatment outcomes of the patients assisted at the Institution.

Methods: It was a retrospective and observational study. Data were collected from medical records available in the hospital Cancer Database Registry Service after the approval from the institution review board.

Results: There was a prevalence among women (71.1%). The average age of the patients was 55 years. The most common histological type was squamous cell carcinoma (81.4%), followed by adenocarcinoma (7%). Regarding patients' origin, approximately 58% came from Curitiba and the metropolitan region. Considering the treatment performed, 95% of the cases did not undergo any form of surgical treatment, only 4.7% underwent surgery, 2.3% only chemotherapy and 4.7% only radiotherapy, and the minority underwent local resection. Combined treatment was applied to 88% of the patients. Regarding the TNM (UICC) clinical staging, the most common was stage III (23.5%), followed by stages II, IV and I (18.6%, 2.3% and 2.3%, respectively). Family history of cancer was found in 34.9% of the patients, alcoholism in 11.7% and smoking in 44.2%. Were alive at the end of the first phase of treatment 92.2% of the patients.

Conclusion: Epidemiological characteristics of patients were in accordance with literature data. Most patients underwent chemoradiotherapy, and more than half of them were alive at the end of treatment.

Keywords: *Cancer; Anal Canal; Treatment; Early Survival*

Introduction

Anal cancer is an uncommon neoplasm, responsible for only 2.5% of neoplasms of the digestive tract [1]. In 2014, the incidence of colon and rectum neoplasms was 15070 new cases for men and 17530 for women, but there were no data on anal canal cancer [2].

Studies have shown an increase in incidence, associated with factors such as female sex, HPV and HIV infection, anal intercourse and smoking [3].

The association with HPV infection, as evidenced in epidemiological studies and clinical trials, was essential in clarifying the pathophysiology and etiology of the most common histological type, squamous cell carcinoma (SCC) [4]. Thus, anal canal cancer is closer to other genital malignancies than other neoplasms of the gastrointestinal tract, requiring a differentiated approach.

The standard treatment of anal cancer for a long time consisted of abdominoperineal resection and dissection of inguinal lymph nodes. Abdominoperineal amputation, which includes resection of the sigmoid colon, rectum and anus, defines the need of a permanent colostomy, which brings complications such as prolapse, stenosis, paraestomal hernias and dermatitis [5-7], as well as producing a significant loss of quality of life [8,9]. The five-year survival expectancy ranges from 40 to 70 percent, with a perioperative mortality rate of 3 percent [10]. With the advent of combined treatment consisting of chemotherapy associated with radiotherapy, the possibility of healing patients and preserving the anal sphincter arose, which significantly reduced the need for definitive colostomy in many patients [11]. The use of combined therapy also increased the expectation of survival in five years from 72 to 89 percent [12-14].

Therefore, the use of combined therapy has become the standard treatment for patients with squamous cell carcinoma of the anal canal, reserving surgical treatment for cases of recurrent or persistent disease after initial treatment, in cases of failure of the treatment and to those who present complications [10].

The main prognostic factors are defined by tumor staging, size and lymph node invasion [15]. However, there is a need to identify other risk factors as well as the prognosis for the treatment outcome. In this sense, the national literature is lacking.

Objective of the Study

The objective of this study is to present data regarding anal cancer collected from the Cancer Database of Hospital Erasto Gaertner, a referred Cancer Center in Brazil, from the period of 2005 to 2013 and analyze the treatment outcomes of the patients assisted at the Institution, information that current lacks in the available literature.

Methods

It was a retrospective and observational study regarding the analysis of data from patients admitted and treated with anal canal cancer at the Erasto Gaertner Hospital from 2005 to 2013. Information was collected, after the approval from the institution review board, between March and May 2015 by independent researchers directly from the medical and physical records available at the Archive Service Physician of the Hospital Registry of Cancer, using field record based on the standard format of the National Cancer Institute [16].

During this period, 120 cases of anal canal cancer were admitted. The following variables were evaluated: prevalence by gender, age, histological type, patient origin, treatment performed, tumor staging, history of alcoholism and smoking, hereditary tendencies and survival after the first phase of treatment.

The absolute and relative frequencies were generated from the SISRHC system and tabulated through the EpiInfo System, version 7.1. The survival rate was calculated using the Kaplan Meier method.

