Anal Cancer Treatment Outcomes: A Single-Center Experience

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SUMMARY

Anal cancer is a relatively uncommon malignancy, accounting for approximately 2.5% of all gastrointestinal cancers.

This retrospective study included patients diagnosed and treated with anal cancer between February 1, 2015 and February 1, 2025 at Sestre milosrdnice University Hospital Center in Zagreb, Croatia. A total of 42 patients met the inclusion criteria.

All 42 patients had histologically confirmed squamous cell carcinoma. At the time of diagnosis, 35 patients (83.33%) had localized or locoregionally advanced disease (stage I–III), 6 patients (14.29%) had metastatic (stage IV) disease, and 1 patient had an unknown disease stage. Most patients (31; 83.78%) received radical-dose (chemo)radiotherapy at some point during their disease. In patients with primary chemoradiotherapy as initial treatment, the complete response rate was 56.52% (13 patients). At the cut-off date (February 1, 2025), 31 patients (73.81%) were alive. Median follow-up was 24.82 months. For the whole study cohort, neither 2-year nor 5-year overall survival was reached.

The findings of our single-center study demonstrate that definitive chemoradiotherapy is an effective treatment for anal cancer, with high rates of local control and overall survival.

KEYWORDS

Anal cancer; *Anal carcinoma*; *Single-center experience*; *Squamous cell carcinoma*; *Human papillomavirus*; *Concomitant chemoradiotherapy*

Introduction

Anal cancer is a relatively uncommon malignancy, accounting for approximately 2.5% of all gastrointestinal cancers[1]. Despite its rarity, the incidence of anal cancer has been steadily increasing worldwide, partly due to changing epidemiological factors, such as an aging population, the prevalence of human papillomavirus infection (HPV) and immunosuppression, particularly in individuals with human immunodeficiency virus (HIV) infections[2]. The disease predominantly arises from the anal canal and is histologically categorized as squamous cell carcinoma in the majority of cases. The current standard of care for most cases of anal cancer is definitive chemoradiotherapy, which has dramatically improved outcomes over the past few decades. This approach, initially established by the pivotal Nigro protocol, combines 5-fluorouracil and mitomycin C with concurrent radiotherapy, providing high rates of local control and sphincter preservation[3]. However, despite these advances, challenges are still present, including treatment-related toxicity, the risk of recurrence, and disparities in outcomes based on patient demographics and comorbidities.

Given the limited number of cases treated at individual institutions, single-center experiences provide valuable insights into real-world treatment outcomes, including response rates, patterns of recurrence and the management of toxicities. This study aims to present the treatment outcomes of anal cancer patients managed at our center, focusing on clinical characteristics, therapeutic approaches and survival outcomes. By analyzing these data, we hope to contribute to the growing body of evidence guiding the management of this challenging malignancy and identify areas for potential improvement in care delivery.

Methods

Study design and setting

This retrospective cohort study was conducted at Sestre milosrdnice University Hospital Center; a large tertiary care center in Zagreb, Croatia. The study was conducted in accordance with ethical standards set by the institution's Ethics Committee and the Helsinki Declaration from 1975, as revised in 1983. The need for informed consent was waived due to the retrospective nature of the research.

Patient population

Patients diagnosed with anal cancer and treated over a 10-year period between February 1, 2015 and February 1, 2025 were included in the study. Eligibility criteria included histologically confirmed anal carcinoma and the availability of relevant medical records and follow-up data. The exclusion criterion was prior treatment for anal cancer at another institution.

Data collection

Data were extracted from electronic medical records as well as from the hospital pathology database and included: demographic information (age, sex, comorbidities), tumor characteristics (size, stage based on the TNM classification, HPV and HIV status where available), treatment details (chemotherapy regimen, radiotherapy dose and modifications), outcomes (treatment response — clinical and radiographic, recurrence and survival data).

Statistical analysis

Descriptive statistics were used to summarize patient characteristics, treatment details and outcomes. An unpaired t-test was used to compare demographic, disease and treatment parameters between different subgroups of patients.

Survival analysis was performed using the Kaplan–Meier method to estimate overall survival (OS). Statistical significance was set at $P < 0.05$.

