Outcomes of locally advanced vulvar cancer patients treated with definitive concurrent chemoradiation at Groote Schuur Hospital from January 2008 – January 2020.

Master's Dissertation

by

Dr Adnaan Sayed

for the degree of

Master of Medicine (Radiation Oncology)

at the

University of Cape Town

Supervisor: Dr Nazia Fakie

Co supervisor: Dr Linda Rogers

Plagiarism Declaration

I, the undersigned, declare that:

1. **Turnitin Submission:** This thesis/dissertation has been submitted to the Turnitin module (or an equivalent similarity and originality checking software) as required for the completion of my degree.

2. **Original Work:** The work presented in this thesis/dissertation is my own, and any references to the work of others have been appropriately cited and acknowledged.

3. **Supervisor Review:** My Turnitin report has been reviewed by my supervisor, and any concerns identified regarding similarity or potential plagiarism have been resolved through consultation.

Name: Adnaan Sayed

Student number: SYDADN001

Signature: Signed by candidate

Date: 22 November 2024

Introduction

Vulvar cancer is a rare form of gynaecological cancer, accounting for only 2-5% of all gynaecological malignancies.[1, 2] With an annual incidence rate of 3 per 100,000 women, there were 45 240 new cases and 17 427 deaths globally in 2020.[2] Although the global incidence is highest in North America and Europe, the African continent leads the world in mortality from vulvar cancer.[3] Factors such as a high human immunodeficiency virus (HIV) and human papillomavirus (HPV) prevalence combined with limited screening and treatment capabilities, facilitate a growing vulvar cancer burden among young women of Sub-Saharan Africa (SSA).[4]

Recent reports from countries like Togo suggest a growing incidence of vulvar cancer among younger women, and this rise is strongly associated with the increasing prevalence of HPV infection.[4] The incidence of high-risk HPV subtypes among countries in SSA range from 10.7 to 97.2%. [5] A study conducted by Kang et al. across 13 high-income countries observed an overall vulvar cancer incidence surge of 38% in women younger than 60, while no notable rise was observed in women over 60 years of age.[6]

Squamous cell carcinoma (SCC) is the most prevalent type of vulvar cancer, representing the vast majority of cases. Less common types, include melanoma, basal cell carcinoma and Paget's disease of the vulva.[7]

Several factors heighten the risk of developing vulvar cancer, including HIV infection, HPV infection, smoking, alcohol use, obesity, Lichen Sclerosis and differentiated vulvar intraepithelial neoplasia (VIN).[8] HPV is also implicated in the development of other malignancies, such as cervical, vaginal, anal, and penile cancers, and its connection to vulvar cancer is now increasingly recognized. Overall, HPV accounts for approximately 40–50% of vaginal and vulvar cancers.[9]

The HPV strains most frequently associated with vulvar cancer are HPV 16 and 18, the same strains implicated in cervical squamous cell carcinoma.[9] In South Africa, HPV infection rates are notably high, with one study estimating a prevalence of 15.5% among women with normal cytology. Given the strong link between HPV, cervical cancer, and vulvar cancer, it is likely that vulvar cancer rates among young South African women may also increase.[10] However, with the introduction of the HPV vaccine, a significant reduction in HPV-related vulvar cancers is expected over the next two decades.[9]

Alongside HPV-related pathways, chronic skin conditions such as Lichen Sclerosis and premalignant conditions such as differentiated VIN also play a significant role in the pathogenesis of vulvar cancer. Early identification, treatment, and close monitoring of women with Lichen Sclerosis and differentiated VIN are vital to effectively reduce the vulvar cancer incidence.[9]

Patients with vulvar cancer often present with persistent itching, non-healing ulcers, skin changes in the vulvar region and pain. Following a thorough medical history and clinical examination, diagnosis is confirmed through a biopsy of the lesion, accompanied by diagnostic imaging to exclude distant metastases.[11] Vulvar cancer is surgically staged and the FIGO (International Federation of Gynaecology and Obstetrics) staging system is used for this purpose, with recent updates in 2021 aimed at simplifying the criteria for stage 3 disease.[6]

The treatment of vulvar cancer depends on the tumour's resectability and the patient's overall health condition. Factors such as age, performance status, and the presence of comorbidities also influence the treatment plan. Decisions should be made by a multidisciplinary team experienced in treating these complex tumours.[6]

In early-stage disease, defined as stages IA-IB, surgery is the primary treatment, involving a radical wide local excision of the tumour and an evaluation of lymph nodes through sentinel lymph node biopsy or inguino-femoral lymphadenectomy.[12] Adjuvant radiotherapy is recommended in cases where surgical margins are close or involved and when further re-excision is not possible. It is also advised when lymph node involvement is present, particularly when multiple nodes are affected or when extracapsular extension is evident.[13]

In contrast to early-stage vulvar cancer, the management of locally advanced disease, defined as stages II-IVA, presents more significant challenges. When central structures such as the anus or urethra are involved, extensive surgery including exenteration with colostomy or urostomy may be required, followed by complex reconstructive procedures. Postoperative complications such as wound breakdown, stoma formation, infections, and lower extremity oedema are common with postoperative mortality being a primary concern.[13]

