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ORIGINAL RESEARCH

Impact of Radiotherapy on Endocrine Function and Gut Microbiota in Cervical Cancer Patients Undergoing Ovarian Transposition

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Objective: This study aims to investigate the effects of radiotherapy on ovarian function, endocrine function, and gut microbiota in cervical cancer patients who underwent ovarian transposition, compared to those who did not.

Methods: This study included 100 cervical cancer patients treated from January to June 2024, divided into a control group (50 cases, radical surgery and radiotherapy) and an observation group (50 cases, ovarian transposition surgery plus radiotherapy). Radiotherapy protocols included conventional, intensity-modulated, or conformal radiotherapy, with 6MVX rays delivering 100–200 cGy per session, 5 sessions per week for 6 weeks. In the observation group, the ovarian region was shielded with a lead plate. Outcomes measured included ovarian and endocrine function, quality of life, adverse reactions, and gut microbiota composition. DNA was extracted from fecal samples for 16S rRNA sequencing and bioinformatics analysis, including α- and β-diversity, taxonomic composition, and LEfSe analysis.

Results: Before radiotherapy, no significant differences in serum sex hormone levels were observed between the groups. After radiotherapy, the control group showed greater increases in FSH and LH and a more pronounced decrease in estradiol (E2) levels. Ovarian function preservation was significantly higher in the observation group (28.00% vs 0.00%). The observation group also had a higher Kupperman score 6 months post-surgery (28.01±10.22 vs 21.91±7.38). Adverse reaction rates were comparable. Gut microbiota analysis revealed differences in taxonomic composition, with higher Firmicutes (66.5% vs 65.56%) and Faecalibacterium (7.0% vs 2.7%) in the observation group, while Proteobacteria (4.1% vs 13.9%) and Shigella (2.7% vs 8.5%) were more abundant in the control group. LEfSe analysis identified notable species differences, including higher Peptoniphilus and Actinomyces in the observation group.

Conclusion: Ovarian transposition surgery effectively preserves ovarian function in cervical cancer patients. Changes in gut microbiota during radiotherapy may influence endocrine outcomes, warranting further research.

Keywords: microbiome, ovarian transposition, cervical cancer radical surgery, radiotherapy, endocrine function

Introduction

Cervical cancer is one of the most common malignant tumors in the female reproductive system, with human papillomavirus (HPV) infection being the primary pathogenic factor.[1] Although surgery, radiotherapy, and chemotherapy are the main treatment modalities for cervical cancer, radiotherapy plays a critical role by controlling tumor growth through the destruction of cancer cell DNA.[2,3] However, radiotherapy may adversely affect ovarian function, particularly in young premenopausal women, potentially leading to early ovarian failure and endocrine dysfunction. While radiotherapy is an effective treatment for advanced cervical cancer, it can severely damage ovarian function due to the ovaries' sensitivity to radiation.[4,5]

To reduce the damage caused by radiotherapy to ovarian function, ovarian transposition surgery has been widely adopted as a method to preserve ovarian function. This surgery relocates the ovaries to a safe position outside the

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radiation field, thereby minimizing direct damage from radiotherapy.[6] However, ovarian transposition surgery does not completely eliminate the risk of radiotherapy-induced ovarian damage, and thus, there remains a risk of changes in endocrine function. Additionally, the surgery itself may impact ovarian blood supply and nerve structures, further complicating the assessment of endocrine function.[7,8]

In recent years, research has revealed a close relationship between the gut microbiota and ovarian function, with dysbiosis of the gut microbiota potentially affecting ovarian endocrine function through various pathways.[9] For example, the gut microbiota can regulate the synthesis and metabolism of ovarian hormones by metabolizing estrogen or secreting hormone-like substances. Furthermore, dysbiosis may trigger intestinal inflammation, leading to abnormal ovarian function. Given this, microbiome research has become a crucial approach to exploring the relationship between the gut microbiota and endocrine function.[10]

This study aims to analyze the mechanisms by which radiotherapy affects endocrine function after ovarian transposition surgery for cervical cancer, using a microbiome-based approach. We will compare the changes in ovarian function, endocrine function, and gut microbiota between patients who underwent ovarian transposition surgery and those who did not, exploring the correlation between microbiota and endocrine function. This study not only contributes to a deeper understanding of the impact of radiotherapy on endocrine function in cervical cancer patients but also provides more scientific evidence for clinical treatment and opens new avenues for the application of microbiome research in cancer therapy.

Research Subjects and Methods

Research Subjects and Grouping Scheme

This study intends to select 100 patients who underwent radical cervical cancer surgery and were hospitalized in the gynecology department of our hospital and affiliated institutions, according to the inclusion and exclusion criteria. We plan to select 100 patients hospitalized in the gynecology department of our hospital and affiliated institutions from January 2024 to June 2024, all of whom underwent radical cervical cancer surgery. Based on the type of surgery, all patients will be divided into a control group and an observation group (ovarian transposition group), with 50 cases in each group. Both groups will undergo radical cervical cancer surgery and lymph node dissection, with the ovarian transposition group additionally undergoing ovarian transposition surgery. Postoperatively, both groups will receive radiotherapy. This study complies with the Declaration of Helsinki and was approved by the Ethics Committee of The First Affiliated Hospital of Hebei North University. Informed consent was obtained from all enrolled patients and their families.

Inclusion criteria:

(1) Age 30–45 years;
(2) Pathological biopsy of the cervix indicating squamous cell carcinoma;
(3) Preoperative B-ultrasound indicating normal morphology and position of both fallopian tubes and ovaries;
(4) Clinical staging by the International Federation of Gynecology and Obstetrics (FIGO 2009) at stage I A2 to II A2;
(5) Normal menstrual cycle before surgery, with no perimenopausal syndrome;
(6) No antibiotic treatment or probiotic intake within the last month;
(7) Complete follow-up data.

