

Comparison of survival outcomes by different treatments for HIV-infected cervical cancer: a real-world study in a single center in China

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Abstract

Background: Information on HIV-infected cervical cancer is very limited in China. The current study investigated long-term follow-up results of HIV-infected cervical cancer patients treated by different methods from an area in southwestern China in which HIV and cervical cancer are endemic.

Methods: All HIV-infected cervical cancer patients registered in Yunnan Cancer Hospital from January 2015 to December 2017 were retrospectively reviewed. Overall survival (OS) was the primary end-point.

Results: A total of 47 patients entered into the study. 7 patients underwent radical surgery. 24 patients received radiotherapy with high palliative intent, including intensity modulated radiotherapy (IMRT)/volume modulated arc therapy (VMAT)/helical tomotherapy (TOMO) with simultaneous integrated boost (SIB) (SIB; n=15), IMRT/VMAT to the pelvis followed by late course boost (LCB) (LCB; n=9) to the gross tumor volume (GTV). 3 patients received simple external beam radiotherapy to the pelvis (EBRT) (SEBRT; n=3). 13 patients gave up anti-tumor therapy at the initial diagnosis. The 3-year OS for patients who received surgery, LCB, SIB, SEBRT, no anti-tumor treatment were 100%, 51.9%, 66.7%, 0%, and 0%. All of the deaths were attributed to cancer. The prognosis of HIV-infected cervical cancer patients was closely related to the treatment methods ($p < 0.05$).

Conclusions: LCB and SIB are effective and safe modality for treatment of HIV-infected cervical cancer in a limited resource setting.

Background

Cervical cancer is a leading cause of cancer related morbidity and mortality afflicting women in less-developed countries. In China, cervical cancer ranks seventh and ninth in cancer prevalence and mortality in women, respectively(1). HIV-infected women have a greater persistence of high-risk human papillomavirus and a greater likelihood of developing invasive cervical cancer compared to HIV-uninfected women(2-4) and cervical cancer has been classified as an AIDS-defining malignancy(5).

Treating patients with two conditions challenges the oncologists. Standard treatments for this set of patients have not been defined, the management of cervical cancer in HIV-infected women were based on best practice for HIV-negative women, while seeking to optimize combination antiretroviral therapy (ART) (6). Some found the tolerance for chemoradiation was lower in HIV-infected patients(7, 8), while others found the majority of these patients can complete standard concomitant chemoradiotherapy used in HIV-uninfected women with comparable tolerability(9). Some studies showed HIV-infected women were at increased risk of relapses or a shortened life expectancy(7, 10, 11). Others found HIV infection did not affect survival(12-15). However, clinical data on treatment and prognosis of HIV-infected cervical cancer in China are scarce.

Yunnan, a province located in southwestern China where cervical cancer is in endemic, has the highest prevalence of HIV infection in the country currently. Yunnan Cancer Hospital is the biggest public cancer

center in this area. The limited brachytherapy equipment was not available to HIV-infected patients for the case of iatrogenic infection prevention. As some studies indicated that external beam radiotherapy (EBRT) techniques, such as intensity-modulated radiotherapy (IMRT), volumetric-modulated arc therapy (VMAT), three dimensional-conformal radiotherapy (3D-CRT), helical tomotherapy (TOMO) and stereotactic radiotherapy, could be reasonable options when it is not possible to perform brachytherapy(16-19), patients undertook external beam boost in place of high dose rate brachytherapy. Either simultaneous integrated boost (SIB) or late course boost (LCB) was performed to the gross tumor volume (GTV) for HIV-infected patients. Here, we analyzed treatment parameters and survival of HIV-infected cervical cancer patients in Yunnan Cancer Hospital.

Methods

Ethical considerations

The study was reviewed and approved by the Research Ethical Committees of the Third Affiliated Hospital of Kunming Medical University (Kunming, China). All patients provided written informed consent following an explanation of the treatment procedures in accordance to institutional requirements. They were fully informed that the radiation therapy was palliative. The confidentiality of the patient status was maintained by avoiding personal identifiers during analysis.

Patient Characteristics

Women were histologically confirmed invasive cervical cancer treated at Yunnan Cancer Hospital (January 2015 to December 2017) were approached for enrollment. Diagnoses of cervical cancer were based on comprehensive cervical cancer control guidelines from the World Health Organization (WHO). Cancers were staged by two experienced gynecologic oncologists on the basis of vaginal examination, chest and abdomen computed tomography (CT) with iodine-containing contrast medium, and pelvic magnetic resonance imaging (MRI) using the system of the International Federation of Gynecology and Obstetrics (FIGO) 2009. A total of 3913 women with a new diagnosis of invasive cervical cancer were enrolled, including 47 (1.2%) HIV-infected patients, 3755 (96.0%) HIV-uninfected patients, and 111 (2.8%) with unknown HIV status. Analyses were restricted to 47 with HIV infection. The HIV status was tested using the enzyme-linked immunosorbent assay method in Yunnan Cancer Hospital and also confirmed in provincial and prefecture-level Center for Disease Control affiliated clinics. Lymph node in imaging study with short-axis diameter over 10mm or relative apparent diffusion coefficient (ADC) values, or image findings of ring enhancement and marked necrosis, were defined as lymphadenopathy. Clinical and pathological variables analyzed included patient age; ethnicity; occupation; marital status; history of blood transfusion; initiated ART before cancer diagnosis; median duration of ART; symptoms; HPV infection; clinical stage; tumor size; pathological type; differentiation; node status; hemoglobin; pregnancy; delivery; CD4 cell count and co-morbidity status (Supplementary Table 1).