Results

In a period of 08 years, between 2005 and 2013, 120 cases of anal canal cancers confirmed by the anatomo-pathology tests were diagnosed.

There was a predominance in the female gender with 86 (71.7%) cases versus 34 (29.3%) in the male gender. The mean age of male patients with anal cancer was 52 years (32 - 82), with a standard deviation of ± 16. Among females, the mean age was 57 years (33 - 82) and standard deviation of ± 14. The main origin of the patients was 70 (58%) from Curitiba and metropolitan region, the capital and largest city of the state.

Regarding risk factors, alcohol abuse was reported by five (11.7%) patients and refused by 24 (55.8%). History of smoking was found in 19 (44.2%) patients and 11 (25.6%) denied exposure to tobacco. There was not information on the history of smoking and alcoholism in the medical records of 30.2% and 32.6% patients, respectively.

In the studied sample, the most common histological type was squamous cell carcinoma in 98 (81.6%) cases, adenocarcinoma in 11 (9.2%) cases and other types of cancer in 11 (9.2%) cases, including 01 non-hodgkin's lymphoma, 01 adeno-squamous carcinoma, 01 carcinoma NOS without further specification and 01 squamous cell carcinoma large non-keratotic cells.

According to the TNM classification of the International Union for Cancer Control (UICC), the most prevalent clinical staging of the patients was stage III in 61 (23.3%) patients, followed by the stage II in 47 (18.6%), and stages IV and I in 6 (2.3%) each.

Regarding the treatment performed, underwent combined chemo-radiotherapy 106 (88.3%) patients, did not undergo any form of surgical treatment 114 (95%) patients; underwent exclusively to radiotherapy 6 (4.7%) patients, received exclusively chemotherapy 2 (2.3%) patients and underwent local resections 6 (4.7%) patients.

Of these patients, 82 (65.1%) were alive without evidence of disease after the first phase of the treatment, 22 (19%) patients presented partial response, 8 (7%) had disease progression and 8 (7%) patients died.

Sex	Female	72%
	Male	28%
Histologic Type	Squamocellular Carcinoma	82%
	Adenocarcinoma	9%
	Other	9%
TNM Clinical Stage	CSI	2%
	CS II	17%
	CS III	22%
	CS IV	2%
Treatment Option	Chemoradiation	88%
	Surgery only	5%
	Radiation only	5%
	Chemotherapy only	2%
Treatment response 1 year after diagnose	Complete response	29%
	Partial response	8%
	Disease progression	3%
	Death	3%

Table 1: *Cases distribution (%) according to analyzed variables.*

Discussion

Anal canal cancer represents a small fraction of gastrointestinal tract tumor, but its different pathophysiology allows treatment options that avoids the surgical approach and makes it a prominent neoplasm within the digestive apparatus [17]. Epidemiological information on this type of tumor is scarce in Brazil's literature and demonstrates the importance of this study.

The large number of cases allows the analysis of cases with diverse treatment options, from combined treatment with chemoradiotherapy to surgical rescue therapy.

The studied sample shows predominance of females, in a ratio of 2.53F:1M, which represents a lower ratio than that found by other reports of the Brazilian literature in previous years [18,19]. Studies in several countries around the world have shown an increase of the incidence of squamous cell carcinoma of the anal canal in the population as a whole, but mainly in men, especially men who have sex with men (MSM), HIV + patients and patients younger than 30 years [20,21]. It is likely that the F:M ratio found in this study is related to these described profile changes of the population nowadays. However, patients over 45 years old still prevail; the mean age found in this study is consistent with descriptions from the literature, including series describing this recent change in the patients' profile [22,23].

Smoking (current or previous) was present in 44.2% of patients and it is a risk factor already established in the pathogenesis of this disease, contributing to genetic alterations with HPV [17]. Although the literature does not establish a clear association between alcohol consumption and increased incidence of anal canal cancer, 11.7% of patients reported alcohol abuse in this study.

Epidermoid carcinoma is the most prevalent histological type and its pathophysiology related to HPV infection is well defined [17]. Large international studies show an increase in all histological subtypes. However, the increase in cases of squamous cell carcinoma was clearly greater than the increase in cases of adenocarcinoma [23,24]. Some authors argue that anal canal adenocarcinoma is treated as a separate disease, very different from epidermoid carcinoma [23]. The rate of epidermoid carcinoma reported in this study (81.5%) shows a higher prevalence of this histological type in the location.