Exclusion criteria:

(1) Severe heart, liver, or kidney dysfunction;
(2) Coagulation disorders;
(3) Inability to tolerate surgery and postoperative radiotherapy;
(4) Pregnancy.

Surgical and Radiotherapy Protocol

Control Group: Radical cervical cancer surgery without ovarian transposition, followed by radiotherapy.

Observation Group (Ovarian Transposition Group): Radical cervical cancer surgery combined with ovarian transposition surgery. The ovarian border is initially incised to free the ovarian arteries and veins, after which the ovaries are moved to the lateral paracolic gutters and fixed to the abdominal wall. Postoperatively, radiotherapy is administered. (High-risk factors exist post-radical surgery in both the control and observation groups).

Radiotherapy Protocol: Patients will select conventional radiotherapy, intensity-modulated radiotherapy, or conformal radiotherapy based on their condition and preference. The distribution of different radiotherapy modalities between the observation and control groups was similar, with no statistically significant difference. The radiotherapy target area will be determined by CT and MRI, with 6MV X-ray external irradiation. The lower boundary will be at the level of the bilateral ischial tuberosities, the upper boundary at the lower edge of the third lumbar vertebra, and the lateral boundary approximately 2.0 cm outside the widest point of the pelvis. The pelvic area will be irradiated with a dose of 100–200 cGy per session, 5 sessions per week, for 6 consecutive weeks. In the ovarian transposition group, the ovaries will be shielded using lead plates. The technical route is illustrated in Figure 1.

Sample Collection and DNA Extraction

Fecal samples from all enrolled patients were collected once within one week before radiotherapy and once after approximately 15 sessions of radiotherapy using a high-pressure sterile fecal collection device. Samples will be immediately stored at −80°C to ensure microbial stability. During sample processing, thawing will be performed on ice to minimize the degradation of related substances. Approximately 500 mg of fecal sample will be taken from each sample and placed in a 2 mL EP tube. Genomic DNA will be extracted using the Mag-Bind Soil DNA Kit, following the instructions. The specific steps include mixing the pretreated sample with glass beads, adding buffer, and vortexing, followed by incubation at 90°C to promote cell lysis. After centrifugation, the supernatant will be transferred to a new centrifuge tube, magnetic beads and binding buffer will be added to purify the DNA, and finally, DNA purification will be performed using a nucleic acid purification instrument, and DNA concentration will be measured to ensure the accuracy of subsequent experiments.

PCR Amplification, Sequencing Library Preparation, and Data Analysis

To amplify the V3-V4 region of the bacterial 16S rRNA gene, universal primers 341F and 806R will be used for PCR amplification. High-fidelity enzymes will be used to ensure amplification accuracy, and a low cycle number strategy will be employed to enhance experimental stability. A pre-experiment will be conducted to determine the minimum number of cycles required to obtain an adequate amount of amplified product. The amplified products will be detected and recovered by 2% agarose gel electrophoresis. The recovered PCR products will be fluorescently quantified using the Quant-iT PicoGreen dsDNA Assay Kit, and the products of different samples will be mixed according to the fluorescence quantification results. The sequencing library will be prepared using the TruSeq Nano DNA LT Library Prep Kit, and library construction will include end repair, adapter ligation, and PCR amplification. The completed library will be quality checked using the Agilent Bioanalyzer, and once qualified, paired-end sequencing will be performed on the MiSeq sequencer. The target fragment length for sequencing is 200–450 bp. Data analysis will include initial screening of high-quality sequences, OTU clustering, species diversity analysis, and analysis of differences in microbial community structure between different samples and groups. Finally, based on the 16S rRNA gene sequencing results, a microbial community association network will be constructed, and its metabolic functions will be predicted.

Gut Microbiota Structure

First, α-diversity indices (Shannon index, Simpson index, and Chao1 index) will be used to assess the richness and evenness of microbial communities in each group, and these indices will be displayed using box plots or bar charts. Statistical analysis of α-diversity differences will be conducted using the Kruskal–Wallis test or Mann–Whitney *U*-test. Next, β-diversity indices (such as Bray-Curtis distance, Unweighted UniFrac distance, and Weighted UniFrac distance) will be calculated to evaluate differences in community structure between samples, and these differences will be visualized using Principal Coordinate Analysis (PCoA) or Non-metric Multidimensional Scaling (NMDS) plots, with the PERMANOVA test used to assess significant differences between groups. Additionally, the taxonomic composition of