Treatment

Cancer treatment details were obtained through reviewing the electronic medical records. All of these patients were advised to accept ART treatment. 13 patients (27.66%) declined to receive any anti-tumor treatment at the time of diagnosis. 4 types of treatment were administered to 34 patients in this study: surgery based treatment (S; n=7), EBRT followed by LCB to GTV (LCB; n=9), EBRT with SIB to GTV (SIB; n=15), simple external beam radiotherapy (EBRT) to the pelvis (SEBRT; n=3) (Fig. 1).

7 patients (14.9%) received radical hysterectomy and lymphadenectomy. Patients with any of high-risk factors including plevic lymph node metastasis, positive surgical margin, positive lymphovascular space involvement, deep stromal invasion, positive parametrial involvement, high differentiation grade, and large tumor size (≥ 4 cm) received postoperative chemotherapy and/or radiotherapy according to the national guidelines. Patient with postoperative local recurrence received radiotherapy.

27 patients (57.4%) received radiation therapy. The standard treatment protocol for cervical cancer patients is 45-50.4Gy in 23-28 fractions of EBRT delivered to the pelvis, with concurrent weekly cisplatin chemotherapy at a dose of 40mg/m² for four to six cycles, and brachytherapy 20-28Gy in four to five fractions starting in week five of EBRT. Patients were immobilized in the supine position with abdominal body thermoplastic masks, and underwent helical computer tomography at 5 mm slice thickness. All planning was performed using the Pinnacle treatment planning system (TPS). The GTV delineation consisted of all clinically and radiologically demonstrable primary tumor. These HIV-infected patients receive the same pelvis EBRT as HIV-negative patients, but the brachytherapy is replaced by supplementary EBRT including LCB and SIB to the primary tumor. 9 patients were treated with a dose of 45-50Gy in 23-25 fractions to the pelvis in phase 1 followed by LCB (18-24Gy in 9-12 fractions) to the GTV (LCB group) in phase 2 (Fig. 1, Supplementary Table 2). 15 patients were treated with 46.8-54Gy in 26-30 fractions to pelvis and SIB 57.2-66Gy (58.1-69.44Gy equivalent dose [EQD2]) in 26-30 fractions to the GTV (SIB group) (Fig. 1, Supplementary Table 3). 3 patient received SEBRT with 46-50.4Gy in 23-28 fractions to the pelvis (Fig. 1). Concurrent chemotherapy is given weekly during radiotherapy as long as the treatment is tolerated according to the doctor's judgment. Some patients received 1 to 3 cycles of neoadjuvant chemotherapy using taxol and cisplatin when there was a waiting list before the start of radiotherapy. If the CD4 count is less than 200cells/ μ l, chemotherapy is omitted. Newly diagnosed HIV-infected patients are referred expeditiously for Yunnan Provincial Infectious Disease Hospital so that they can begin to receive ART therapy as soon as possible.

Surveillance after treatment

After primary treatment, patients were asked to come back for examination every 3 months for the first 2 years, every 6 months for the nest 3 years, and annually thereafter. As some of these patients received subsequent follow-up care at local facilities or did not have examinations, the exact onset of disease recurrence is unknown. All the participants were contacted by phone in June of 2019 and May of 2020, and their survival was confirmed. In the event of patient death, families were questioned about the cause of death.

Statistical analysis

Overall survival (OS) was the primary endpoint evaluated, and was calculated from the first day of diagnosis to death for non-censored observations. If such information could not be obtained, data after the last contact were censored. OS was evaluated using the Kaplan-Meier method with Log Rank and Breslow test. Patient age, ethnicity, occupation, marital status, initiated ART before cancer diagnosis, FIGO stage, macroscopic tumor growth, tumor size, lymphadenopathy, histological type, histological differentiation, hemoglobin, CD4 cells count, and treatment method were also assessed using univariate analysis to determine their impact on OS. Univariate and multivariate analysis were performed using the Cox regression method. Hazard ratios (HR) with their 95% confidence intervals (CI) are reported. SPSS software (version 17.0, SPSS Inc., Chicago, IL) was used for all statistical analyses. For all analyses, a $p < 0.05$ was considered statistically significant.