Results

Patient characteristics

A total of 42 patients met the inclusion criteria and were included in the study. The vast majority of the patients were female (33 patients, 78.57%). The average age of the study patients was 62.9 years (median age 62.5 years; range 40–93 years; standard deviation (SD) 12.03). On average, female patients were older than male patients (64.48 years with SD 12.18 and 57.11 years with SD 9.99, respectively), however the difference was not statistically significant ($P = 0.1037$; 95% CI -1.58–16.32). HPV status was available for 6 patients, and all were HPV positive. HIV status was available for 1 patient (negative).

Disease stage and treatment

All 42 patients had histologically confirmed squamous cell carcinoma; there were no other types. Regarding TNM status, 3 patients (7.14%) had an unknown T stage, 2 patients (4.76%) had stage T1, 13 patients (30.95%) stage T2, 9 patients (21.43%) stage T3, and 15 patients (35.71%) stage T4. When looking at the primary anal tumor size, the average diameter was 44.2 mm (median 39.5 mm; range 16–90 mm; SD 20.04). Three patients (7.14%) had an

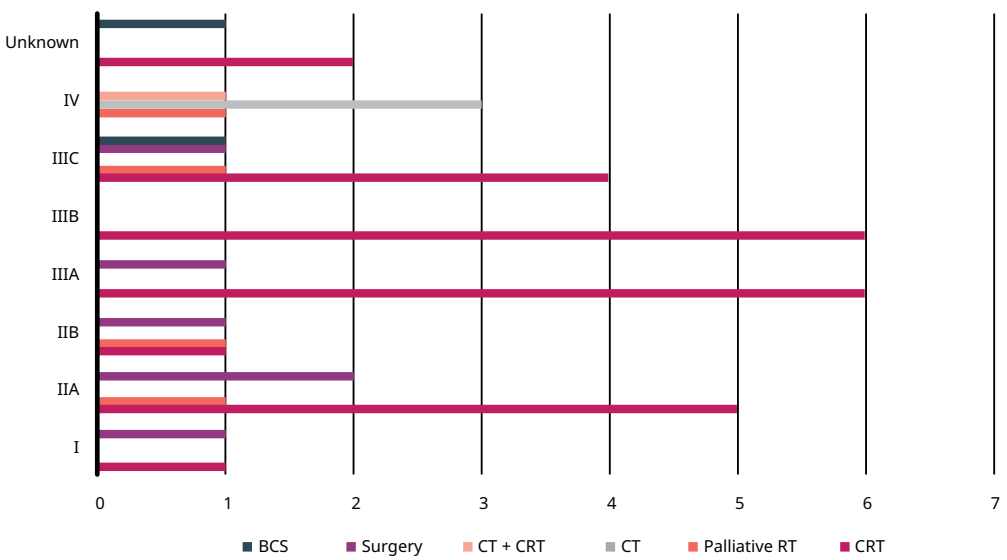

Fig. 1. First-line therapy in study patients subdivided by stage.

CRT = concomitant chemoradiotherapy; CT = chemotherapy; RT = radiotherapy; BSC = best supportive care.

unknown N stage, 21 patients (50.00%) had stage N0, and 18 patients (42.86%) had stage N1. Anal cancer can be subdivided into anal canal and anal margin (perianal skin) cancer. In this study population, 16 patients (38.10%) had anal canal cancer and 14 patients (33.33%) anal margin cancer (arising from the ± 5 cm of perianal skin caudal from the anal margin); in 12 (28.57%) patients the exact location of the primary tumor was unknown. Most of the patients (35 patients; 83.33%) had a localized or locoregionally advanced disease (stage I–III) and for 2 of them it was not possible to determine the definitive disease stage (I–III), but they did not have metastatic disease. Only 6 patients (14.29%) had metastatic (stage IV) disease at the time of diagnosis, and for 1 patient it was not possible to determine the definitive disease stage. Figure 1 summarizes initial therapies that different patient subgroups received, relative to stage.