The patients' presentation regarding TNM Clinical Staging at the time of diagnosis showed a difference in comparison to the values of the literature. We observed a prevalence of stage III in 50% of the cases. However, other national and international studies show a prevalence of stage II [18,25,26].

Since the early 1980s, with the publication of Norman Nigro showing complete remission of the disease by using combined therapy (chemoradiotherapy), anal canal carcinoma therapy has changed dramatically. The Nigro scheme proposes a dose of 30 Gy divided into 3 weeks, associated with 1000 mg/m^2/day of 5-fluoracil given on continuous infusion on days D1-D4 and D29-D32 and at a dose of mitomycin-C 15 mg/m^2 given in D1. This strategy caused complete remission of the disease, although this regimen was idealized as neoadjuvant [27]. The use of mitomycin-C or other cytotoxic drugs together with 5-fluoracil is still discussed; however, the superiority of combined treatment compared to surgical treatment is already well established in the literature, especially in terms of overall survival and colostomy-free survival [28].

Combined therapy was performed in 88.4% of patients in this study. Avoiding the surgical approach for these patients, as well as for patients who underwent chemotherapy or radiotherapy exclusively, ultimately resulted in 95% of patients without a surgical approach. Surgical approach, with abdominoperineal amputation of the rectum (Miles surgery), presents a great disadvantage in this type of tumor due to the loss of the sphincter function and the need for definitive colostomy [27].

It is observed that at the end of the first treatment phase (defined by the period from 8 to 12 months after starting treatment), 65% of the patients presented no evidence of disease. This means that, with the proposed treatment, more than half of the patients certainly preserved anal function, requiring no surgical approach, and did not require a definitive colostomy for the effective treatment of cancer. Data from the literature corroborate this rate as an acceptable rate of colostomy-free survival [26,28,29]. Are undeniable the beneficial effects of preserving anal function without requiring a colostomy for patients, not only physiologically but also psychologically by improving the social well-being of these patients [30].

The study limitations are the use of records that were not designed for the study, so the available data may be of poor quality. Also there were frequently an absence of data on potential confounding factors since the data were recorded in the past. Differential losses to follow up coulod also bias this retrospective studies.

Conclusion

Combined treatment in anal canal carcinoma can provide high success survival rates without requiring a definitive colostomy surgery.

An adequate initial evaluation of the case and performing a successful treatment based on well-established cancer protocols can improve survival rates and increase higher quality of life outcomes.

Patients presented with anal canal carcinoma evolved with a high early survival rate (at the end of the first phase of the proposed treatment).

Patient follow-up for longer time will allow concrete conclusions of the benefits of combined treatment.

Bibliography

1. Siegel R., *et al*. "Cancer statistics, 2015". *CA: A Cancer Journal for Clinicians* 65.1 (2015): 212-254.
2. Instituto Nacional de Cancer José Alencar Gomes da Silva. Estimativa 2014. Ministério da Saúde (2014): 124.
3. Palefsky JM. "Anal human papillomavirus infection and anal cancer in HIV-positive individuals: an emerging problem". *AIDS* 8.3 (1994): 283-295.
4. Ryan DP and Christopher GW. "Classification and Epidemiology of Anal Cancer". *UptoDate* (2013): 1-17.
5. Londono-Schimmer EE., *et al*. "Life table analysis of stomal complications following colostomy". *Diseases of the Colon and Rectum* 37.9 (1994): 916-920.
6. Robertson I., *et al*. "Prospective analysis of stoma-related complications". *Colorectal Disease* 7.3 (2005): 279-285.
7. Shabbir J and Britton DC. "Stoma complications: a literature overview". *Colorectal Disease* 12.10 (2010): 958-964.
8. Nugent KP., *et al*. "Quality of life in stoma patients". *Diseases of the Colon and Rectum* 42.12 (1999): 1569-1574.
9. Schaube J., *et al*. "The quality of life after extirpation of the rectum for carcinoma". *Deutsche Medizinische Wochenschrift* 121.6 (1996): 153-158.
10. Ghosn M. "Anal cancer treatment: Current status and future perspectives". *World Journal of Gastroenterology* 21.8 (2015): 2294-2302.
11. De Bari B., *et al*. "External beam radiotherapy ± chemotherapy in the treatment of anal canal cancer: a single-institute long-term experience on 100 patients". *Cancer Investigation* 32.6 (2014): 248-255.
12. Doci R., *et al*. "Primary chemoradiation therapy with fluorouracil and cisplatin for cancer of the anus: results in 35 consecutive patients". *Journal of Clinical Oncology* 14.12 (1996): 3121-3125.
13. Northover JMA., *et al*. "ACT-1 Epidermoid anal cancer: Results from the UKCCCR randomised trial of radiotherapy alone versus radiotherapy, 5-fluorouracil, and mitomycin". *Lancet* 348.9034 (1996): 1049-1054.

