Journal of
Gynecology and Women's Health
ISSN 2474-7602

Juniper Publishers
key to the Researchers

Research Article
Volume 22 Issue 2 - October 2021
DOI: 10.19080/JGWH.2021.22.556085

J Gynecol Women's Health

Disease-Free Survival after Wertheim-Meigs Radical Hysterectomy Vs. Robotic-Assisted Radical Hysterectomy for Early-Stage Cervical Squamous Cell Carcinoma

Alin Popescu[1], Stelian Pantea[2]*, Felix Bratosin[2], Mircea Selaru[2], Ciprian Duta[2], Sorin Dema[3], Manuela Popescu[4], Mirela Loredana Grigoras[5], Adrian Gluhovschi[1], Elena Bernad[1], Adelina Geanina Mocanu[1] and Marius Craina[1]

[1]*Department of Obstetrics and Gynecology, "Victor Babes" University of Medicine and Pharmacy, Romania*

[2]*Department of General Surgery, "Victor Babes" University of Medicine and Pharmacy, Romania*

[3]*Service of Radiotherapy, Emergency City Hospital, Romania*

[4]*Department of Neonatology, "Victor Babes" University of Medicine and Pharmacy, Romania*

[5]*Department of Anatomy and Embryology, "Victor Babes" University of Medicine and Pharmacy, Romania*

Submission: September 29, 2021; **Published:** October 08, 2021

***Corresponding author:** Stelian Pantea, Department of General Surgery, "Victor Babes" University of Medicine and Pharmacy, Romania

Abstract

Cervical cancer is the second most common cancer in young women, being responsible for more than 200 thousand deaths worldwide. The pap-smear test provides a cheap and accessible method of screening, thus allowing the early diagnosis in most of the cases and the possibility of curative approaches through surgical interventions. The aim of this study was to evaluate the surgical outcomes and the 5-year disease-free survival after Wertheim-Meigs radical hysterectomy vs. robotic-assisted radical hysterectomy. In this longitudinal study, we operated 160 patients with stage IA2-IB1 squamous cell carcinoma on a 4 to 1 frequency matching, 128 by open surgery, and 32 respectively by the robot-assisted technique. The Clavien-Dindo scale was used to assess postoperative complications and a 5-year systematic follow-up for patient surveillance. The 5-year disease-free-survival was not statistically different between the two surgical methods Patients in the robot-assisted group had better postoperative outcomes, and the proportion of relapses at 2 years was lower than in the open surgery arm, the difference was not significant. The open surgery method correlated with lower hemoglobin levels and higher rates of post-interventional infections. The robotic-assisted radical hysterectomy appears to be superior at short term in this particular population by number of postoperative complications and relapses, but the 5-year disease-free survival was not influenced by the promising approach of robot-assisted surgery.

Keywords: Cervical cancer; Disease-free survival; Radical hysterectomy; Robotic surgery; Squamous cell carcinoma

Abbreviations: SCC: Squamous-Cell Carcinoma; ADC: Adenocarcinomas; HPV: Human Papillomavirus; CIN: Cervical Intraepithelial Neoplasia; HIV: Human Immunodeficiency Virus; SEER: Surveillance, Epidemiology, and End Results; FIGO: Federation of Gynecology and Obstetrics; BMI: Body Mass Index

Introduction

Cervical cancer currently occupies a second place as the most common cancer in young women between 15 and 44 years old, and it is responsible for more than 500 thousand cases every year worldwide [1], ranking third as the most common cancer type. Globally, around 200 thousand women die every year from cervical cancer, where both the mortality rates and incidence rates have the highest count in developing countries from the sub-Saharan countries [2]. Women in the 35-66 years old age group account for two-thirds of all cervical cancers, with a median age of diagnosis at 49 years [3]. The prognosis in developed countries such as the UK is excellent, where more than 60% of women survive ten years after diagnosis. The 5-year relative survival for FIGO stage I is 96% in the UK and 92% in the USA [3-4]. On the other side, 87% of all deaths caused by cervical cancer happen in developing countries [2].

Squamous-cell carcinoma (SCC) accounts for 90% of all cervical cancers, while the remaining part being represented by adenocarcinomas (ADC) in around 9% of cases, and other histology variants 1% [5]. The sexually transmitted human papillomavirus (HPV) is the main contributor to the development of SCC of the cervix [6], being classified as low-risk and high-risk, also known as oncogenic HPV type. If the viral infection is not cleared within 12 to 24 months, it will tend to progress to precancerous states [7], starting at cervical intraepithelial neoplasia (CIN) and evolving to cancer. According to the VIVIANE study [8], the highest risk strains are in descending order HPV33, HPV16, HPV 18, HPV 31, and HPV45. The high-risk HPV is found in 99.7% of cervical cancers [9], but other risk factors such as Chlamydia trachomatis were discovered in 40% of SCC [10], or the human immunodeficiency virus (HIV) and Herpes simplex virus 2 (HSV-2) infections being associated to cervical cancer [11]. Nutritional behavior, oral contraceptive pills use, smoking, obesity, and inflammatory diseases were also correlated with a higher chance of developing cervical cancer [12].