Several retrospective studies have demonstrated the effectiveness of chemoradiation in treating locally advanced vulvar cancer. A 2008 trial by Beriwal et al. showed promising clinical outcomes with concurrent chemoradiotherapy (CCRT), coupled with low morbidity.[14] Similarly, a Phase II trial from Van Triest et al. found that Capecitabine-based chemoradiation offers an effective alternative to extensive surgery, providing substantial locoregional control with manageable levels of acute and long-term toxicity.[12] Landrum et al. further indicated that there were no significant differences in overall survival, progression-free survival, or recurrence rates between patients treated with primary chemoradiation and those who underwent surgery.[15]

At Groote Schuur Hospital (GSH) in Cape Town, South Africa, the Oncology Department has been utilizing concurrent chemoradiation for the treatment of locally advanced vulvar cancer since the 1980s.[16] This retrospective study aims to evaluate the overall survival (OS) and disease-free survival

(DFS) in patients with locally advanced vulvar cancer who were treated with definitive chemoradiation at GSH between January 2008 to January 2020, as well as explore factors which may influence survival in this population.

Methods

Patient Data Collection

All newly diagnosed patients with locally advanced vulvar cancer who presented to the Gynaecology Oncology Combined Clinic at GSH between 2008 and 2020, who underwent radical concurrent chemoradiation were eligible for inclusion in this study. Treatment included radiotherapy doses of 45-50.4 Gy for the base plan and 10-14 Gy for the boost plan with concurrent Cisplatin or Mitomycin C. Patient data was obtained from hospital records and the Gynaecology Oncology database in accordance with electronic patient records (EPR). Collected data included patient age, HIV status, FIGO 2021 cancer stage, ECOG performance status, OS, DFS, treatment response and specific treatment details. Data collection was facilitated through a RedCap data collection sheet, which was securely password-protected and accessible only to the author. (HREC-ref number: R016/2013)

Statistical analysis

Statistical analysis was performed using SPSS version 29. The Kaplan-Meier method was used to describe survival characteristics and the log rank test was used to compare the OS and DFS. In all cases a p-value of less than 0.05 was required for statistical significance. Test of equality of survival distributions for the different levels of HIV status was achieved with Log Rank (Mantel-Cox).

Ethics

Given the retrospective nature of this study, a waiver of consent was sought and granted by the Human Research Ethics Committee (HREC) at the University of Cape Town. All data used was extracted from patient files, ensuring anonymity to protect patient identities.

The study protocol received ethical approval from the Faculty of Health Sciences HREC at the University of Cape Town, and permission to access the medical records of participants was obtained from the administration of Groote Schuur Hospital. Throughout the study, patients were not contacted, and the confidentiality and privacy of their data were safeguarded by utilizing a password-protected computer system. (HREC-ref number:400/2023)

Results

Patient Demographic Data and Treatment Characteristics

Twenty-nine patients were retrospectively included in this study with a mean (± 1SD) age of 48 (± 16) years (Table 1). Among participants(n=29), 28 (86%) had a ECOG performance status of 1 with the other 14% having a score of 2 (Table 1). Regarding HIV status(n=29) 14 (48%) were HIV positive with 10 (71%) of them using antiretroviral therapy (ART). Among the other 15 participants, 12 (41%) were HIV negative, with 3 (10%) having an unknown HIV status. Furthermore, 9 had an unspecified viral load and 4 had a viral load lower than detectable limit. Considering smoking status(n=29) 9 (31%) reported to be smoking, with 16 (55%) reporting no smoking and 4 (14%) providing no response (Table 1). Upon tumour staging based on FIGO 2021, 6 patients (21%) presented with stage II with 23 (79%) presenting with stage III/IVA vulvar cancer (Table 1). Among these 29 patients, 25 (86%) participants completed their full treatment with concurrent chemoradiation. The mean (± 1SD) radiotherapy dose for the 25 patients who completed their course was 57.33 Gy, 15 (60%) of those patients receiving doses above 60 Gy. 90% of the patients had concurrent chemotherapy with either Cisplatin or Mitomycin C (Table 1). 15 participants (52%) had a complete response to treatment, 11 (38%) had a partial response and 3 (10%) had progression of disease.