Most patients (59.52%) received concomitant chemoradiotherapy (CRT) as initial treatment. The second and third most common initial treatments were surgery (14.29%) and palliative radiotherapy (11.90%). Two patients (4.76%) received only best supportive care due to their poor performance status. A total of 29 patients (69.05%) received chemotherapy (CT) as primary treatment (alone or in combination with other modalities). CT protocols that were used as initial treatment are shown in Table 1. Concomitant CRT was performed according to institutional guidelines; CT included 5-fluorouracil or capecitabine with mytomycin. Mitomycin C (10 mg/m²) was delivered on days 1 and 29 of radiotherapy (RT), together with 5-fluorouracil (1,000 mg/m²/day on days 1–4 and 29–32) or capecitabine (825 mg/m² 2 × daily on days of radiation treatment only). RT was delivered using the 3D conformal approach to a total dose of 50.4–54 Gy in 28 to 30 fractions, depending on disease stage. In 2 patients, the therapy was interrupted due to toxicity; one patient with disease stage IIIA received a total RT dose of 16 Gy, and another patient with stage IIIA started CRT, but due to toxicity (deterioration of performance status, dermatitis) further CT was omitted and only RT was continued up to the full planned dose. Out of the 6 patients with an initially metastatic disease, 3 patients were treated with CT, 2 had only palliative RT due to a poor performance status, and one patient with initially stage IV disease received CT which downstaged the disease to stage III, and subsequently received CRT.

Out of the 37 patients who received RT during the course of their disease, 31 of them (83.78%) received radical-dose (chemo)radiotherapy, 5 (13.51%) received palliative RT, and 1 patient (2.70%) with metastatic disease received a stereotactic body RT. The mean dose in patients who received CRT was

Table 1. Chemotherapy protocols in different subpopulations of study patients, given as initial oncology therapy in the study population.

Chemotherapy regimen	Localized disease – Initial CRT	Localized disease – Initial surgery	Initial Stage IV disease	Total
Mitomycin + capecitabin	15	2	1	18
Mitomycin + 5-FU	6	0	0	6
Capecitabine	1	0	0	1
Paclitaxel + carboplatin	0	0	2	2
Unknown	2	0	0	2

CRT = concomitant chemoradiotherapy; CT = chemotherapy

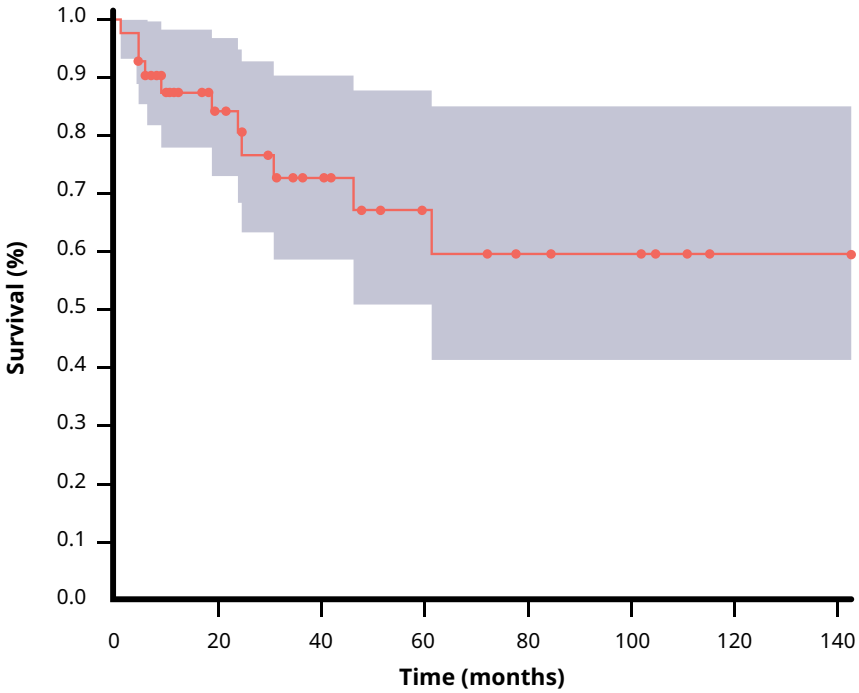

Fig. 2. Overall survival, all stages. The blue area represents the 95% confidence interval.