Cervical cancer starts as confined to the cervix uteri and locally develops to the parametrium, uterus, and vagina, having an initial lymphatic spread to the obturator, external and internal iliac, then further to the para-aortic lymph nodes, while distant metastasis occurs in later stages of the disease by hematogenous spread to lungs, liver, and skeleton, most commonly [13]. The Surveillance, Epidemiology, and End Results (SEER) staging of the American Cancer Society groups cervical cancer as localized, regional, and distant, while the International Federation of Gynecology and Obstetrics (FIGO) is the most developed staging system currently available, ranging from stage I to stage IVB [14]. The early-stage cervical cancer is defined by FIGO as IA-IB1, while the recommendations stand for radical surgery for stages IA2-IB1, associated with radiotherapy in selected cases based on parameters such as lymph node metastasis local parametrial invasion, tumor size, deep stromal invasion, and positive surgical margins [15].

The Wertheim-Meigs procedure stands for radical hysterectomy with pelvic lymphadenectomy in an open surgery fashion, which was implemented more than 100 years ago and was slightly modified over time according to the advances of surgical and medical practice [16]. The development of surgical robots allowed multiple procedures to be performed in a minimally invasive manner, including the robotic-assisted hysterectomy that has the same purpose as the Wertheim-Meigs procedure. Although several studies suggest the superiority of open surgery for cervical cancer [17-19], it is still a debate in comparing between open surgery and robot-assisted surgery in specific histological types of cervical cancer considering the DFS that our study aims to clarify.

Materials and Methods

A longitudinal cohort study without random treatment allocation was designed according to the STROBE guidelines [20] to include patients with cervical cancer that qualify for radical hysterectomy with pelvic lymphadenectomy in the Obstetrics and Gynecology Department of the Timis County Emergency Clinical Hospital "Pius Brinzeu" from Timisoara, Romania. The study consisted of two stages; the initial recruitment and intervention phase between 9 February 2014 and 31 August 2016, and the later follow-up phase between 1 September 2016 and 1 September 2021.

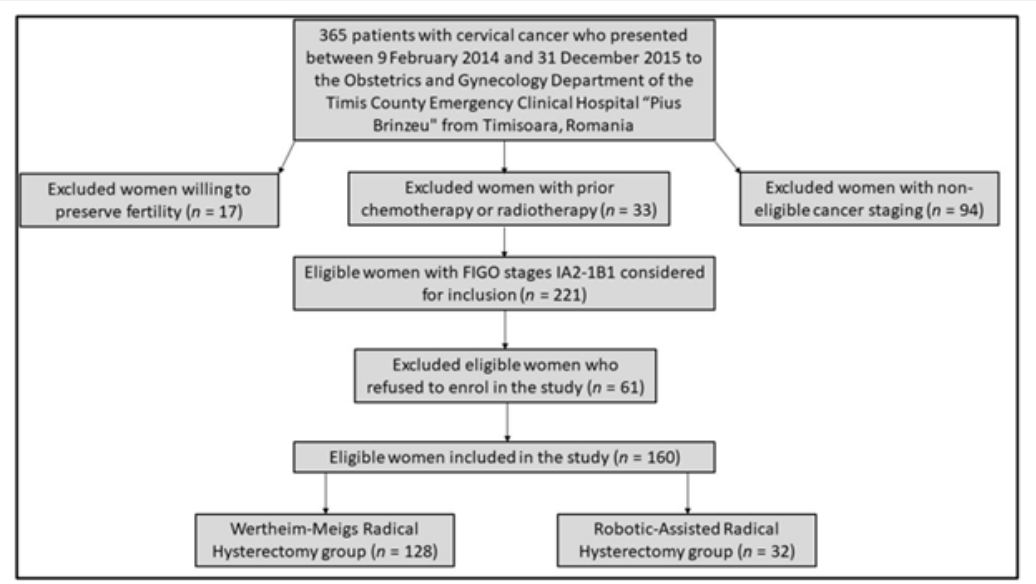

Figure 1: Flowchart of the study inclusion and eligibility criteria.

The inclusion criteria (Figure 1) consisted of fulfilling the following: (1) obtaining patient's informed consent to participate in the study and willingness to undergo radical hysterectomy with pelvic lymphadenectomy, (2) histopathologic diagnosis of

How to cite this article: Alin P, Stelian P, Felix B, Mircea S, Ciprian D, et al. Disease-Free Survival after Wertheim-Meigs Radical Hysterectomy Vs. Robotic-Assisted Radical Hysterectomy for Early-Stage Cervical Squamous Cell Carcinoma. J Gynecol Women's Health. 2021: 22(2): 556085.
DOI: 10.19080/JGWH.2021.21.556085

squamous cell carcinoma, (3) FIGO stages IA2-1B1, according to the FIGO staging system prior to the 2018 version. The women willing to preserve fertility, the recurrent cases, and those undergoing chemotherapy or radiotherapy were excluded from the study. We also excluded patients suffering from associated systemic inflammatory diseases and those under immunosuppressant therapy. During phase 1 of the study, a number of 221 patients were considered for inclusion based on the eligibility criteria, although 61 women refused to enroll. Case-matching was not possible due to financial constraints and availability of the da Vinci robot equipment used in the study, although frequency matching based on cancer staging was considered in a 4 to 1 manner to avoid confounding effects of an unequal distribution [21]. Considering that our department had 32 available sets for the da Vinci robot, a total of 32 eligible patients were operated using the robotic-assisted hysterectomy method, while the other 128 patients were included in the Wertheim-Meigs open surgery group. An even mix of teams with equivalent surgical expertise performed both types of surgeries involved in the study.