Table 1: Patient demographic and treatment characteristics

Parameter	N (%) or mean±SD
Age	48,17 ± 16,04
ECOG performance status	
1	25 (86%)
2	4 (14%)
HIV status	
Positive	14 (48%)
Negative	12 (41%)
Unknown	3 (10%)
Antiretroviral Therapy (ART)	
Yes	10 (71%)
No	3 (22%)
Unknown	1 (7%)
Smoking	
Yes	9 (31%)
No	16 (55%)
Unknown	4 (14%)
FIGO staging	
Stage II	6 (21%)
Stage III / IVA	23 (79%)
Concurrent chemotherapy	
Yes	26 (90%)
No	3 (10%)
Mitomycin C	11 (38%)
Cisplatin	15 (52%)
Completed radiotherapy	
Yes	25 (86%)
No	4 (14%)
Radiotherapy dose	57,33 ± 7,73
Clinical response	
Partial	11 (38%)
Complete	15 (52%)
Progression of disease	3 (10%)

Survival Outcomes

Among the overall cohort (n=29), the median OS was 41.0 months (95% CI 11.61-70.39 months) (Figure 1). The cumulative 3-year and 5-year OS survival rate was 50%(0.50) and 40%(0.40), respectively (Figure 1). For the same cohort (n=29), the median DFS was 21.0 months (95% CI 4.63 to 37.38 months) (Figure 2). The cumulative 3-year and 5-year DFS survival rate was 38%(0.38) and 27%(0.27), respectively (Figure 2).

Treatment response

A total of 15 patients had a complete treatment response (Table 1). The median OS for these patients was 75.0 months. The cumulative 3-year and 5-year OS survival rate was 77%(0.77) and 0.68 (68%) respectively (Figure 3). The median DFS for these patients was 59.0 months (95% CI 10.73-107.27 months) (Figure 4). The cumulative 3-year and 5-year DFS was 58%(0.58) and 46%(0.46), respectively (Figure 4). A total of 11 patients had a partial treatment response (Table 1). The median OS for these patients was 12.0 months (95% CI 10.16-13.84 months). The cumulative 3-year and 5-year OS survival rate 24%(0.24) and 0%(0.00), respectively. The median DFS for these patients was 12.0 months (95% CI 10.53-13.47 months) (Figure 4). The cumulative 3-year and 5-year DFS was 21%(0.21) and 0%(0.00) respectively (Figure 4). Patients with a complete response to treatment had a statistically significant increase in OS and DFS when compared to those with a partial response. ($p = 0.001$) (Figure 3, Figure 4).

HIV status

A total of 15 patients were HIV-positive (Table 1). The median OS for these patients was 41.0 months (Figure 5). The cumulative 3-year and 5-year OS survival rate was 54%(0.54) and 45%(0.45), respectively (Figure 5). The median DFS for these patients was 29.0 months (95% CI 6.10-51.90 months) (Figure 6). The cumulative 3-year and 5-year DFS was 36%(0.36) and 18%(0.18), respectively (Figure 6). A total of 12 patients were HIV-negative (Table 1). The median OS for these patients was 21.0 months (95% CI 13.57-28.43 months). The cumulative 3-year and 5-year OS survival rate was 41%(0.41) and 28%(0.28), respectively. The median DFS for these patients was 12.0 months (95% CI 3.62-20.38 months) (Figure 6). The cumulative 3-year and 5-year DFS was 21%(0.21) and 0%(0.00) respectively (Figure 6). There was no statistically significant difference in OS or DFS between HIV-positive and HIV-negative patients ($\chi2(1)=0.72$, $p=0.40$, $\chi2(1)=0.56$, $p=0.46$, respectively) (Figure 6).

Table 2: Multivariate cox regression analysis on all patients

Parameter		5-year OS rate	Multivariant: Cox regression	
			Hazard ratio (95% CI)	*p*-value
Stage	Stage II	71%	2,14 (0,47 - 9,65)	0,33
	Stage III/IVA	32%		
Total radiotherapy dose	Less than 55 Gy	56%	1,73 (0,50 - 6,06)	0,39
	55 Gy and higher	24%		
Clinical response	Partial/progressive	0%	0,11 (0,03 - 0,37)	**<0,001**
	Complete	68%		

Parameter		5-year DFS rate	Multivariant: Cox regression	
			Hazard ratio (95% CI)	*p*-value
Stage	Stage II	57%	1,35 (0,38 - 4,80)	0,64
	Stage III/IVA	20%		
Total radiotherapy dose	Less than 55 Gy	50%	2,23 (0,74 - 6,72)	0,15
	55 Gy and higher	0%		
Clinical response	Partial/progressive	0%	0,16 (0,05 - 0,50)	**0,002**
	Complete	46%		

Those with earlier stage disease had a 71% 5-year OS rate compared to those with later stage disease who had an OS of 32% (HR: 2.14, p=0.33) (Table 2). The 5-year DFS was also increased in the earlier

stage group with 57% compared to the later stage group at 20% (HR: 1.35, p=0.64). Patients who received radiotherapy doses of less than 55 Gy had a 56% 5-year OS rate compared to 24% of for those who received doses of more than 55 Gy (HR: 1.73, p=0.39). Patients who received radiotherapy doses of less than 55 Gy also had a 50% 5-year DFS rate compared to 0% for those who received doses of more than 55 Gy (HR: 2.23, p=0.15). Participants with a complete response to treatment had a 5-year OS rate of 68%, while there were no survivors beyond 5 years in the partial response/progression of disease group (HR: 0.11, p<0.001). The DFS between these two groups was significant with the complete response group having a DFS of 46% compared to 0% for the partial response/progression of disease group (HR: 0.16, p=0.002) (Table 2).