Results

Clinical features

Table 1 summarizes the characteristics of these patients and their tumors. The median patient age was 48 (range, 33 to 69 years). Han population accounted for the majority of study participants (40/47; 85.1%), the minority populations including Dai, Wa, Yi, Bai ethnic groups accounts for 14.9% of these patients. Nearly all (95.7%, 45/47) participants had symptomatic cancer, with only two (4.3%, 2/47) cancers detected through routine screening. Most patients presented with vaginal bleeding (n=45). The time from first symptom to diagnosis varied from 0.5 to 24 months. More than two-thirds patients had parametrial involvement (stage IIB or greater) at the time of diagnosis. 26 (55.3%) participants had started ART before the cervical cancer diagnosis and had received ART for several years (media, 3.5 years; range, 1 to 10 years). In 21 of the 47 patients, HIV was detected at the time of cervical cancer diagnosis. Tumor diameters ranged from 0 to 7 cm, and most (42.6%, 20/47) were cauliflower-like in shape. Co-morbidity status was detected in 11 cases, including Hepatitis B virus (HBV) infection in 5 cases, hepatitis C virus (HCV) infection in 3 cases, tuberculosis (TB) in 3 cases and syphilis in 5 cases. The median CD4 cell count was 243 cells/ μ l (range, 9 to 806); 14 patients had a CD4 count above 350 cells/ μ l, 14 patients had a CD4 count below 200 cells/ μ l and 9 patients had missing data on CD4 count.

Survival outcomes

The median follow-up period for the 47 patient cohort was 33.5 months and the maximum follow-up duration was 54 months. It should be noted that 2 types of follow-up were employed in this study. One group of patients underwent physical examination and/or imaging examination for recurrent disease as scheduled. In contrast, the other group of patients did not come back for examination. These patients did not come back for examination and their survival were confirmed through telephone contact, the exact onset of disease recurrence is unknown. Overall, 21 (44.7%) patients survived with tumor free, 21 (44.7%) died, and 5 (10.6%) patients were withdrawn. All of the deaths were attributed to cancer. 3-year OS rate was 48% and median OS was 33 months. The 3-year OS rates for patients who received surgery

with/without chemotherapy and radiotherapy, LCB group, SIB group, PEBRT group and no anti-tumor treatment were 100%, 51.9%, 66.7%, 0%, and 0%, respectively ($p < 0.001$; Fig. 2).

Prognostic factors

To identify potential prognostic factors associated with survival in HIV-infected cervical cancer patients, various clinicopathologic variables were evaluated using univariate analysis. Cox regression analysis revealed that clinical stage, lymphadenopathy, hemoglobin were factors significantly associated with OS in addition to the treatment methods (Table 2). Kaplan-Meier analysis revealed the 3-year OS rates for patient with FIGO IA-IIA and IIB-IV were 83.1% and 33.4%, respectively ($p = 0.007$, Breslow; $p = 0.005$ Log Rank, Fig. 3A). The 3-year OS rates for patients with tumor $< 4\text{cm}$ and $\geq 4\text{cm}$ were 72% and 37.2%, respectively ($p = 0.043$, Breslow; $p = 0.051$, Log Rank; Fig. 3B). The 3-year OS rates for patients with and without lymphadenopathy were 81.4% and 30%, respectively ($p = 0.002$, Breslow; $p = 0.001$, Log Rank, Fig. 3C). The 3-year OS rates for patients hemoglobin $> 118\text{g/L}$ and $\leq 118\text{g/L}$ were 70.7% and 24.1%, respectively ($p = 0.002$, Breslow; $p = 0.002$, Log Rank, Fig. 3D). Multivariate analysis revealed that the treatment method was an independent prognostic factor for these HIV- infected patients ($p = 0.036$). Compared with none anti-tumor treatment, EBRT to the pelvis plus LCB (hazard ratio [HR], 0.140; 95% confidence interval [CI], 0.025 to 0.785; $p = 0.025$) or SIB (HR, 0.102; 95% CI, 0.022 to 0.497; $p = 0.004$) to the primary tumor is a significant favorable prognostic factor for OS. These analyses are summarized in Table 3.

Radiotherapy group analyzes

In the radiotherapy group, the median GTV dose, fractions and total treatment time in SIB group were less than those in LCB group, (62.6Gy vs. 66Gy, $p = 0.003$, Mann-Whitney U-test, Fig. 4A; 28 fractions vs. 33 fractions, $p < 0.001$, Mann-Whitney U-test, Fig. 4B; 38.5 days vs. 56 days, $p < 0.001$, Mann-Whitney U-test, Fig. 4C). Of the 9 patients in LCB group, 2 received weekly platinum-based treatment and only 1 complete 4 weekly cycles of cisplatin during radiation therapy (Supplementary Table 2). In SIB group, 6 received concurrent chemotherapy and also only 1 complete 4 cycles cisplatin (Supplementary Table 3). Patients in SIB group had a higher 3-year overall survival than the LCB group (66.7% vs. 51.9%, $p = 0.994$, Fig. 2). There were no casualties related to radiotherapy in both group. Complications related to radiotherapeutic procedures included femoral head necrosis, proctitis, myelosuppression, gastrointestinal tract reaction and hyperpigmentation. Femoral head necrosis occurred in 1 patient in LCB group. Proctitis occurred in 2 patients with 1 from LCB group who also experienced the femoral head necrosis (11.1%, 1/9) and the other from SIB group (6.7%, 1/15). Acute grade 3 leukopenia occurred in 1 from SIB group. Grade 1-2 leukopenia, gastrointestinal tract reaction and hyperpigmentation were common complications in both LCB group and SIB group. No grade 3-4 gastrointestinal tract reaction and hyperpigmentation were recorded in both groups.