Prior to patient inclusion, cervical biopsy or conization was performed to assess the histology and staging of the disease based on stromal invasion [22]. Computed tomography was done to assess the lymph node involvement, as well as to define the local and regional extent [23]. Before undergoing radical hysterectomy, patients were thoroughly checked to ensure that there are no major medical contraindications to surgery. Preparation for surgery consisted of placing a central venous catheter and ensured for the availability of cross-matched blood to prepare for any potential blood loss. Patients received 5000 units of Heparin prior to surgery and a 5000 units daily dose in the postoperative period for thromboembolic prophylaxis. A prophylactic first-generation cephalosporin was given within 30 minutes of skin incision or clindamycin for those allergic to the first option [24]. Complete pelvic lymphadenectomy was executed in all 160 cases, removing the obturator, external, internal, common iliac lymph nodes, and the presacral lymphatic tissues. Preoperative external radiotherapy or brachytherapy was not performed.

The study variables included demographic data, comorbidities, antibiotic use, com-plications after surgery, FIGO staging, chemotherapy, radiotherapy, and follow-up results. Complications after surgery were classified according to the Clavien-Dindo scale [25]. All patients were followed up for at least five years under regular surveillance based on recent recommendations [26], having followed–up visits every two months in the first two years, and every 6-12 months in years 3-5, defining the DFS as the time elapsed from surgery until local recurrence, lymph node recurrence, or metastasis. Follow-up by phone or e-mail to patients or patients' relatives was a solution to determine the status of those who failed to attend checkup appointments. The follow-up visits included general physical and pelvic examination with cytology and determining the squamous cell carcinoma antigen (SCC Ag) marker specific for squamous cell carcinoma [27]. The cytology test and abdominal computed tomography were performed once a year. All patients with pelvic lymph node metastasis diagnosed on CT/MRI after surgery underwent external radiation therapy using 50.4Gy for the nodes smaller than 2cm and radiation boost over 50.4Gy for the nodes bigger than 2cm [28], while patients with grade 3 squamous cell carcinoma received early adjuvant chemotherapy three weeks after surgery [29].

Statistical analysis was performed using the IBM SPSS software version 26.0. Categorical variables were represented as absolute and percentage values. Student's t-test and Mann-Whitney U-test were used for continuous and discrete variables, respectively. Spearman's (rho) correlation coefficient was determined for non-parametric variables, while Pearson correlation was used to analyze parametric data. The $\chi 2$ and Fisher's exact tests were used for statistical analysis of proportions. A Kaplan-Meier analysis estimated the disease-free survival rate based on cancer staging [30]. The significance threshold was set for $\alpha=0.05$.

The Local Commission of Ethics for Scientific Research from the Timis County Emergency Clinical Hospital "Pius Brinzeu" from Timisoara, Romania operates under article 167 provisions of Law no. 95/2006, art. 28, chapter VIII of order 904/2006 and with EU GCP Directives 2005/28/EC, International Conference of Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), and with the Declaration of Helsinki – Recommendations Guiding Medical Doctors in Biomedical Re-search Involving Human Subjects. The current study was approved on the 9 February 2014, with the approval number 4. All study participants agreed to be involved in this study by signing an informed consent form.

Result

During phase one of the study, a total of 160 eligible patients were considered for surgery, where 32 (20%) were assigned to the robotic surgery group, and the other 128 (80%) in the open surgery group. From the 160 cases of squamous cell carcinoma of the cervix, 50 (31.2%) patients had IA2 staging and 110 (68.8%) IB1 staging, respectively. In the robotic surgery arm, ten patients were assigned with IA2 staging, while the other 40 cases of IA2 staging went into the open surgery arm. A total of 22 patients with cancer stage IA2 were assigned to the robotic surgery arm, and the remaining 88 went to the open surgery arm to allow for a 4 to 1 proportional distribution between the two groups (Table 1).