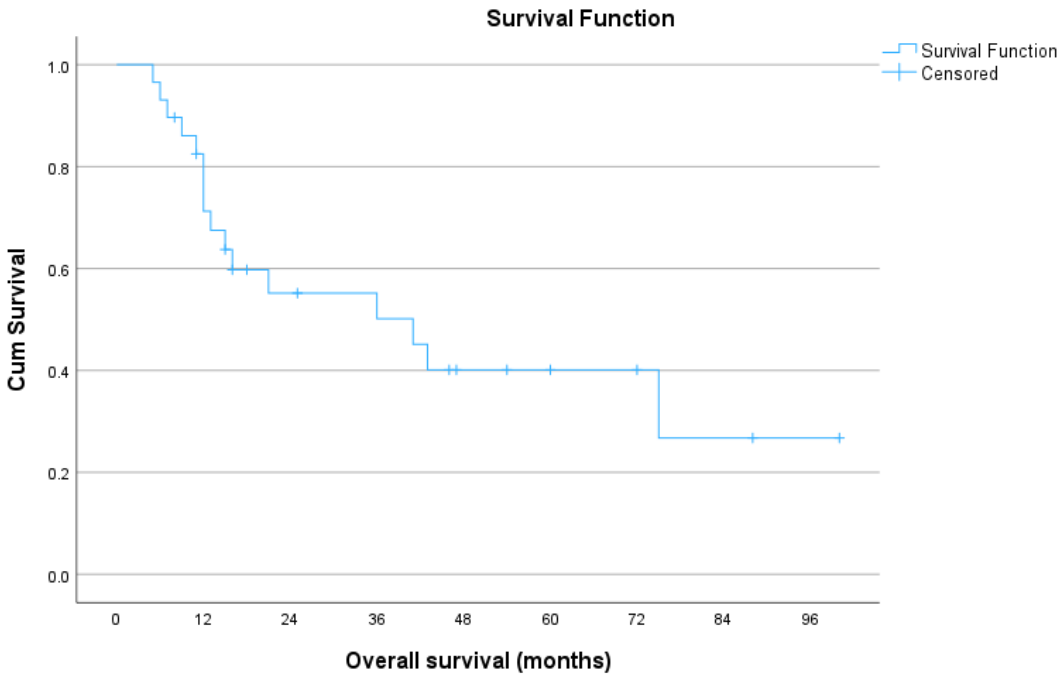

Figure 1: Kaplan-Meier estimate of overall survival

The median OS was 41 months (95% CI, 11.61 to 70.39)

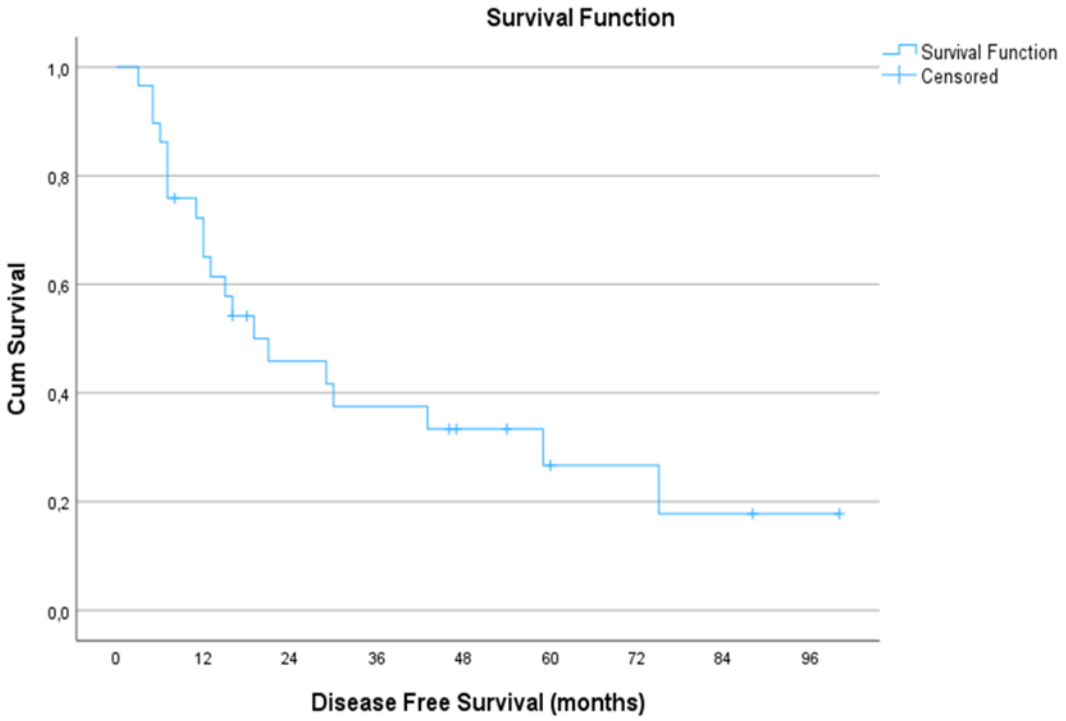

Figure 2: Kaplan-Meier estimate of Disease-Free survival

The median DFS was 21 months (95% CI, 4.63 to 37.38)