Discussion

There is a lack of study on the treatment and outcomes of HIV-infected cervical cancer in China. A lot of oncologists have a poor understanding on the treatment significance of HIV malignancy consortium. This study is the first to report long-term follow-up results of HIV-infected cervical cancer patients in Yunnan, China, which is an epicenter of both HIV and cervical cancer.

The median age of HIV-uninfected cervical cancer patients was 49 (range, 17 to 86 years) in this hospital, HIV-infected patients were similar in age (median age 48 years). Although previous studies showed that HIV infection shortens the latent period in the progression of pre-malignant cervical lesions to invasive and HIV-infected patients were substantially younger than HIV-uninfected(10), the study found no difference in age. Consistent with characteristics described in previously(10), nearly all (95.74%) patients presented with symptoms due to the cervical cancer and most (70.21%) had parametrial involvement (stage IIB or greater) at the time of diagnosis. HIV-infected women in Mangshi prefecture have been provided with free cervical cancer screening services since 2009(20), but most HIV-infected women are never screened in this study. Our results emphasize the need for regular cervical cancer screening of women in HIV programmes in more areas in Yunnan.

Gynaecological oncology surgeons provide open radical surgery for 6 early-stage patients and 1 IIB stage patient. No complication related to surgical procedures were recorded. Although 1 patient had vaginal recurrence 4 months after surgery, she got complete remission again after radical doses of radiotherapy. All 7 patients live without tumor until the last follow up. On this basis, we suggest radical surgery for HIV-infected patients with early-stage cervical cancers.

24 patients receiving EBRT boost instead of intracavity therapy for the limited applicator. EBRT boost techniques performed in this study were IMRT/VMAT/TOMO SIB and LCB with 3D-CRT following pelvic IMRT. The rectum, bladder, and small bowel are the organs at risk and limit the dose that can be given with EBRT(21). The radiation doses here were much lower than guideline-concordant treatment and the concurrent chemotherapy is not enough. The 3-year OS survival rates for LCB group and SIB group in our study were 51.9% and 66.7%, which seems not inferior to those receiving standard concurrent chemoradiotherapy previously (Supplementary Table 4)(7, 10, 13). Although the difference is not significant, the 3-year OS rate in SIB group is better than LCB group. The prolongation of overall treatment time has a well-documented detrimental effect on tumor control and survival(22), we speculated that the OS advantage in SIB were due to shorter treatment time.

However, the OS of LCB or SIB was significantly poorer than HIV-uninfected patients receiving guideline-concordant curative radiotherapy in the center (64.6% vs. 79.4%, $p=0.038$, Breslow; $p=0.060$, Log Rank, Supplementary Fig. 1). We could not tell the differences were HIV-related or treatment method related or both. Vaginal multi-channel individual model made by 3D printing technology makes it possible for to have personal applicator. We hope to study the efficacy of curative radiotherapy using 3D printing applicator brachytherapy for HIV-infected cervical cancer patients in the future.

For the 13 patients who gave up antitumor therapy at primary diagnosis and 3 patients who received SEBRT, the median survival is 7 months. Cox analysis showed that EBRT to the pelvis plus LCB or SIB to

the primary tumor is a significant favorable prognostic factor for OS compared with no anti-tumor treatment. So we suggested HIV-infected cervical cancer patients should be actively treated even to receive high palliative radiation such as LCB or SIB, rather than giving up therapy or receiving low palliative radiation such as SEBRT.

To the best of our knowledge, the present study is the first study of HIV-infected cervical cancer with long-term follow-up results in southwestern China, where both diseases are endemic. However, it has some important limitations. First, the HIV-infected sample consisted of only 47 women and the small size may therefore influence our findings. Secondly, no guideline-concordant curative radiotherapy was applied. We did not know the feasibility, safety, tolerability and efficacy of guideline-concordant chemoradiotherapy in Chinese HIV-infected cervical cancer patients. Thirdly, information about tumor control and relapse were incomplete, which restricted analysis to disease free survival.

Conclusion

In conclusion, our findings suggest that both surgery and radiotherapy are effective and safe treatment methods for HIV-infected cervical cancer patients. Although the total dose of radiation is not enough, SIB and LCB treatment shows reasonable efficacy and safety. The feasibility and tolerability of guideline-concordant curative radiotherapy for HIV-infected patients need to be evaluated in the future in Chinese population.

Declarations

Ethics approval and consent to participate

This study confirmed strictly to the ethical guidelines of the Declaration of Helsinki and was approved by the Research Ethics Committee of the third affiliated hospital of Kunming Medical University

Consent for publication

Not applicable.

Availability of data and materials

The data used in this study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no potential conflicts of interest associated with the publication of this manuscript.

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Authors' contributions

Lan Zhang, Wen-Hui Li, Kang-Ming Li and Mei-Ping Jiang conceived the study. Lan Zhang, Mei-Ping Jiang, Yun-Fun Li participated in the study design, case collection, drafting, and revising the manuscript. Yan-Qing Li participated in case collection. Xing-Rao Wu, Zheng Li, Hong-Ping Zhang, Wei Xiong, and Ming Zhang participated in interpretation of the data and revising the manuscript. All authors read and approved the final manuscript.