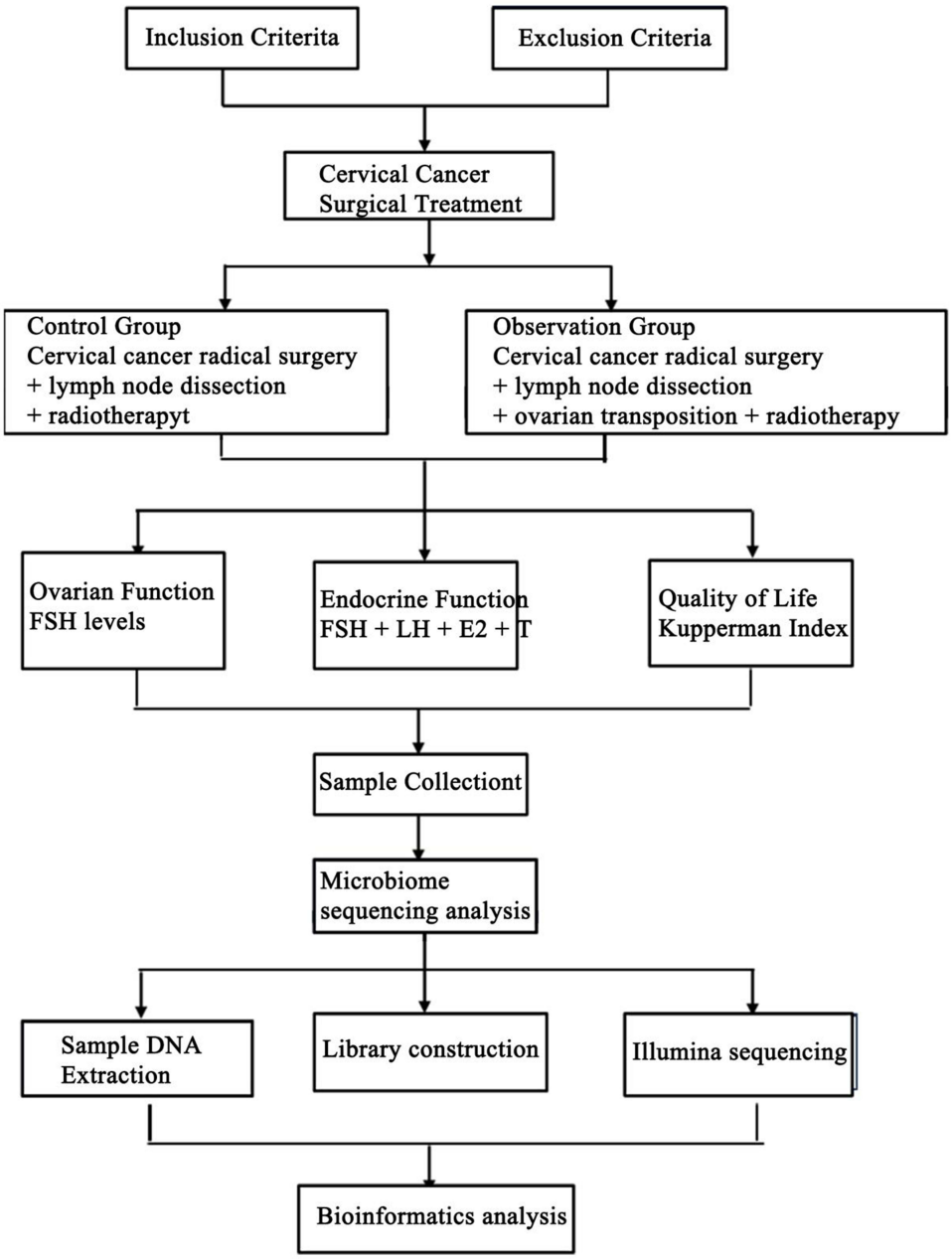

Figure 1 The technical route.

the microbial community will be analyzed, and the relative abundance of major microbial phyla, families, and genera in different groups will be displayed using stacked bar charts or pie charts. Finally, Linear Discriminant Analysis Effect Size (LEfSe) will be used to identify microbial species with significant differences between groups, and these differences will be visualized using LDA plots.

Endocrine Function Assessment

(1) The ovarian function of the two groups will be evaluated based on serum follicle-stimulating hormone (FSH) levels before and after radiotherapy. Normal: FSH < 10 IU/L with no menopausal symptoms; Declined function: 10 IU/L ≤ FSH < 40 IU/L with menopausal symptoms; Lost function: FSH ≥ 40 IU/L. Ovarian function preservation will be considered if FSH ≥ 10 IU/L occurs once within one year, with no menopausal symptoms.

(2) Radioimmunoassay will be used to detect the levels of FSH, luteinizing hormone (LH), estradiol (E2), and testosterone (T) before and after radiotherapy in both groups to assess endocrine function.

(3) Six months after treatment, the Kupperman index will be used to assess the quality of life in both groups. The menopausal index: hot flashes and sweating are scored 4 points, insomnia, dyspareunia, urinary system symptoms, irritability, and paresthesia are scored 2 points, depression, dizziness, fatigue, palpitations, and tiredness are scored 1 point; symptom severity is divided into four levels: no symptoms = 0 points, occasional symptoms = 1 point, persistent symptoms = 2 points, symptoms affecting life = 3 points. The Kupperman score = menopausal index × symptom severity, with higher scores indicating poorer quality of life.

(4) Record adverse reactions during the follow-up period for both groups.

Statistical Analysis

In this study, all relevant data will be analyzed using SPSS 14.0 statistical software. For quantitative data, results will be expressed as mean ± standard deviation ($\bar{x} \pm s$), and *t*-tests will be conducted. Categorical data will be expressed as frequency and percentage [n (%)], and comparisons between data will be performed using the chi-square test. A P-value of less than 0.05 will be considered statistically significant in all statistical analyses. Additionally, the graphical presentation will be processed and displayed using GraphPad Prism 9 software. Sequencing data will be statistically processed and analyzed using the R programming language and QIIME 2 software. Group differences in microbial relative abundance, α-diversity, and β-diversity indices will be analyzed using non-parametric test methods, including the Kruskal–Wallis test and Wilcoxon rank-sum test. The statistical analysis results will be displayed through box plots, with data expressed as mean ± standard error (SE). All statistical tests will be two-sided, with a significance level of $P < 0.05$. In the LDA effect size analysis, the discrimination threshold for feature differences will be set at 2.0, with a significance level of 0.05 for the Kruskal–Wallis test.

Results

Baseline Data

There were no statistically significant differences between the two groups in terms of age, BMI, pathological type, or stage (P>0.05), as shown in Table 1.