The median age of enrollment in the study was 54 years, being equivalent to the date of cancer diagnosis, ranging from 24 to 83 years, with the open-surgery group averaging 54 years at diagnosis versus 55 years in the robot-surgery group (p-value = 0.768). Overall, the body mass index (BMI) of patients in the open-surgery arm was 26, compared to 27 in the robot-surgery arm (p-value = 0.603). There was no significant difference in the median follow-up period between the two study groups (53 months vs. 54 months, p-value = 0.698), as well as no significant difference in the median DFS between open surgery and robotic surgery (42 months vs. 47 months, p-value = 0.461). The analysis of tumor size

How to cite this article: Alin P, Stelian P, Felix B, Mircea S, Ciprian D, et al. Disease-Free Survival after Wertheim-Meigs Radical Hysterectomy Vs. Robotic-Assisted Radical Hysterectomy for Early-Stage Cervical Squamous Cell Carcinoma. J Gynecol Women's Health. 2021: 22(2): 556085.
DOI: 10.19080/JGWH.2021.21.556085

showed no significant difference in proportions between the two study arms at the 2cm threshold for tumor size (p-value = 0.871), although a bigger tumor size was significantly correlated to cancer relapsing within five years (rho = 0.465, p-value = 0.001). A bigger tumor size was also correlated with a higher cancer grade (rho = 0.240, p-value = 0.032). The cancer relapse (Table 2) was positively associated to a high tumor grade (p-value = 0.001), overall survival (p-value = 0.001), number of lymph nodes involved (p-value = 0.001), and postoperative complications (p-value = 0.001). There was no significant difference between the study groups in proportions of lymph nodes involved (p-value = 0.141), tumoral differentiation grade (p-value = 0.967), and adjuvant treatment received. The postoperative complications evaluated by the Clavien-Dindo scale ranging from a score of 0 (no significant complications) to a score of 5, evaluated the minimally-invasive robotic-surgery technique as having better outcomes than the classic open-surgery technique (p-value = 0.001), with 24 (75%) patients from the robot-surgery arm experiencing no complications, versus 42 (33%) patients from the open-surgery arm with no postoperative complications.

Table 1: Baseline sample characteristics and comparison of outcomes between study groups.

Characteristics	Full Cohort (N = 160)	Open Surgery (N = 128)	Robotic Surgery (N = 32)	P-Value
Age, years	54	54	55	0.768
BMI, kg/m^2	26	26	27	0.603
Overall survival, n (%)	136 (85.0)	108 (84.3)	28 (87.5)	0.554
Median 5-year DFS (months)	45	42	47	0.461
Median follow-up (months)	54	53	54	0.698
Tumor Size, n (%)				**0.871**
<2cm	62 (38.7)	50 (39.0)	12 (37.5)	
≥2cm	98 (61.3)	78 (61.0)	20 (62.5)	
Lymph Node Involvement				**0.141**
0	112 (70.0)	94 (73.4)	18 (56.3)	
1	18 (11.3)	12 (9.4)	6 (18.7)	
>1	30 (18.8)	22 (17.2)	8 (25.0)	
FIGO Stage, n (%)				**1**
IA2	50 (31.2)	40 (31.3)	10 (31.2)	
IB1	110 (68.8)	88 (68.7)	22 (68.8)	
Differentiation Grade, n (%)				**0.967**
Grade 1	92 (57.5)	74 (57.8)	18 (56.3)	
Grade 2	50 (31.3)	40 (31.2)	10 (31.3)	
Grade 3	18 (11.3)	14 (11.0)	4 (12.4)	
Relapse (n = 38), n (%)				**0.868**
Local	20 (12.5)	16 (12.5)	3 (9.4)	
Regional	10 (6.3)	8 (6.3)	2 (6.3)	
Distant	8 (5.0)	8 (6.3)	1 (3.2)	
Total	38 (23.7)	32 (25.0)	6 (18.8)	
Adjuvant Treatment, n (%)				
Radiotherapy-only	28 (17.5)	20 (14.0)	8 (31.3)	0.211
Chemotherapy-only	8 (5.0)	5 (3.1)	3 (12.5)	0.204
Radio-chemotherapy	10 (6.3)	6 (4.7)	4 (12.5)	0.102
Clavien-Dindo Scale, n (%)				**0.001**
No complications	66 (41.2)	42 (32.8)	24 (75.0)	
Score 1	64 (40.0)	60 (46.8)	4 (12.4)	
Score 2	24 (15.0)	22 (17.2)	2 (6.3)	
Score 3	6 (3.8)	4 (3.2)	2 (6.3)	
Score 4	0 (0.0)	0 (0.0)	0 (0.0)	
Score 5	0 (0.0)	0 (0.0)	0 (0.0)	

How to cite this article: Alin P, Stelian P, Felix B, Mircea S, Ciprian D, et al. Disease-Free Survival after Wertheim-Meigs Radical Hysterectomy Vs. Robotic-Assisted Radical Hysterectomy for Early-Stage Cervical Squamous Cell Carcinoma. J Gynecol Women's Health. 2021: 22(2): 556085. DOI: 10.19080/JGWH.2021.21.556085

Table 2: Correlation analysis.