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Abbreviations

OS: Overall survival; IMRT: intensity modulated radiotherapy; VMAT: volume modulated arc therapy; TOMO: helical tomotherapy; SIB: simultaneous integrated boost; LCB: late course boost; GTV: gross tumor volume; EBRT: external beam radiotherapy; SEBRT: simple external beam radiotherapy

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Tables

Table 1 Patient characteristics

Characteristics	No.of patients (%)	
Age, year	48 (33 - 69)	
Ethnicity		
Han	40	85.11
Dai	4	8.51
Yi	1	2.13
Wa	1	2.13
Bai	1	2.13
Occupation		
Salaried position	3	6.38
Unemployed	44	93.62
Marital status		
Married	42	89.36
Divorced	1	2.13
Widowed	4	8.51
Married age	21 (16 - 28)	
History of blood transfusion		
Yes	7	14.89
No	37	78.72
Unknown	3	6.38
Initiated ART before cancer diagnosis		
Yes	26	55.32
No	21	44.68
Median duration of ART	3.5 (1 - 10)	
Initial symptoms leading to diagnosis		
Bleeding	45	95.74
Pain	1	2.13
Other	2	4.26
HPV infection		

Positive	30	63.83
Negative	2	4.26
Unknown	15	31.91
FIGO stage		
IA	3	6.38
IB	6	12.77
IIA	4	8.51
IIB	21	44.68
IIIA	0	0.00
IIIB	8	17.02
IV	4	8.51
X	1	2.13
Tumor size [cm]		
≥4	30	63.83
<4	15	31.91
Undefined	2	4.26
Macroscopic tumor growth		
Erosive	4	8.51
Cauliflower-like	20	42.55
Nodular	9	19.15
Ulcerative	11	23.40
Undefined	3	6.38
Lymphadenopathy		
Yes	24	51.06
No	19	40.43
Undefined	4	8.51
Histological type		
Squamous cell carcinoma	44	93.62
Adeno cell carcinoma	3	6.38

Histological differentiation		
Well	6	12.77
Moderate	22	46.81
Poor	6	12.77
Undefined	13	27.66
Hemoglobin (g/L)		
≤118	24	51.06
>118	23	48.94
Pregnancy	3 (1 - 15)	
Delivery	2 (1 - 5)	
Recent CD4, median cells/ul	243 (9 - 806)	
Treatment		
Surgery	7	14.89
LCB	9	19.15
SIB	15	31.91
SEBRT	3	6.38
No anti-tumor treatment	13	27.66

Table 2 Univariate analysis of overall survival based on risk factors

Characteristics	No.	3-year OS rate (%)	Median survival (mo)	p-value
Age, year				0.951
<48	23	45.2	33	
≥48	24	50.1	/	
Ethnicity				0.238
Han	40	52.3	/	
Minorities	7	28.6	23	
Occupation				0.247
Salaried position	3	100.0	/	
Unemployed	44	42.1	26	
Marital status				
Married	42	42.7	26	0.276
Divorced	1	100.0	/	
Widowed	4	100.0	/	
Initiated ART before cancer diagnosis				0.224
Yes	26	51.9	/	
No	21	42.1	10	
FIGO stage				0.017
IA-IIA	3	83.1	/	
IIB-IV	21	33.4	19	
X	1			
Tumor size [cm]				0.058
<4	15	72.0	/	
≥4	30	37.2	23	
Undefined	2			
Macroscopic tumor growth				0.674
Erosive	4	100.0	/	
Cauliflower-like	20	49.2	33	
Nodular	9	50.0	12	

Ulcerative	11	30.0	8
Undefined	3		/
Lymphadenopathy			0.005
Yes	24	30.0	12
No	19	81.4	/
Undefined	4		
Histological type			0.207
Squamous cell carcinoma	44	50.8	/
Adeno cell carcinoma	3	0.0	6
Histological differentiation			0.533
Well	6	60.0	/
Moderate	22	39.8	29
Poor	6	33.3	8
Undefined	13	63.6	/
Hemoglobin (g/L)			0.005
≤118	24	24.1	10
≥118	23	70.7	/
Recent CD4 cells/ul			0.485
≥200	13	46.2	10
≥200	22	49.0	33
Treatment			0.005
Surgery	7	100.0	/
LCB	9	51.9	/
SIB	15	66.7	/
SEBRT	3	0.0	7
No anti-tumor treatment	13	0.0	7

Table 3 Multivariate analysis of overall survival based on risk factors

Risk factor	Harzard ratio	95% confidence interval	<i>p</i> -value
FIGO stage			0.194
IA-IIA	Reference		
IIB-IV	4.1	0.487-34.550	
Tumor size [cm]			0.473
<4	Reference		
≥4	1.553	0.466-10.362	
Lymphadenopathy			0.216
No	Reference		
Yes	2.296	0.615-8.565	
Hemoglobin (g/L)			0.331
≤118	1.795	0.572-5.236	
>118	Reference		
Treatment			0.036
Surgery	∞0.001	0.000-3.27E260	0.966
LCB	0.14	0.025-0.785	0.025
SIB	0.102	0.022-0.497	0.004
SEBRT	0.791	0.155-4.043	0.779
No anti-tumor treatment	Reference		