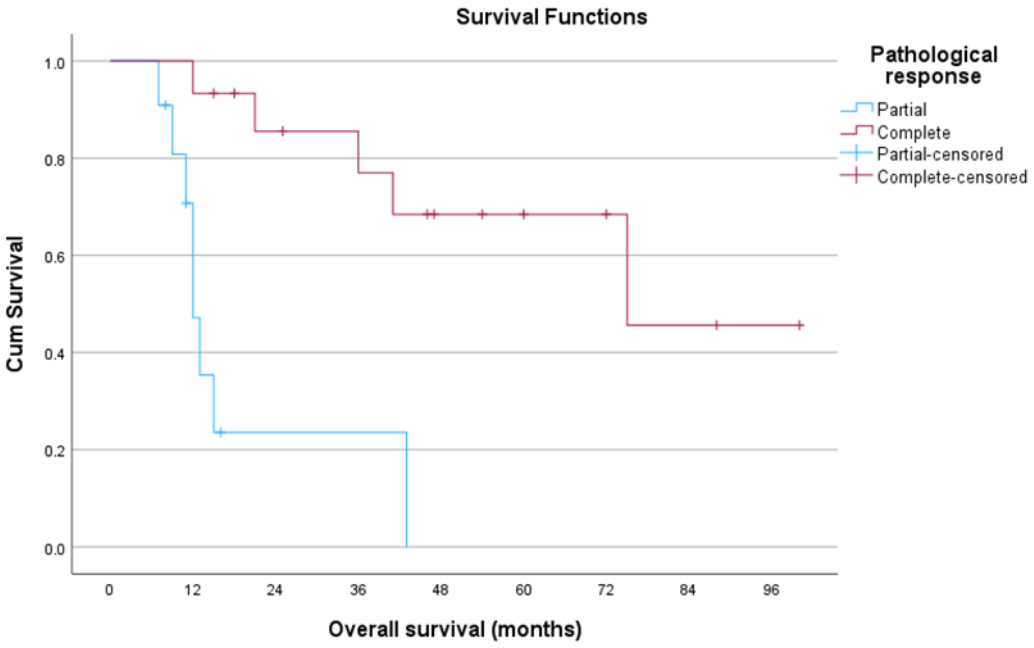

Figure 3: Kaplan-Meier estimate of overall survival in participants with complete and partial response to treatment

(HR: 0.11, p<0.001)

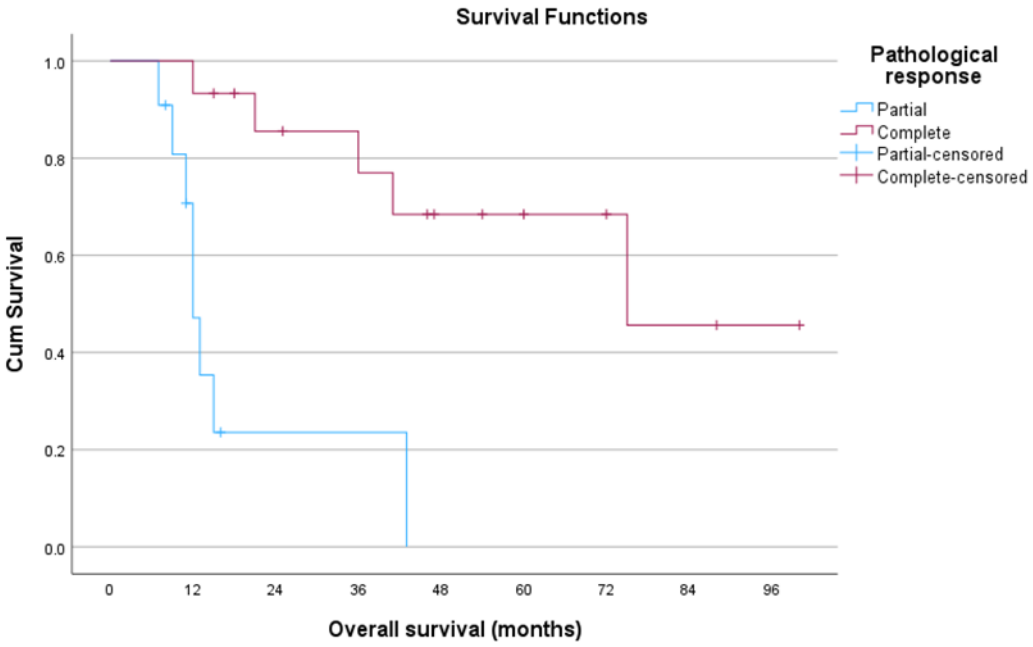

Figure 4: Kaplan-Meier estimate of disease-free survival in participants with complete and partial response to treatment

(HR: 0.16, p=0.002)