Table 1 Comparison of Baseline Data Between the Two Groups

Item	Observation Group (n=50)	Control Group (n=50)	t/χ^2	p
Age				
Range	30–45	30–45		
Mean Age	36.93±5.71	37.11±5.69	0.158	0.875
BMI	23.17±2.04	23.16±2.05	0.024	0.981
Pathological Type (%)			0.045	0.832
Squamous Cell Carcinoma	16	17		
Non-Squamous Cell Carcinoma	34	33		
Stage			0.102	0.749
IA2	6	5		
IB1	5	5		
IB2	9	11		
IB3	7	7		
IIA1	10	10		
IIA2	13	12		

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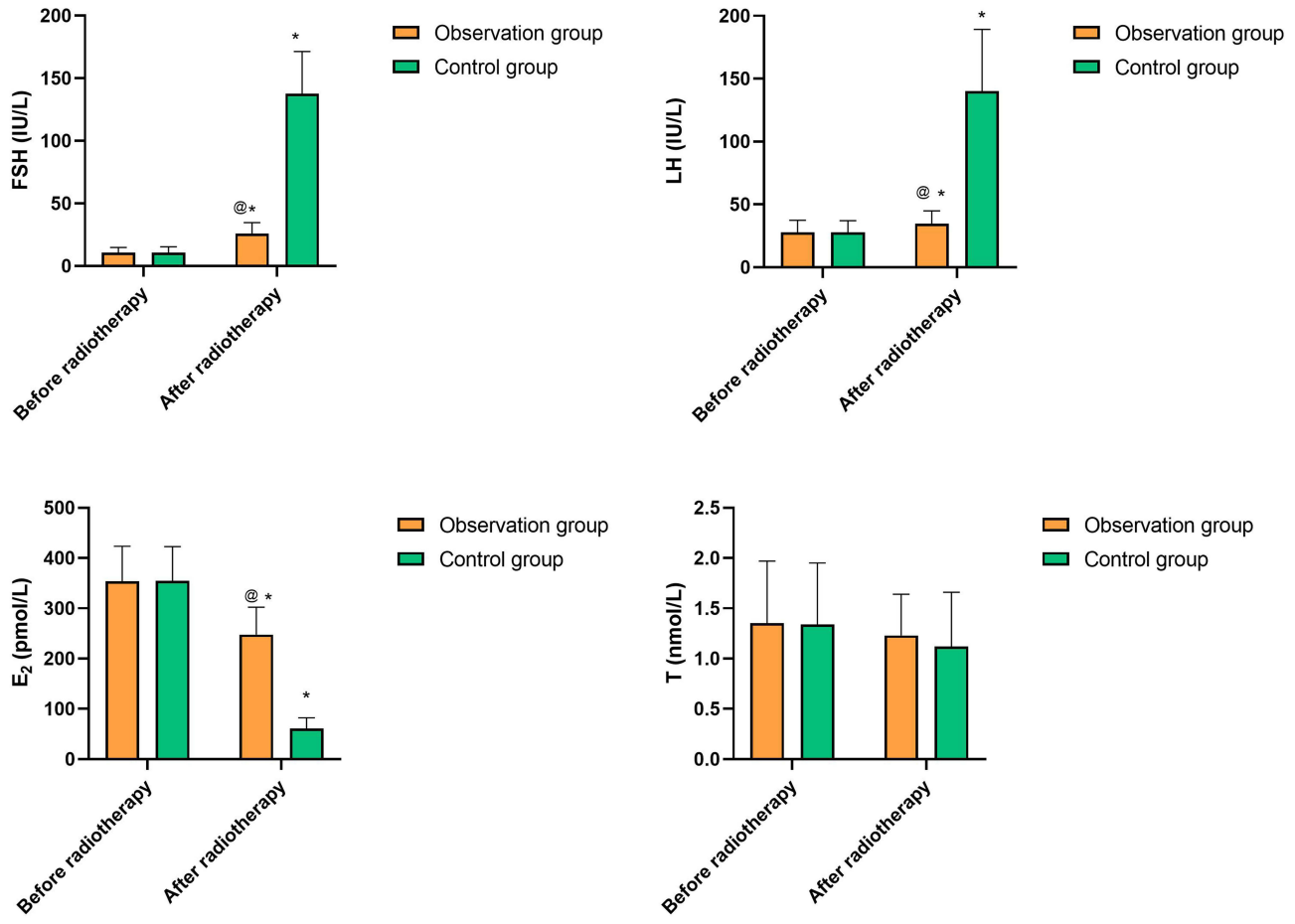

Figure 2 Comparison of Endocrine Function Between the Two Groups. *P<0.05 compared to pre-radiotherapy within the same group, @P<0.05 compared to post-radiotherapy in the control group.

Comparison of Endocrine Function Between the Two Groups

Before radiotherapy, there were no statistically significant differences in serum hormone levels between the two groups (all P>0.05). After radiotherapy, serum FSH and LH levels significantly increased in both groups, with the control group showing a more pronounced increase (both P<0.05). Simultaneously, serum E2 levels significantly decreased in both groups, with a more substantial decline in the control group (P<0.05). Serum T levels did not change significantly before and after radiotherapy in either group, and the differences between the groups were not statistically significant (all P>0.05). See Figure 2.

Comparison of Ovarian Function Between the Two Groups

In the observation group, 6 patients had normal ovarian function, 8 had decreased function, and 36 had lost function. In the control group, no patients had normal or decreased ovarian function, and 50 had lost function. The ovarian function preservation rate in the observation group was 28.00%, significantly higher than the 0.00% in the control group (p<0.05), as shown in Table 2.

Table 2 Comparison of Ovarian Function Between the Two Groups

Group	Normal	Decreased Function	Lost Function	Ovarian Function Preservation
Observation Group (n=50)	6	8	36	14 (28.00%)
Control Group (n=50)	0	0	50	0 (0.00%)
χ^2				16.279
p				0.001

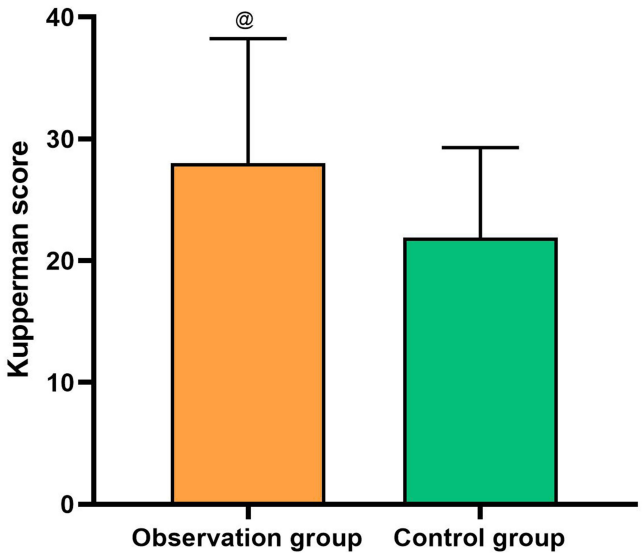

Figure 3 Comparison of Kupperman Scores Between the Two Groups. @P<0.05 compared to post-radiotherapy in the control group.