Figures

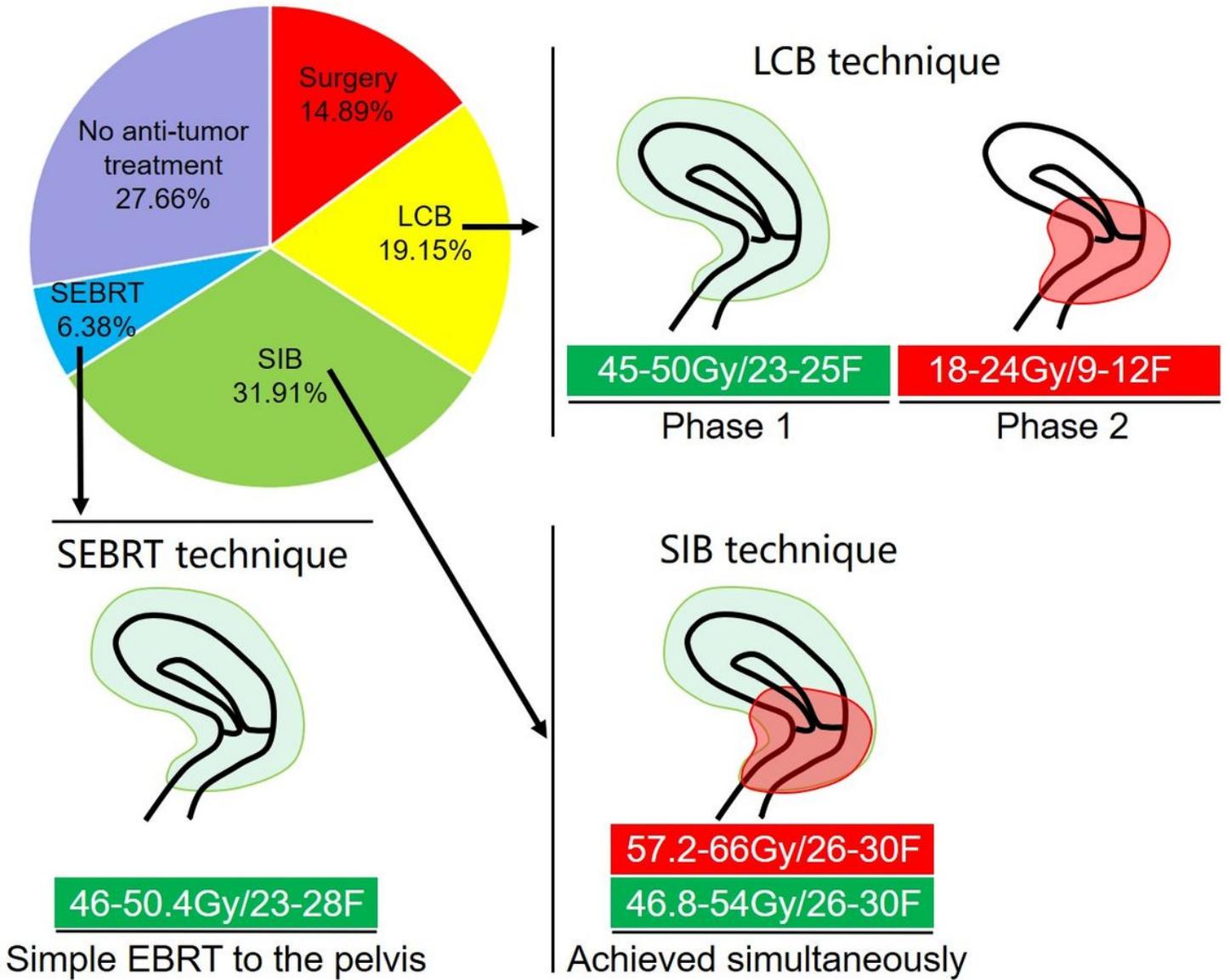


Figure 1

Diagrams showing the percentage of each treatment method and the procedures for late course boost (LCB) radiotherapy, simultaneous integrated boost (SIB) radiotherapy, simple external beam radiotherapy (SEBRT)