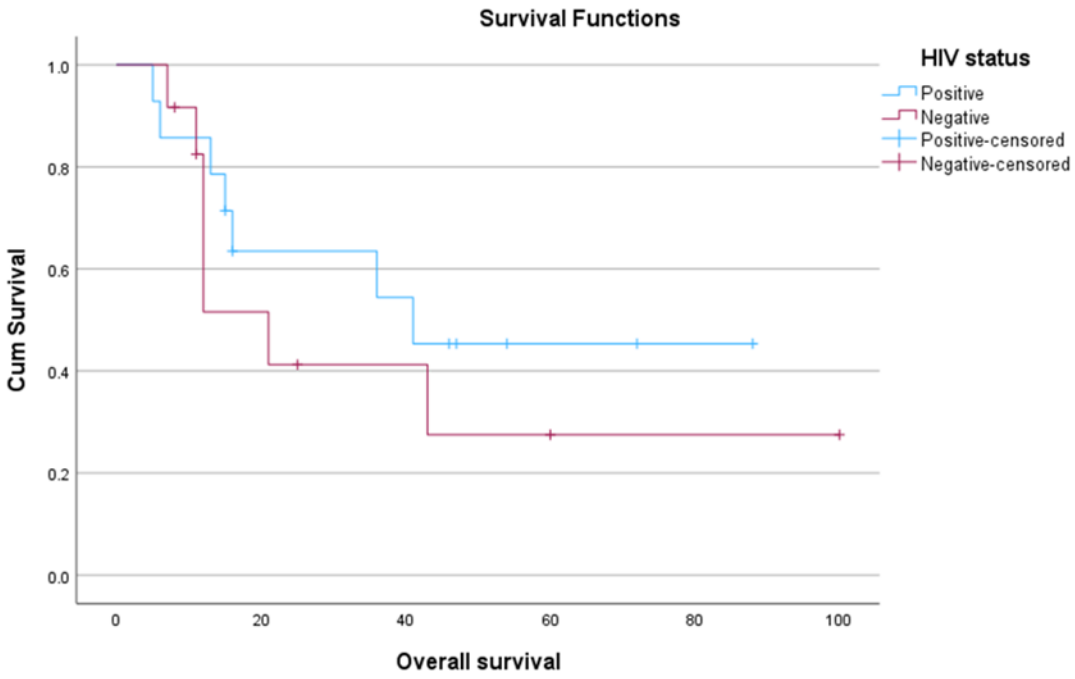

Figure 5: Kaplan-Meier estimate of overall survival in participants with HIV positive and negative disease

(HR: 1.09, p=0.74)

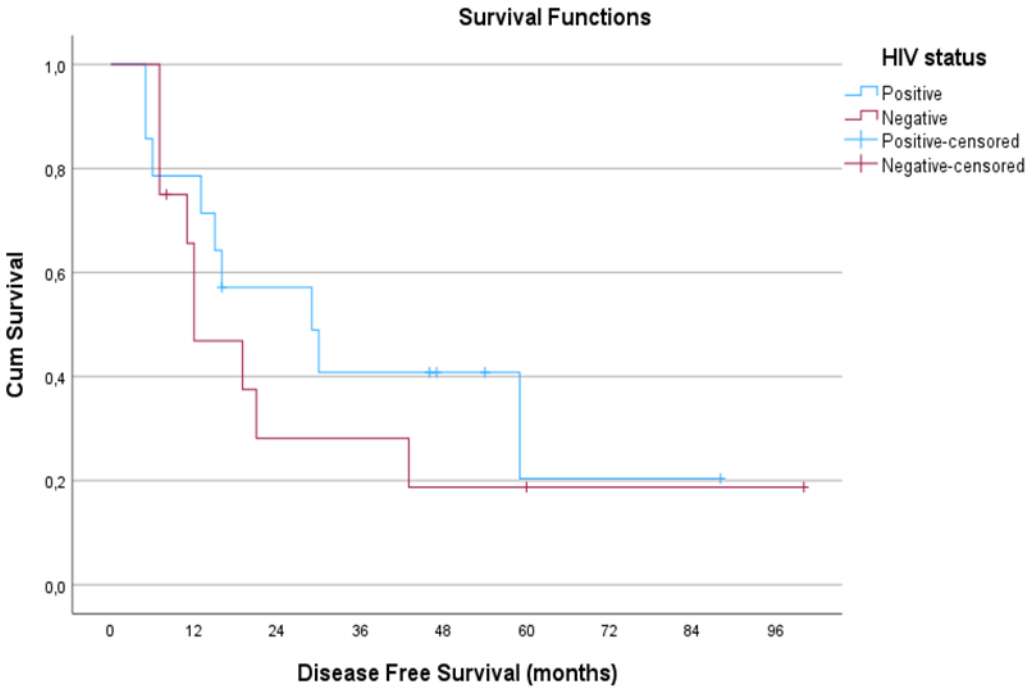

Figure 6: Kaplan-Meier estimate of disease-free survival in participants with HIV positive and negative disease

(HR: 1.60, p=0.78)

Discussion

The aim of this study was to assess the efficacy of primary chemoradiation in treating patients with locally advanced vulvar cancer at Groote Schuur Hospital by evaluating overall and disease-free survival, as well as highlighting factors contributing to survival.