Comparison of Kupperman Scores Between the Two Groups

Six months after surgery, the Kupperman score was (21.91±7.38) in the control group and (28.01±10.22) in the observation group. The score in the observation group was significantly higher than that in the control group, with a statistically significant difference (P<0.05), as shown in Figure 3.

Comparison of Adverse Reactions Between the Two Groups

There was no statistically significant difference in the overall incidence of adverse reactions between the two groups (P=0.194>0.05). The total incidence of adverse reactions was 36.00% (18/50) in the observation group and 24.00% (12/50) in the control group. The specific adverse reactions were as follows: in the observation group, there were 2 cases of ovarian cysts, 7 cases of cystitis, 4 cases of intestinal obstruction, and 5 cases of abdominal pain; in the control group, there were 0, 5, 4, and 3 cases, respectively. See Table 3.

Changes in Gut Microbiota Before and After Radiotherapy

The sequencing overview of gut microbiota in patients with cervical cancer after radiotherapy was conducted using the Illumina MiSeq platform (PE150) to study the microorganisms in the samples. A total of 100 fecal samples were analyzed for the 16S rRNA V4 gene sequence. The average number of sequencing reads was 28,640 (range 23,167–-30,000 reads), and a total of 1,009,963 sequences were obtained. A total of 2806 ASVs (amplicon sequence variants) were detected across the 100 samples, with 2558 (91.16%) detected before radiotherapy and 2246 (80.04%) after radiotherapy in the observation group. A total of 2039 (72.67%) were detected both before and after radiotherapy in the observation group. There were no statistically significant differences in the alpha diversity indices, including the Simpson index, Shannon entropy index, and Chao1 index, between the two groups before and after radiotherapy

Table 3 Comparison of Adverse Reactions Between the Two Groups

Group	Ovarian Cyst	Cystitis	Intestinal Obstruction	Abdominal Pain	Total Incidence of Adverse Reactions
Observation Group (n=50)	2	7	4	5	18 (36.00%)
Control Group (n=50)	0	5	4	3	12 (24.00%)
χ^2					1.714
P					0.194

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(P>0.05), indicating no significant difference in the richness of gut microbiota between the two groups before and after radiotherapy (P>0.05). See Figure 4. Bray-Curtis, Unweighted UniFrac, and Weighted UniFrac distance matrices Anosim analysis methods were used to perform significance analysis of beta diversity indices between the two groups before and after radiotherapy, and the results showed no statistically significant differences in beta diversity indices before and after radiotherapy in either group (P>0.05). See Figure 5.

Changes in the Relative Abundance of Major Gut Microbiota Between the Observation and Control Groups During Radiotherapy

Differences in microbial species composition were observed between the two groups. First, taxonomic composition analysis was performed at both the phylum and genus levels to analyze the differences in taxonomic composition between the two groups (Figure 6A and B). Second, LEfSe analysis revealed significant differences in species between the two groups (Figure 6C and D). Finally, a taxonomic hierarchy tree was used to visually represent the comparison of species composition at each phylum, class, order, family, and genus level between the two groups (Figure 6E).

Impact of Radiotherapy on Endocrine Function and Gut Microbiota

After radiotherapy, serum FSH and LH levels significantly increased in both groups, while serum E2 levels significantly decreased, with no significant change in serum T levels. Additionally, there were no statistically significant differences in