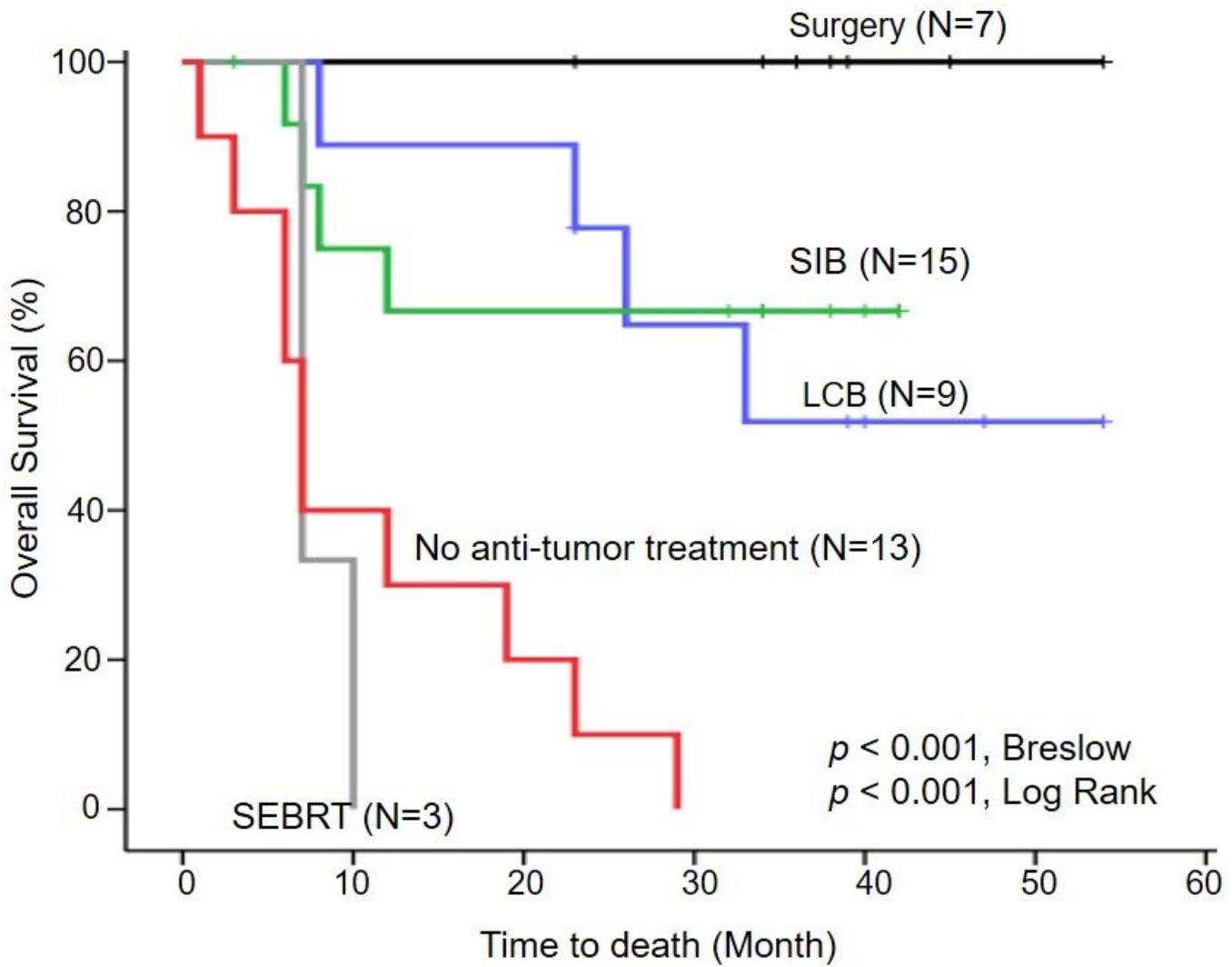


Figure 2

Kaplan-Meier overall survival curves for treatments including surgery, late course boost (LCB) radiotherapy, simultaneous integrated boost (SIB) radiotherapy, simple external beam radiotherapy (SEBRT) and none anti-tumor treatment.