		Tumor Size	Relapse	Grading	OS	Lymph Nodes	Clavien-Dindo
Tumor Size	Rho	1	.465**	.240*	-0.19	0.15	-0.069
	P-value		0.001	0.032	0.09	0.185	0.54
Relapse	Rho	.465**	1	.469**	-.489**	.486**	.305**
	P-value	0.001		0.001	0.001	0.001	0.001
Grading	Rho	.240*	.469**	1	-.315**	0.171	0.036
	P-value	0.001	0.001		0.004	0.127	0.746
OS	Rho	-0.19	-.489**	-.315**	1	-.499**	-.363**
	P-value	0.09	0.001	0.004		0.001	0.009
Lymph Nodes	Rho	0.149	.486**	0.171	-.499**	1	.229*
	P-value	0.185	0.001	0.127	0.001		0.041
Clavien-Dindo	Rho	-0.069	.305**	0.036	-.363**	.229*	1
	P-value	0.54	0.005	0.746	0.009	0.041	

** Correlation is significant at the 0.01 level (2-tailed); * Correlation is significant at the 0.05 level (2-tailed).

The median follow-up duration was 54 months, ranging from 19 to 66 months. Cancer relapse was observed in 38 (23.7%) individual patients during phase 2 of the study, with local relapse being the most common finding in 20 (12.5%) of all patients, followed by regional relapse in 10 (6.3%) cases, and lastly distant metastasis in 8 (5%) women. The average time observed from surgical intervention until cancer relapse was 42 months, ranging from 28 to 54 months. The Kaplan-Meier survival analysis (Figure 2) showed a statistically insignificant difference in DFS between the robotic-surgery study arm (p = 0.049), where the average DFS was 42 months in the open-surgery arm, compared to the average 47 months in the robotic-surgery arm (Table 1).

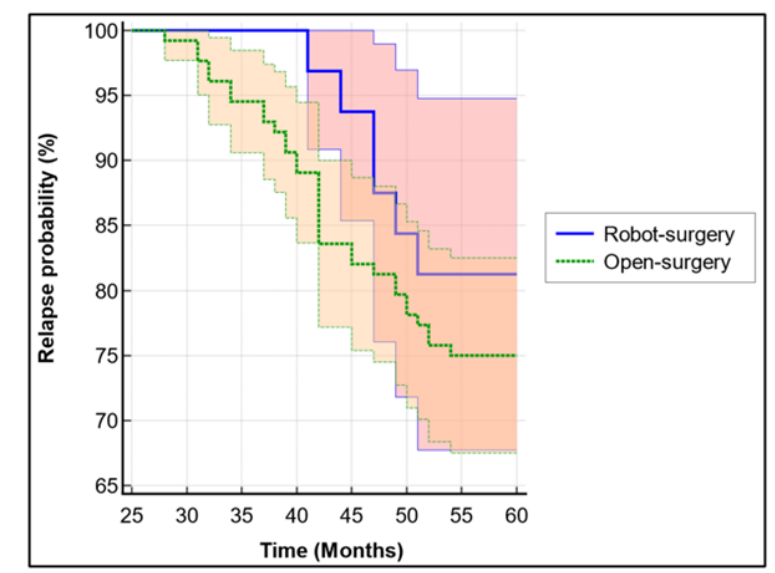

Figure 2: Disease-free survival plot.

The overall 5-year survival was 85%, with 24 deaths (15%), where the full cohort analysis observed a relatively equal survival rate in the open-surgery group when com-pared to the robot-surgery group (84.3% vs. 87.5%, p-value = 0.554) (Table 1). Out of the 24 recorded deaths, four patients died in the first 28 months due to causes unrelated to the malignant process. The Kaplan-Meier survival analysis estimated an insignificant difference in the 5-year overall survival (Figure 3) between patients from the robotic-assisted hysterectomy study arm and open-surgery study arm (p = 0.440), with the average survival estimate at 58 months for patients operated using the Wertheim-Meigs technique, and 59 months respectively for those undergoing the robotic surgery. The average time of death in the robotic-surgery arm occurred at 49 months, versus 46 months in the open-surgery group.

How to cite this article: Alin P, Stelian P, Felix B, Mircea S, Ciprian D, et al. Disease-Free Survival after Wertheim-Meigs Radical Hysterectomy Vs. Robotic-Assisted Radical Hysterectomy for Early-Stage Cervical Squamous Cell Carcinoma. J Gynecol Women's Health. 2021: 22(2): 556085. DOI: 10.19080/JGWH.2021.21.556085

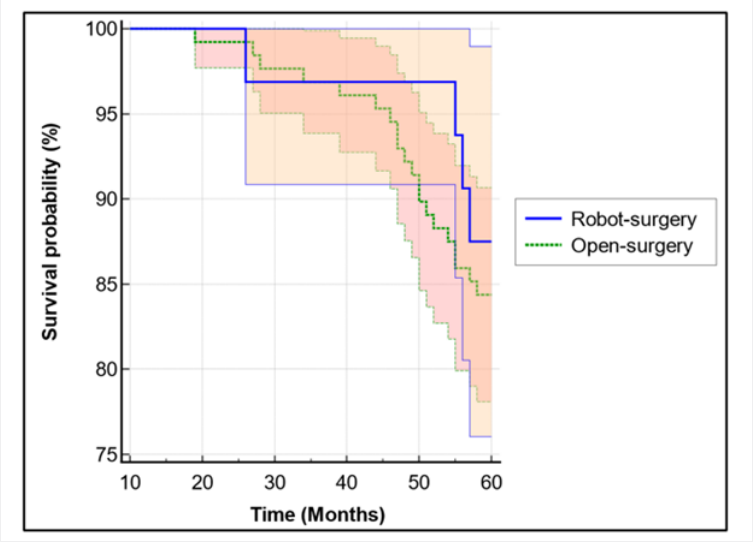

Figure 3: Overall survival plot.