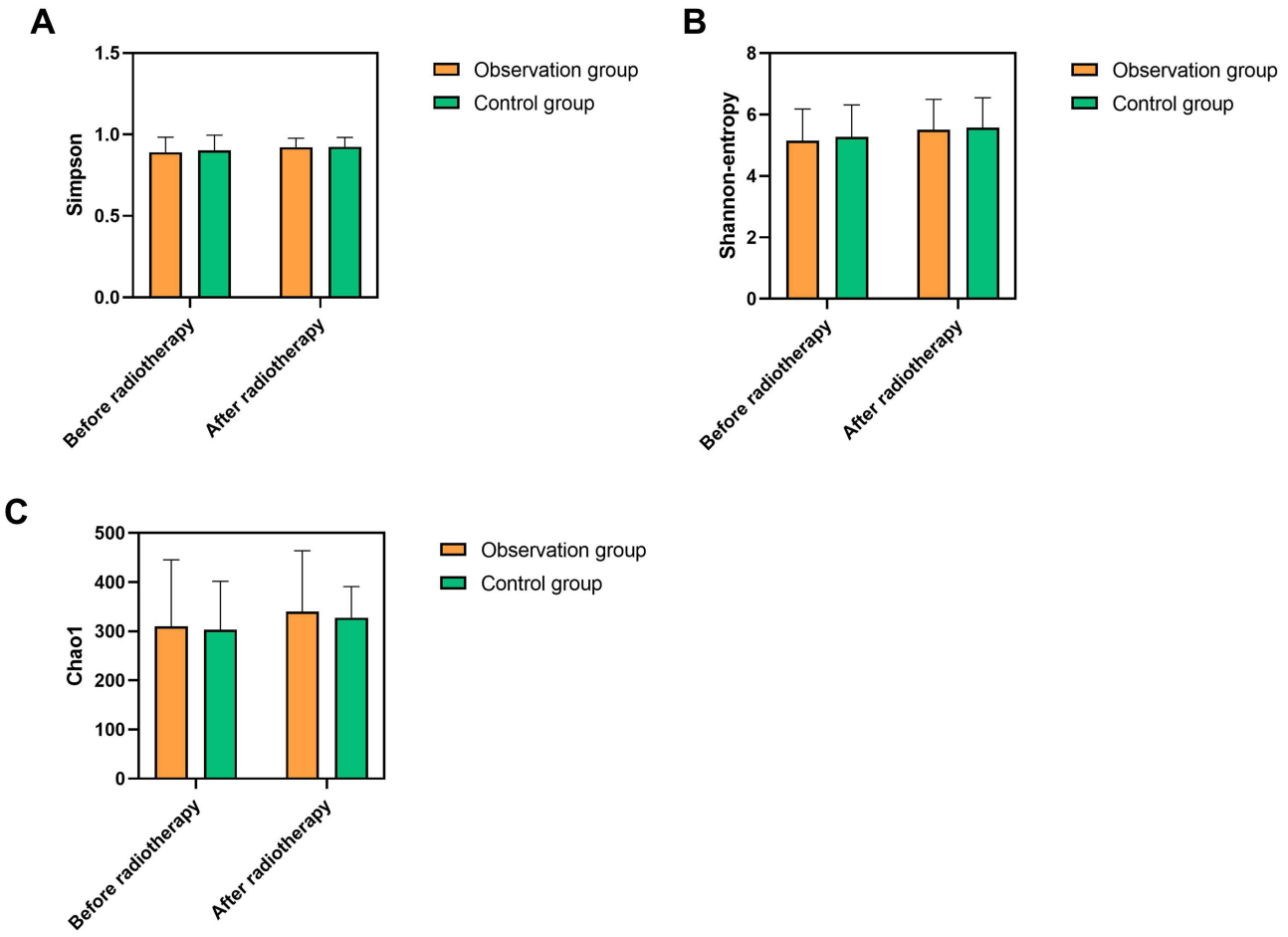

Figure 4 Comparison of Alpha Diversity Indices Before and After Radiotherapy in the Two Groups. The alpha diversity indices, including the Simpson index, Shannon entropy index, and Chao1 index, between the two groups before and after radiotherapy (P>0.05), The richness of gut microbiota between the two groups before and after radiotherapy (P>0.05) (**A-C**).

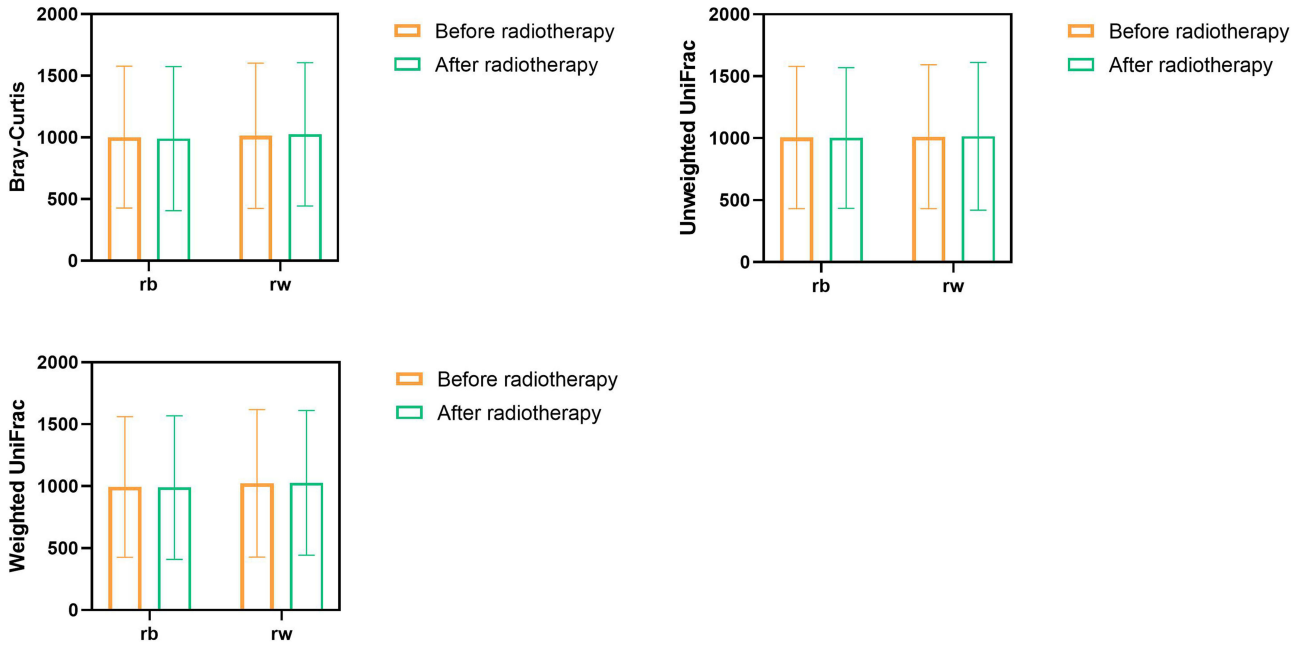

Figure 5 Comparison of Beta Diversity Indices Before and After Radiotherapy in the Two Groups.
Abbreviations: rb, Rank of Inter-group Distance; rw, Rank of Intra-group Distance.

alpha and beta diversity indices of gut microbiota before and after radiotherapy, but differences in microbial species composition were observed between the observation and control groups.