14. Peiffert D., *et al*. "Preliminary results of a phase II study of high-dose radiation therapy and neoadjuvant plus concomitant 5-fluorouracil with CDDP chemotherapy for patients with anal canal cancer: a French cooperative study". *Annals of Oncology* 8.6 (1997): 575-581.

15. Ajani JA., *et al*. "Prognostic factors derived from a prospective database dictate clinical biology of anal cancer: the intergroup trial (RTOG 98-11)". *Cancer* 116.17 (2010): 4007-4013.

16. Brasil - Ministerio da Saúde - Instituto Nacional de Cancer. Registros Hospitalares de Câncer - Planejamento e Gestão (2010): 536.

17. Salati SA and Al Kadi A. "Anal cancer - a review". *International Journal of Health Sciences* 6.2 (2012): 206-230.

18. Matheus C., *et al*. "Carcinoma Epidermóide de Canal Anal: Resultados do Tratamento de 46 Pacientes". *Revista Brasileira de Coloproctologia* 17.3 (1997): 180-185.

19. Torres Neto JDR., *et al*. "Estudo demográfico do câncer de canal anal e ânus no estado de Sergipe". *Revista Brasileira de Coloproctologia* 27.2 (2007): 190-195.

20. Robinson D., *et al*. "An analysis of temporal and generational trends in the incidence of anal and other HPV-related cancers in South-east England". *British Journal of Cancer* 100.3 (2009): 527-531.

21. Shiels MS., *et al*. "Impact of the HIV epidemic on the incidence rates of anal cancer in the United States". *Journal of the National Cancer Institute* 104.20 (2012): 1591-1598.

22. Brewster DH and Bhatti LA. "Increasing incidence of squamous cell carcinoma of the anus in Scotland, 1975-2002". *British Journal of Cancer* 95.1 (2006): 87-90.

23. Jin F., *et al*. "Trends in anal cancer in Australia, 1982-2005". *Vaccine* 29.12 (2011): 2322-2327.

24. Nielsen A., *et al*. "Trends in incidence of anal cancer and high-grade anal intraepithelial neoplasia in Denmark, 1978-2008". *International Journal of Cancer* 130.5 (2012): 1168-1173.

25. Nakamura RA., *et al*. "Tratamento conservador do carcinoma do canal anal". *Revista do Colégio Brasileiro de Cirurgiões* 32.1 (2005): 23-31.

26. Tomaszewski JM., *et al*. "Twenty-Five-Year Experience With Radical Chemoradiation for Anal Cancer". *International Journal of Radiation Oncology* 83.2 (2012): 552-558.

27. Blumetti J and Bastawrous AL. "Epidermoid Cancers of the Anal Canal: Current Treatment". *Clinics in Colon and Rectal Surgery* 22.2 (2009): 77-83.

28. Shridhar R., *et al*. "Anal cancer: current standards in care and recent changes in practice". *CA: A Cancer Journal for Clinicians* 65.2 (2015): 139-162.

29. McElvanna K., *et al*. "Anal Cancer Management and Outcomes in Northern Ireland 2002-2006". *Gut* 62.2 (2013): A27.

30. Chiao EY., *et al*. "A population-based analysis of temporal trends in the incidence of squamous anal canal cancer in relation to the HIV epidemic". *Journal of Acquired Immune Deficiency Syndromes* 40.4 (2005): 451-455.

Volume 5 Issue 8 August 2018
©All rights reserved by Phillipe Abreu-Reis*., et al.*