Discussion

The current study provides a comprehensive analysis of the disease-free survival and overall survival in early-stage squamous cell cervical cancer, as well as the postoperative outcomes in comparison between two surgical approaches, the classic open surgery for radical hysterectomy with pelvic lymphadenectomy and the modern robotic surgery radical hysterectomy with pelvic lymphadenectomy. Several wider studies [31] have analyzed the same research question to compare the abdominal surgery versus a minimally-invasive surgical approach, although radical laparoscopic hysterectomy with pelvic lymphadenectomy replaced the robotic minimally-invasive method. In this nationwide study from the Netherlands, there was a higher mortality and cancer recurrence in the open abdominal surgery study arm, but there was no statistically significant difference in the disease-free survival and overall survival.

Although the 5-year overall survival of FIGO stage I cervical cancer is reported to stand above 90% [32], our study reported lower OS (85%) that can be attributed to a higher incidence of high-grade squamous cell carcinoma (11%). A recent comprehensive study [33] published the analysis of over 30 thousand women with cervical cancer, where the results indicated grade 3 tumors having a 4.48 hazard ratio (HR) as an independent association with a lower survival rate. The lower OS reported by our study may also be at-tributed to the old age of participants, having three patients older than 75 years and 25 patients older than 60. Literature findings [34] suggest that women over 70 are less likely to receive aggressive treatment for cervical cancer due to associated comorbidities, thus the potential of faster disease progression and negative outcomes. The same study observed an HR of 1.46 for the patient age group 50-69 in relation to a negative prognostic value.

Cervical cancer stages IA2-IB1 stand as the main indication for radical hysterectomy, although some studies suggest the same results when non-bulky IA1 and IB2 stage tumors undergo the same treatment scheme [35]. Our study is in accordance with another research made on the management of early-stage cervical carcinoma through radical hysterectomy [36] that achieved similar results but including stages IA1 and IB2 in the study cohort. Over 1500 patients were surveilled for a minimum of 60 months, with results showing an 88.7% OS. The same study reported that cancer grading isn't a significant predictor for DFS and OS, as found observed here.

Robot-assisted surgery is a fairly new approach that is meant to step further into the minimally-invasive world of surgery, being proven superior to the laparoscopic method [37]. Our study confirmed the superiority of robotic surgery regarding postoperative com-plications and fewer relapses at 2 years, with the concern of involving a small sample. We had better expectations from the robotic-surgery approach in terms of DFS, but the results were insignificant compared to the open-surgery method, although poor results involving the minimally-invasive robotic surgery can be attributed to this method having a longer learning curve [38], thus intervention outcomes might be influenced by subjective factors such as surgeon preparedness and prior experience in open and laparoscopic surgery, as previously observed [39].

Probably the biggest study to date comparing the two surgical methods discussed in our research was a clinical trial performed in 2017 on a number of 631 patients eligible for radical hysterectomy for stages IA1-IA2-IB1 cervical cancer [18]. In that study, minimally invasive radical hysterectomy was linked with poorer rates of disease-free and overall survival in women with early-stage cervical cancer than open abdominal radical

How to cite this article: Alin P, Stelian P, Felix B, Mircea S, Ciprian D, et al. Disease-Free Survival after Wertheim-Meigs Radical Hysterectomy Vs. Robotic-Assisted Radical Hysterectomy for Early-Stage Cervical Squamous Cell Carcinoma. J Gynecol Women's Health. 2021: 22(2): 556085. DOI: 10.19080/JGWH.2021.21.556085

hysterectomy. However, differences in our studies might occur due to our focus on the squamous cell cervical carcinoma, while the bigger study included all histological types in re-search. Also, another difference is the use of both laparoscopic and robotic-assisted methods of minimally assisted radical surgery in the clinical trial by Ramirez et al., while we used solely the da Vinci robot. It is important to mention a randomized controlled trial coordinated in Sweden by Falconer et al. [40] comparing robot vs open radical hysterectomy, estimated to close in 2027, since we believe its results will certainly be of fundamental importance to reinforce the conclusions of the present study, or to bring new and surprising observations.