Discussion

The Role of the Microbiome in Cancer Development and Treatment

The interplay between cancer development and treatment and the human microbiome is an emerging area of research.[11] Dysbiosis of microbial communities can lead to the generation of harmful metabolites and an increased expression of antigenic microbes, which may alter anticancer immune responses through the promotion of mucosal inflammation or systemic disorders, thereby affecting cancer treatment outcomes.[12,13] Microbial communities within and around the tumor, as well as those distant from the tumor, can influence cancer susceptibility and progression through various mechanisms, such as modulating inflammatory responses, inducing DNA damage, and producing metabolites associated with either tumorigenesis or suppression.[14] These mechanisms play crucial roles in the onset and progression of cancer. Studies have shown a correlation between bacterial communities in the reproductive tract and the etiology, severity, and treatment outcomes of gynecological malignancies.[15] Moreover, factors such as inflammation, cancer, chemotherapy, and radiotherapy may lead to changes in the number, diversity, richness, and balance of microbial communities, thereby impacting the efficacy and prognosis of cancer treatment.[16,17]

Impact of Ovarian Transposition on Endocrine Function

The ovary, as a vital endocrine organ in females, secretes various hormones that are crucial for maintaining reproductive function.[18] This study compared the endocrine function, ovarian function, and quality of life of patients before and after radiotherapy following ovarian transposition. The results showed no significant difference in serum sex hormone levels between the two groups before radiotherapy, suggesting that maintaining blood flow during ovarian transposition and moving the ovaries to a region distant from radiation exposure can effectively protect ovarian function, keeping hormone levels post-transposition similar to those of patients who did not undergo transposition.[19] After radiotherapy, the serum FSH and LH levels in both groups increased significantly, with a more pronounced increase in the control group; serum E2 levels decreased significantly, with a larger decrease in the control group. Serum T levels did not change significantly

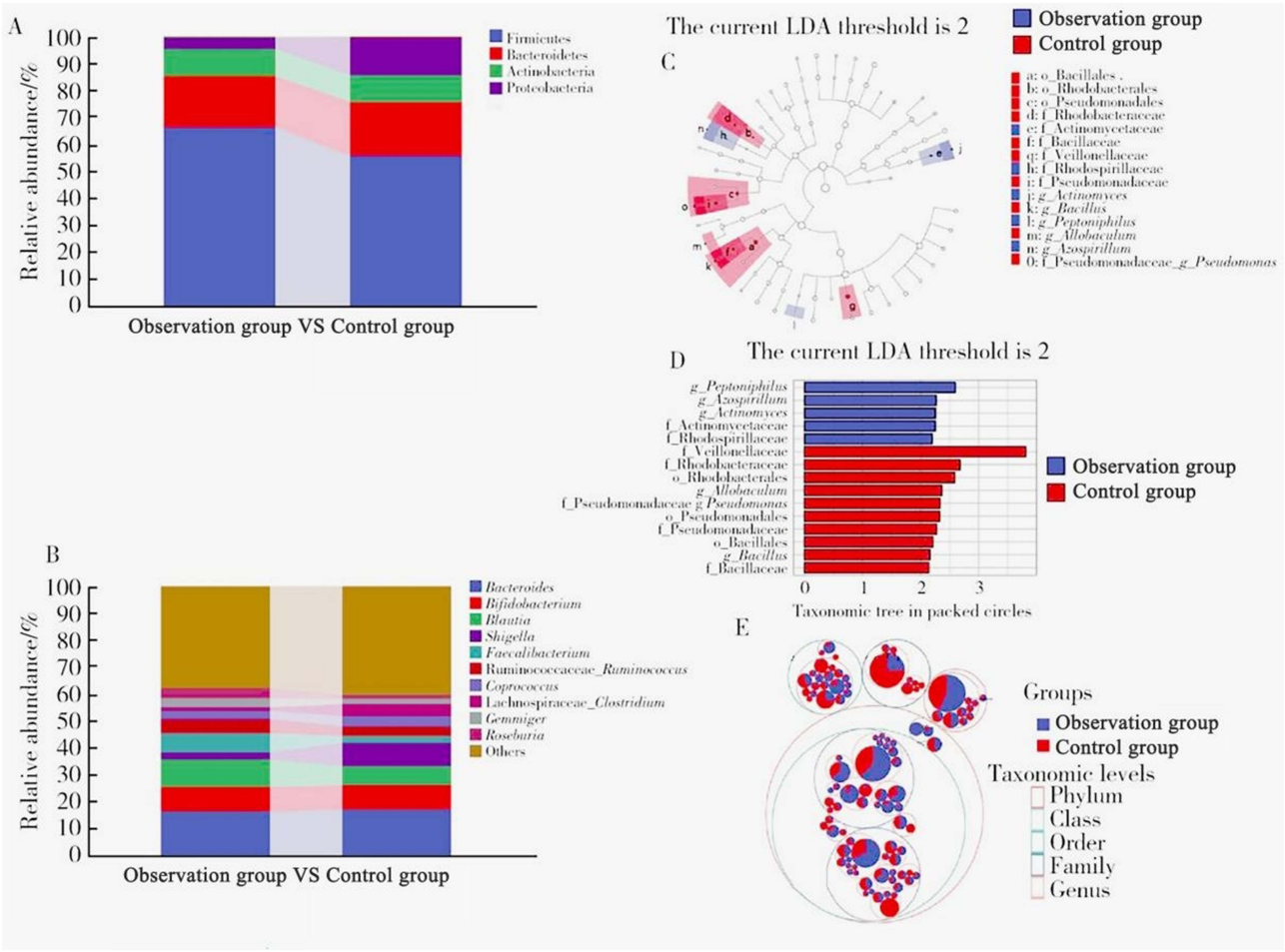

Figure 6 Analysis of Differences in Microbial Species Between the Two Groups. (**A**) Relative abundance of the observation group and control group at the phylum level; (**B**) Relative abundance of EHOUL analysis of the observation group and control group. Cladogram (**C**) shows the taxonomic hierarchy of the major taxa from phylum to genus. Histogram (**D**) shows the logarithmic score values of LDA analysis of each taxon; (**E**) Taxonomic hierarchy tree diagram of the observation group and control group. Large circles with different colors in the figure indicate different taxonomic levels, including phylum, class, order, family, and genus. The position of microbial species differences between the two groups at each classification grade can be intuitively seen.
Abbreviations: LEfSe, LDA effect size; LDA, linear discriminant analysis.

before and after radiotherapy, and there was no significant difference between the two groups. These results indicate that ovarian transposition offers some protection for ovarian endocrine function. The discrepancy with previous studies may be related to factors such as the distance of ovarian transposition, radiation dose, and timing.[20,21] The Kupperman score was significantly higher in the observation group, and the ovarian function retention rate was significantly higher compared to the control group. Furthermore, there was no significant difference in the incidence of abdominal pain, ovarian cysts, bowel obstruction, and cystitis between the two groups during follow-up, indicating that radiotherapy significantly improves the quality of life of cervical cancer patients after ovarian transposition without increasing the incidence of related adverse effects, suggesting a certain degree of safety.