Survival outcomes

The survival outcomes for women treated with concurrent chemoradiation at Groote Schuur Hospital were suboptimal. This study reports a 5 year OS of 40% and 5 year DFS of 27%. These results echo the findings from Van Triest et al. who reported a 5 year OS of 52% and 5 year DFS of 45% for locally advanced vulvar cancer treated with CCRT.[12] Together, these studies emphasize the need for continued global improvement in the efficacy of primary CCRT in treating locally advanced vulvar cancer.

Factors Influencing Outcomes

Age

This study reported a median age of diagnosis to be 48 years, a significantly younger value than reported in American and English studies where the average age ranged between 64 and 68 years.[15, 17] Additionally, age of presentation and HPV status are linked in vulvar cancer pathogenesis. While most patients in North America and Europe present with vulvar cancer at older ages through a Lichen Sclerosis-like pathway, the younger population in this study likely presented with HPV-induced vulvar cancer, often accelerated by HIV coinfection. In fact, the trend of rising incidence of vulvar cancer among younger women in low- and middle-income countries is, primarily attributed to the high prevalence of HIV and the increasing rates of HPV infections within these populations.[18] This underscores the critical

actions needed to combat vulvar cancer, like HIV screening, early diagnosis, and the prompt initiation of ART, along with counselling to ensure adherence to treatment. Additionally, it emphasizes the importance of administering HPV vaccinations at a young age, which could significantly reduce the incidence of vulvar cancer.[9]

HIV Status

HIV has been established as a driver of vulvar cancer, particularly with HPV co-infection.[18] Nearly half of the patients in this study were HIV-positive, underscoring the strong link between HIV and vulvar cancer. However, there was no significant difference in OS or DFS between HIV-positive and HIV negative groups. This aligns with findings from a Botswana study where survival was similarly unaffected by HIV status.[18] These results are likely due to the high rate of HIV-control in these populations. Thus, the importance of ART initiation and adherence counselling in these populations for the prevention of vulvar cancer cannot be overstated.

Stage at Presentation

This study reported that over 75% of patients presented with stage III disease or higher. Previous studies both in South Africa and Botswana have linked later disease presentation to poorer survival outcomes.[16, 18] Several factors may explain this late presentation, including limited access to healthcare, particularly for patients in rural areas. Geographic barriers, lack of transportation, and extended wait times to see specialists often delay diagnosis. Additionally, socioeconomic challenges such as poverty, unemployment, and inadequate living conditions make it difficult for individuals to prioritize their health, while financial constraints further hinder timely access to medical care.

Treatment Completion and Response

This study reported a treatment completion rate of 86%, with 52% achieving a complete response, leading to significantly better survival outcomes for these patients compared to those without a complete response. These reported rates of treatment completion and response come in contrast to a 2001 study by Rogers et al. at GSH who reported that 70% of patients completed CCRT, with a 28% complete response rate.[16] The increase in complete response relative to treatment completion may be due to higher radiotherapy doses, as patients in this study's cohort received 50-64 Gy compared to 45 Gy in Rogers' study. Additionally, more advanced radiotherapy techniques were used in this study such as intensity-modulated radiotherapy (IMRT). Despite improvements in treatment completion

and response among studies at GSH, other international studies have reported an even higher complete response rate.

Horowitz et al. in America reported a 73% complete response rate, which may be attributed to their more intensive chemotherapy regimen combining weekly Cisplatin and Gemcitabine, compared to this study's use of single-agent Cisplatin or Mitomycin C.[19] Additionally, this study's lower response rates may also be explained by patient presentation, as patients presented with more advanced disease. Lastly, all of Horowitz et al.'s patients were treated with advanced radiotherapy techniques such as IMRT, whereas some of this study's patients received 3D conformal radiotherapy (3DCRT).[19]

Beriwal et al. reported a 64% complete response rate using IMRT, highlighting its several advantages over 3DCRT, combined with a chemotherapy regimen of 5-FU and Cisplatin.[14] GSH has since adopted IMRT exclusively as the preferred radiotherapy technique, aiming to enhance treatment complete response rates. Thus, limitations in radiotherapy techniques could have also influenced the outcomes of treatment completion and response.

Study Limitations

The limitations of this study stem from its retrospective design and its focus on a single institution. The study population, consisting of patients with locally advanced vulvar cancer treated with CCRT, was relatively small at 29. Additionally, treatment protocols, particularly for chemoradiation, evolved throughout the study period. Cisplatin replaced Mitomycin C as the concurrent chemotherapy of choice, while IMRT supplanted 3DCRT, introducing variability that may have impacted patient outcomes.