53.63 Gy (median 54 Gy; range 16–59,4 Gy; SD 7.53). Most of these 31 patients received 3D conformal RT, only 2 received intensity-modulated RT with simultaneous-integrated boost. Also, the mean time to start of CRT after diagnosis was 4.35 months (median 3 months; range 0.43–29 months; SD 5.77). The mean dose in patients who received palliative RT was 22 Gy (median 20 Gy; range 20–25 Gy; SD 2.74).

Treatment outcomes

Twenty-three patients completed planned CRT as the primary treatment. In this subset of patients, the complete response (CR) rate following CRT was 56.52% (N = 13 patients). A partial response (PR) was observed in 13.04% (N = 3), 8.70% (N = 2) had stable disease, while 4.35% (N = 1) experienced progressive disease and developed metastatic disease. In 4 patients, relevant medical documentation was not available to assess treatment outcomes after CRT. In patients who could be evaluated (N = 19), the 6-month local control rate was 94.74%, while the 2-year local control rate was 78.95%. Data on treatment-related toxicities were scarce and it was not possible to objectively assess potential side effects in the study population. No treatment-related mortality was reported.

Ultimately, 9 patients (39.13%) had disease recurrence after primary CRT. Among them, 4 had complete response to primary CRT. Mean time to recurrence in this subgroup of patients was 20 months (median 18 months; range 8–36 months; SD 12.65). One of these 4 patients also developed distant metastasis later on. Eight patients had surgery due to disease recurrence or residual disease after primary CRT: 6 of them underwent abdominoperineal resection, 2 local tumor excision, and 1 dissection of the inguinal lymph nodes. Seven patients with initial local or locoregional disease

developed metastatic disease at some point during the course of the disease. All of these patients received first-line chemotherapy for metastatic disease with paclitaxel + carboplatin.

The cut-off date for the study analysis was February 1, 2025. At the cut-off date, 31 patients (73.81%) were alive and 11 died. The median follow-up was 24.82 months (range 1.23–120 months). For the whole study patient group, neither 2-year nor 5- year overall survival was reached, as shown in Figure 2. A separate survival analysis per disease stage was not done due to the small number of patients, along with high survival rates.

Discussion

To the best of our knowledge, this is the largest investigation on patients with anal cancer performed in Croatia so far. The findings of our single-center study demonstrate that definitive chemoradiotherapy is an effective treatment for anal cancer, with high rates of local control and overall survival consistent with those reported in larger, multi-institutional trials. The complete response rate of 56.52% aligns with previously published data[4,5,6], highlighting the efficacy of the Nigro protocol in achieving tumor eradication. Despite these positive outcomes, the recurrence rate of 39.13% underscores the need for vigilant post-treatment surveillance and potential strategies to address high-risk features, such as advanced stage or persistent HPV infection.

The role of HPV in anal cancer prognosis remains an area of active investigation. In our cohort, HPV status was unfortunately available only in a small proportion of patients, since medical records underwent severe changes (introduction of a new medical records system) and some data were lost or were not adequately recorded. Further research is needed to explore the prognostic implications of HPV status and its potential role in guiding individualized treatment strategies.

This study had several limitations, most notably its retrospective design and the relatively small sample size, which limited the generalizability of our findings. However, the single-center setting allows for a detailed and uniform analysis of treatment protocols and outcomes, providing valuable insights into real-world clinical practice.

Conclusion

Our study reinforced the efficacy of chemoradiotherapy as the standard of care for local and locoregionally advanced anal cancer, while highlighting ongoing challenges related to recurrence. Future efforts should focus on optimizing treatment regimens, incorporating HPV-directed therapies and addressing disparities in access to care to improve outcomes for all patients.

DISCLOSURE OF CONFLICT OF INTEREST The authors report no conflicts of interest.