Conclusion

There is an apparent superior performance of the robotic-assisted surgical method for radical hysterectomy with pelvic lymphadenectomy compared with the classic open surgery in what regards short-term survival in patients with stage IA2-IB1 squamous cell cervical cancer, although the study showed no significant difference at the 5-year follow-up. Also, the overall survival was not influenced by the modern surgical approach. The minimally-invasive robotic surgery brought significantly fewer immediate post-operative complications, but did not show any differences in long-term complications, since the patients included in this study had no statistically significant differences in relapses and the need for adjuvant treatment. Lastly, the small cohort size of the robotic-surgery arm can affect the reliability of our findings and justifying the presented conclusions, making any superiority of the minimally invasive approach hard to support.

Institutional Review Board Statement

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Local Commission of Ethics for Scientific Research from the Timis County Emergency Clinical Hospital "Pius Brinzeu" from Timisoara, Romania, no. 95/2006 and approved on 2 February 2014.

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patient(s) to publish this paper.

Data Availability Statement

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

References

1. Escobar N, Plugge E (2020) Prevalence of human papillomavirus infection, cervical intraepithelial neoplasia and cervical cancer in imprisoned women worldwide: a systematic review and meta-analysis. J Epidemiol Community Health 74(1): 95-102.
2. Memon A, Bannister P (2019) Epidemiology of Cervical Cancer. In: Farghaly S (Ed), Uterine Cervical Cancer. Springer, Cham, pp. 1-16.
3. (2020) The Surveillance, Epidemiology, and End Results (SEER) Program.
4. (2020) Cancer Research UK.
5. Nowakowski A, Cybulski M, Buda I, Iwona J, Olszak-Wąsik K, et al. (2016) Cervical Cancer Histology, Staging and Survival before and after Implementation of Organised Cervical Screening Programme in Poland. PLoS One 11(5): e0155849.
6. Stanley M (2010) Pathology and epidemiology of HPV infection in females. Gynecologic Oncology 117(2 suppl): S5-S10.
7. Reid R, Stanhope CR, Herschman BR, Booth E, Phibbs GD, et al. (1982) Genital warts and cervical cancer. I. Evidence of an association between subclinical papillomavirus infection and cervical malignancy. Cancer 50(2): 377-387.
8. Skinner RS, Wheeler CM, Romanowski B, Castellsagué X, Lazcano-Ponce E, et al. (2016) Progression of HPV infection to detectable cervical lesions or clearance in adult women: Analysis of the control arm of the VIVIANE study. Int J Cancer 138(10): 2428-2438.
9. McLaughlin-Drubin ME, Munger K (2008) Viruses associated with human cancer. Biochim Biophys Acta 1782(3): 127-150.
10. Koskela P, Anttila T, Bjørge T, Brunsvig A, Dillner J, et al. (2000) Chlamydia trachomatis infection as a risk factor for invasive cervical cancer. Int J Cancer 85(1): 35-39.
11. Smith JS, Herrero R, Bosetti C, Munoz N, Bosch FX, et al. (2002) Herpes simplex virus-2 as a human papillomavirus cofactor in the etiology of invasive cervical cancer. J Natl Cancer Inst 94(21): 1604-1613.
12. Momenimovahed Z, Salehiniya H (2017) Incidence, mortality and risk factors of cervical cancer in the world. Biomedical Research and Therapy 4(12): 1795-1811.
13. Zhou S, Peng F (2020) Patterns of metastases in cervical cancer: a population-based study. Int J Clin Exp Pathol 13(7): 1615-1623.
14. Bhatla N, Berek J, Cuello M (2018) New revised FIGO staging of cervical cancer. Abstract S020.2. Presented at the FIGO XXII World Congress of Gynecology and Obstetrics. Int J Gynecol Obstet 143(3): 12584.
15. Thomakos N, Trachana SP, Davidovic-Grigoraki M, Rodolakis A (2016) Less radical surgery for early-stage cervical cancer: To what extent do we justify it?-Our belief. Taiwan J Obstet Gynecol 55(4): 495-498.
16. Swailes AL, Gockley AP, Kesterson R, Joshua P (2017) The Wertheim hysterectomy: Development, modifications, and impact in the present day. Gynecol Oncol 145(1): 3-8.
17. Wang Y, Li B, Ren F, Song Z, Ouyang L, et al. (2020) Survival After Minimally Invasive vs. Open Radical Hysterectomy for Cervical Cancer: A Meta-Analysis. Front Oncol 10.
18. Ramirez PT, Frumovitz M, Pareja R, Lopez A, Vieira M, et. al. (2018) Minimally Invasive versus Abdominal Radical Hysterectomy for Cervical Cancer. N Engl J Med 379(20): 1895-1904.
19. Qin M, Siyi L, Huang HF, et al. (2020) A Comparison of Laparoscopies and Laparotomies for Radical Hysterectomy in Stage IA1-IB1 Cervical Cancer Patients: A Single Team With 18 Years of Experience. Front Oncol 10: 1738.
20. Cuschieri S (2019) The STROBE guidelines. Saudi J Anaesth 13(Suppl 1): S31-S34.
21. de Graaf MA, Jager KJ, Zoccali C, Dekker FW (2011) Matching, an Appealing Method to Avoid Confounding? Nephron Clinical Practice 118(4): c315-c318.
22. Freeman SJ, Aly AM, Kataoka MY, Addley HC, Reinhold C, et al. (2012) The revised FIGO staging system for uterine malignancies: implications for MR imaging. Radiographics 32(6): 1805-1827.