Conclusions

The survival outcomes for women treated with concurrent chemoradiation at Groote Schuur Hospital were suboptimal, with a median overall survival of 41 months and a disease-free survival of 21 months. Several factors may have contributed to these outcomes, including age at presentation, HIV status, disease stage at presentation, and treatment completion and response rates. Notably, patients who achieved a complete response to treatment demonstrated significantly better survival compared to those with only a partial response. This study enforces the need for further interventions for vulvar cancer including enhanced screening, HPV vaccination, HIV control, and

timely intervention. Enhancing education and improving access to healthcare in South Africa are critical to encouraging these interventions for vulvar cancer.

References

1. Shylasree TS, Bryant A, Howells RE. Chemoradiation for advanced primary vulval cancer. Cochrane Database Syst Rev. 2011;2011(4):CD003752-CD.
2. Woelber L, Trillsch F, Kock L, Grimm D, Petersen C, Choschzick M, et al. Management of patients with vulvar cancer: a perspective review according to tumour stage. Ther Adv Med Oncol. 2013;5(3):183-92.
3. Zhu B, Gu H, Mao Z, Beeraka NM, Zhao X, Anand MP, et al. Global burden of gynaecological cancers in 2022 and projections to 2050. J Glob Health. 2024;14:04155.
4. Darre T, Sama B, Djiwa T, Afantodji-Agbeti WED, Bombone M, Kambote Y, et al. Factors associated with vulvar cancer from 2005 to 2021 in Togo, sub-Saharan Africa. BMC Womens Health. 2023;23(1):514.
5. Seyoum A, Assefa N, Gure T, Seyoum B, Mulu A, Mihret A. Prevalence and Genotype Distribution of High-Risk Human Papillomavirus Infection Among Sub-Saharan African Women: A Systematic Review and Meta-Analysis. Front Public Health. 2022;10:890880.
6. Olawaiye AB, Cuello MA, Rogers LJ. Cancer of the vulva: 2021 update. International Journal of Gynecology & Obstetrics. 2021;155(S1):7-18.
7. Tan A, Bieber AK, Stein JA, Pomeranz MK. Diagnosis and management of vulvar cancer: A review. J Am Acad Dermatol. 2019;81(6):1387-96.
8. Deppe G, Mert I, Belotte J, Winer IS. Chemotherapy of vulvar cancer: a review. Wien Klin Wochenschr. 2013;125(5-6):119-28.
9. Mazzotta M, Pizzuti L, Krasniqi E, Di Lisa FS, Cappuzzo F, Landi L, et al. Role of Chemotherapy in Vulvar Cancers: Time to Rethink Standard of Care? Cancers. 2021;13(16):4061.
10. Butt JL, Botha MH. Vulvar cancer is not a disease of the elderly: Treatment and outcome at a tertiary referral centre in South Africa2017.
11. Kumar N, Ray MD, Sharma DN, Pandey R, Lata K, Mishra A, et al. Vulvar cancer: surgical management and survival trends in a low resource setting. Journal of the Egyptian National Cancer Institute. 2020;32(1):4.

12. van Triest B, Rasing M, van der Velden J, de Hullu J, Witteveen PO, Beukema JC, et al. Phase II study of definitive chemoradiation for locally advanced squamous cell cancer of the vulva: An efficacy study. Gynecologic Oncology. 2021;163(1):117-24.
13. Nooij LS, Brand FAM, Gaarenstroom KN, Creutzberg CL, de Hullu JA, van Poelgeest MIE. Risk factors and treatment for recurrent vulvar squamous cell carcinoma. Critical Reviews in Oncology/Hematology. 2016;106:1-13.
14. Beriwal S, Coon D, Heron DE, Kelley JL, Edwards RP, Sukumvanich P, et al. Preoperative intensity-modulated radiotherapy and chemotherapy for locally advanced vulvar carcinoma. Gynecologic Oncology. 2008;109(2):291-5.
15. Landrum LM, Skaggs V, Gould N, Walker JL, McMeekin DS. Comparison of outcome measures in patients with advanced squamous cell carcinoma of the vulva treated with surgery or primary chemoradiation. Gynecologic Oncology. 2008;108(3):584-90.
16. Rogers LJ, Howard B, Van Wijk L, Wei W, Dehaeck K, Soeters R, et al. Chemoradiation in advanced vulval carcinoma. Int J Gynecol Cancer. 2009;19(4):745-51.
17. Leung E, Tremblay C, Liao D, Burnett M, Huang L, Sun SZ, et al. Treatment patterns and outcomes of patients with locally advanced vulvar or vaginal cancer in British Columbia. Gynecologic Oncology. 2023;175:107-13.
18. MacDuffie E, Sakamuri S, Luckett R, Wang Q, Bvochara-Nsingo M, Monare B, et al. Vulvar cancer in Botswana in women with and without HIV infection: patterns of treatment and survival outcomes. Int J Gynecol Cancer. 2021;31(10):1328-34.
19. Horowitz NS, Deng W, Peterson I, Mannel RS, Thompson S, Lokich E, et al. Phase II Trial of Cisplatin, Gemcitabine, and Intensity-Modulated Radiation Therapy for Locally Advanced Vulvar Squamous Cell Carcinoma: NRG Oncology/GOG Study 279. J Clin Oncol. 2024;42(16):1914-21.