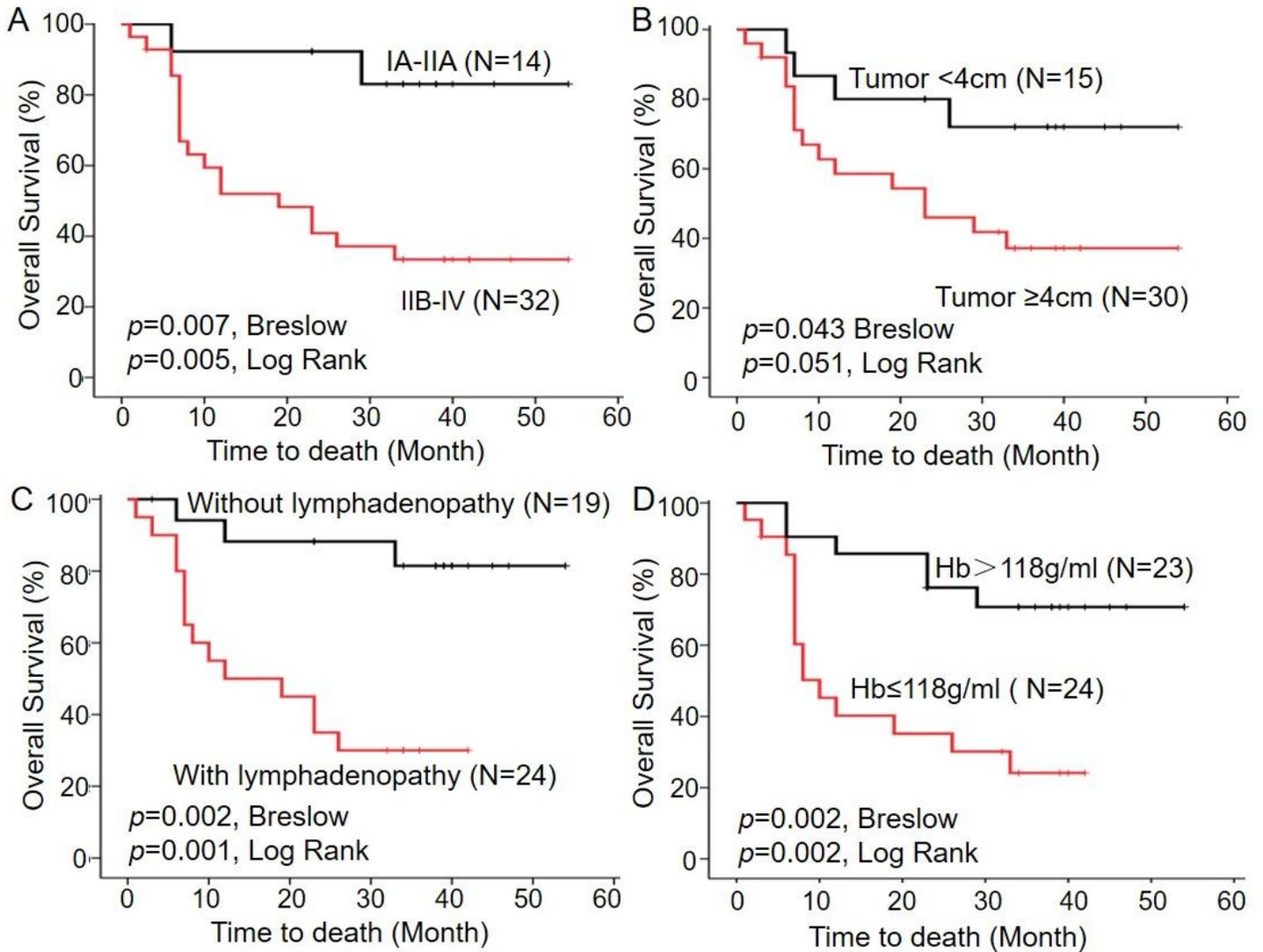


Figure 3

Kaplan-Meier overall survival curves for HIV-positive cervical cancer patients stratified by various clinicopathologic factors. (A) Survival curves for patients stratified by clinical stage; (B) for patients with tumor size \geq 4 cm and $<$ 4cm; (C) for patients with and without lymphadenopathy; (D) for patients with hemoglobin $>$ 118g/L and \leq 118g/L.

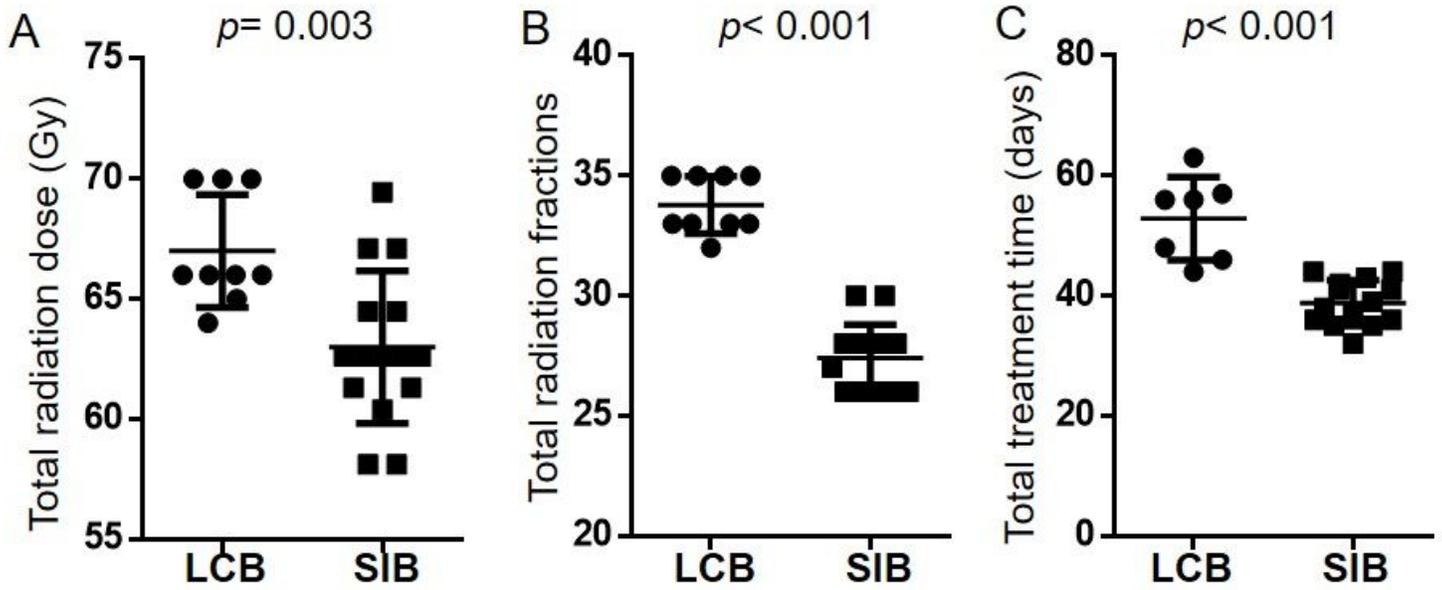


Figure 4

(A) Total radiation dose (B) fractions and (C) treatment time in late course boost (LCB) group and simultaneous integrated boost (SIB) group.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementaryTable1.xls](#)
- [SupplementaryFig.1.doc](#)
- [SupplementaryTable2.xls](#)
- [SupplementaryTable3.xls](#)
- [SupplementaryTable4.xls](#)