References

1. Gondal TA, Chaudhary N, Bajwa H, Rauf A, Le D, Ahmed S. Anal Cancer: The Past, Present and Future. Curr Oncol. 2023 Mar 11;30(3):3232-3250. doi: 10.3390/curroncol30030246.
2. Mokos M, Coric M, Silovski H, Basic-Jukic N. Anal cancer in a renal transplant recipient: A case report and literature review. Acta Clin Croat. 2023 Nov;62(3):556-560. doi: 10.20471/acc.2023.62.03.19. PMID: 39310683; PMCID: PMC11414003.
3. Nigro ND, Vaitkevicius VK, Considine B Jr. Combined therapy for cancer of the anal canal: a preliminary report. Dis Colon Rectum. 1974 May-Jun;17(3):354-6. doi: 10.1007/BF02586980.
4. Slørdahl KS, Klotz D, Olsen JÅ, Skovlund E, Undseth C, Abildgaard HL, Brændengen M, Nesbakken A, Larsen SG, Hanekamp BA, Holmboe L, Tvedt R, Sveen A, Lothe RA, Malinen E, Kaasa S, Guren MG. Treatment outcomes and prognostic factors after chemoradiotherapy for anal cancer. Acta Oncol. 2021 Jul;60(7):921-930. doi: 10.1080/0284186X.2021.1918763.
5. Tachibana I, Nishimura Y, Inada M, Fukuda K, Ishikawa K, Nishikawa T, Yokokawa M, Nakamatsu K, Kanamori S, Hida JI. Definitive chemoradiotherapy for anal canal cancer: single-center experience. Int J Clin Oncol. 2018 Dec;23(6):1121-1126. doi: 10.1007/s10147-018-1316-1. Epub 2018 Jul 10. PMID: 29992389.
6. Khosla D, Kapoor R, Dey T, Kataria V, Singh R, Kumar D, Oinam AS, Gupta R, Rana SS, Shah J, Singh H, Irrinki S, Madan R. Simultaneous Integrated Boost (SIB) Versus Sequential Boost in Anal Cancer Patients: A Single-Center Experience. J Gastrointest Cancer. 2024 Jun;55(2):759-767. doi: 10.1007/s12029-024-01019-5. Epub 2024 Jan 18. PMID: 38236375.

SAŽETAK

Ishodi liječenja raka anusa: iskustvo jednog centra

Jasmina Marić Brozić, Davor Kust, Alma Demirović, Željko Soldić, Jasna Radić, Marin Šunjić, Andrea Burić i Ana Fröbe

Rak anusa relativno je rijedak zloćudni tumor, koji čini oko 2,5 % svih karcinoma probavnog sustava. Ovo retrospektivno istraživanje provedeno u KBC-u Sestre milosrdnice u Zagrebu uključilo je pacijente kojima je dijagnosticiran i liječen rak anusa između 1. veljače 2015. i 1. veljače 2025. Ukupno 42 pacijenta zadovoljila su kriterije te su uključena u ispitivanje.

Svi uključeni bolesnici imali su histološki potvrđen planocelularni karcinom. U vrijeme dijagnoze 35 bolesnika (83,33 %) imalo je lokaliziranu ili lokoregionalno uznapredovalu bolest (stadij I-III), 6 bolesnika (14,29 %) imalo je metastatsku bolest (stadij IV), a 1 je bolesnik imao nepoznat stadij bolesti. Većina bolesnika (njih 31, odnosno 83,78 %) u nekom je trenutku tijekom bolesti primila (kemo)radioterapiju u radikalnoj dozi. U bolesnika s primarnom kemoradioterapijom kao inicijalnim liječenjem stopa potpunog odgovora bila je 56,52 % (13 bolesnika). Na granični datum (1. veljače 2025.) živ je bio 31 bolesnik (73,81 %). Medijan praćenja bio je 24,82 mjeseca. Za cijelu ispitivanu skupinu pacijenata nije dosegnuto ni dvogodišnje ni petogodišnje ukupno preživljenje.

Naši rezultati pokazuju da je definitivna kemoradioterapija učinkovit tretman za karcinom anusa, s visokim stopama lokalne kontrole i ukupnog preživljenja.

KLJUČNE RIJEČI

Rak anusa; *Analni karcinom*; *Iskustvo jednog centra*; *Planocelularni karcinom*; *Humani papiloma virus*; *Konkomitantna kemoradioterapija*