Changes in Gut Microbiota Before and After Radiotherapy

Sequencing analysis of gut microbiota in patients with cervical cancer after radiotherapy showed no significant difference in α and β diversity indices between the two groups before and after radiotherapy, indicating that the overall richness and community structure of gut microbiota did not change significantly before and after radiotherapy. However, there were notable differences in the composition of gut microbiota between the observation group and the control group. At the phylum level, the relative abundance of Firmicutes was higher in the observation group, while Proteobacteria was relatively lower. At the genus level, significant differences were observed in Shigella, Faecalibacterium, and members of

the Lachnospiraceae family between the two groups. LEfSe analysis identified statistically significant differences in certain species between the two groups, such as higher abundances of Ruminococcaceae, Lachnospiraceae, and Actinobacteria in the observation group, whereas the Verrucomicrobia family, Rhodobacteraceae, and Rhodospirillales were more abundant in the control group. The cladogram also visually demonstrated differences in species composition at various taxonomic levels between the two groups.[22]

The lack of significant changes in the richness and community structure of gut microbiota before and after radiotherapy might be attributed to the inherent stability and adaptability of gut microbiota.[23] During radiotherapy, the interactions among microbiota, the regulation of metabolic products, and the body's own immune system and physiological metabolism may protect the stability of gut microbiota to some extent, meaning that the dose and duration of radiotherapy have not yet reached levels that significantly affect gut microbiota.[24] The differences in microbial composition between the observation group and the control group might result from complex mechanisms. On one hand, individual differences in baseline gut microbiota before radiotherapy, influenced by factors such as diet, lifestyle, and genetic background, might lead to varied responses of gut microbiota to radiotherapy across individuals.[25] On the other hand, radiotherapy might alter the gut microenvironment by changing factors like pH, redox potential, and immune cell distribution, thereby altering the composition of gut microbiota.[26] For example, the higher relative abundance of Firmicutes in the observation group might be related to the advantage of this phylum in certain metabolic processes, which could be affected by radiotherapy, leading to changes in its relative abundance. The higher abundance of Proteobacteria in the control group might be due to differences in the adaptability of this phylum to changes in the gut microenvironment caused by radiotherapy.[27] Additionally, radiotherapy might directly or indirectly affect the function of intestinal epithelial cells, thus influencing the interaction between gut microbiota and the host. The differences in species identified through LEfSe analysis could be due to varying sensitivities of these species to radiotherapy.[28,29]

Relationship Between Microbiota and Endocrine Function Before and After Radiotherapy and Future Research Directions

Currently, we can only speculate on the possible relationships between microbiota and endocrine function before and after radiotherapy based on the results: First, radiotherapy may alter the composition of gut microbiota by changing the gut microenvironment, and the changes in gut microbiota may indirectly affect the endocrine system by influencing gut metabolic function and immune regulation. For example, certain gut microbiota may be involved in the metabolism of sex hormones, and changes in microbiota composition could lead to hormonal metabolic disorders, thereby affecting endocrine function. Second, the gut microbiota is closely related to the body's immune system; radiotherapy may influence the immune regulatory function of gut microbiota, and changes in the immune system could affect the function of endocrine organs. Differences in gut microbiota composition between the observation and control groups might lead to different immune responses, thus affecting the degree of changes in endocrine function. Third, gut microbiota might affect the endocrine system's signal transduction by producing specific metabolites or signaling molecules, and changes in gut microbiota composition after radiotherapy might alter the production of these metabolites or signaling molecules, thereby affecting endocrine function.[30–32]

Future studies should focus on the mechanisms underlying microbiota-endocrine interactions, including animal and cell studies to uncover direct links between specific gut microbiota and endocrine organs. Additionally, investigating whether microbiota modulation can mitigate endocrine dysfunction or radiotherapy side effects could have clinical significance. Further research is also needed to identify the roles of different microbial taxa during radiotherapy and their potential as therapeutic targets.

Study Strengths and Limitations

This study highlights the novel association between gut microbiota and endocrine function in cervical cancer patients undergoing radiotherapy, utilizing advanced 16S rRNA sequencing and robust statistical analyses. However, limitations include the short study duration, lack of long-term follow-up, and inability to establish causality. Additionally, a sub-

analysis of microbiome differences in patients retaining ovarian function versus those who did not was limited by small sample size. Future research with larger cohorts and extended follow-up is needed to validate these findings and explore underlying mechanisms.

Conclusion

This study conducted a controlled analysis of 100 patients undergoing radical surgery for cervical cancer, evaluating the effects of ovarian transposition on ovarian function, endocrine function, quality of life, adverse reactions, and gut microbiota composition. The results showed that after radiotherapy, the control group had higher increases in serum FSH and LH levels and greater decreases in serum E2 levels compared to the ovarian transposition group, while the ovarian function retention rate was significantly higher in the ovarian transposition group. There was no significant difference in the incidence of adverse reactions between the two groups. Additionally, gut microbiota sequencing results indicated that although there were no significant differences in α and β diversity indices between the two groups before and after radiotherapy, there were distinct differences in microbiota composition at the phylum and genus levels. LEfSe analysis identified species with statistically significant differences. In summary, ovarian transposition offers some degree of protection for ovarian function in cervical cancer patients, and radiotherapy affects gut microbiota composition, though its specific relationship with endocrine function requires further research to elucidate the mechanisms and clinical significance.

Disclosure

The authors report no conflicts of interest in this work.

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