How to cite this article: Alin P, Stelian P, Felix B, Mircea S, Ciprian D, et al. Disease-Free Survival after Wertheim-Meigs Radical Hysterectomy Vs. Robotic-Assisted Radical Hysterectomy for Early-Stage Cervical Squamous Cell Carcinoma. J Gynecol Women's Health. 2021: 22(2): 556085. DOI: 10.19080/JGWH.2021.21.556085

23. Hricak H, Gatsonis C, Chi DS, Amendola MA, Brandt K, et al. (2005) Role of imaging in pretreatment evaluation of early invasive cervical cancer: results of the intergroup study American College of Radiology Imaging Network 6651-Gynecologic Oncology Group 183. J Clin Oncol 23(36): 9329-9337.

24. Van EN, Schalkwyk VJ, Yudin MH, Allen VM, Bouchard C, et al. (2012) Antibiotic Prophylaxis in Gynaecologic Procedures. J Obstet Gynaecol Can 34(4): 382-391.

25. Dindo D, Demartines N, Clavien PA (2004) Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 240(2): 205-213.

26. Elit L, Fyles AW, Oliver TK, Devries-Aboud MC, Fung-Kee-Fung M, et al. (2010) Members of the Gynecology Cancer Disease Site Group of Cancer Care Ontario's Program in Evidence-Based Care. Follow-up for women after treatment for cervical cancer. Curr Oncol 17(3): 65-69.

27. Fu J, Wang W, Wang Y, Chengeng L, Peichang W, et al. (2019) The role of squamous cell carcinoma antigen (SCC Ag) in outcome prediction after concurrent chemoradiotherapy and treatment decisions for patients with cervical cancer. Radiat Oncol 14(1): 146.

28. Hata M, Koike I, Miyagi E, Numazaki R, Asai-Sato M, et al. (2013) Radiation therapy for pelvic lymph node metastasis from uterine cervical cancer. Gynecol Oncol 131(1): 99-102.

29. Asano H, Todo Y, Watari H (2016) Adjuvant chemotherapy for early-stage cervical cancer. Chin J Cancer Res 28(2): 228-234.

30. Kaplan EL, Meier P (1958) Nonparametric estimation from incomplete samples. J Am Stat Assoc 53(282): 457- 481.

31. Wenzel HHB, Smolders RGV, Beltman JJ, Lambrechts S, Trum HW, et al. (2020) Survival of patients with early-stage cervical cancer after abdominal or laparoscopic radical hysterectomy: a nationwide cohort study and literature review. European Journal of Cancer 133: 14-21.

32. Yan DD, Tang Q, Chen JH, Tu YQ, Lv XJ, et al. (2019) Prognostic value of the 2018 FIGO staging system for cervical cancer patients with surgical risk factors. Cancer Manag Res 11: 5473-5480.

33. Matsuo K, Mandelbaum RS, Machida H, Purushotham S, Grubbs BH, et al. (2018) Association of tumor differentiation grade and survival of women with squamous cell carcinoma of the uterine cervix. J Gynecol Oncol 29(6): e91.

34. Quinn BA, Deng X, Colton A, Bandyopadhyay D, Carter JS, et al. (2019) Increasing age predicts poor cervical cancer prognosis with subsequent effect on treatment and overall survival. Brachytherapy 18(1): 29-37.

35. Tsai CS, Lai CH, Wang CC, Chang JT, Chang TC, et al. (1999) The prognostic factors for patients with early cervical cancer treated by radical hysterectomy and postoperative radiotherapy. Gynecol oncol 75(3): 328-333.

36. Michalas S, Rodolakis A, Voulgaris Z, Vlachos G, Giannakoulis N, et al. (2002) Management of early-stage cervical carcinoma by modified (Type II) radical hysterectomy. Gynecol oncol 85(3): 415-422.

37. Singh H, Modi HN, Ranjan S, Dilley JWR, Dimitrios A, et al. (2018) Robotic Surgery Improves Technical Performance and Enhances Prefrontal Activation During High Temporal Demand. Ann Biomed Eng 46(10): 1621-1636.

38. Soomro NA, Hashimoto DA, Porteous AJ, Ridley JA, Marsh WJ, et al. (2020) Systematic review of learning curves in robot-assisted surgery. BJS Open 4(1): 27-44.

39. Cumpanas AA, Bardan R, Ferician OC, Latcu SC, Duta C, et al. (2017) Does previous open surgical experience have any influence on robotic surgery simulation exercises? Wideochir Inne Tech Maloinwazyjne 12(4): 366-371.

40. Falconer H, Palsdottir K, Stalberg K, Dahm-Kähler P, Ottander U, et al. (2019) Robot-assisted approach to cervical cancer (RACC): an international multi-center, open-label randomized controlled trial. Int J Gynecol Cancer 29(6): 1072-1076.

DOI: 10.19080/JGWH.2021.21.556085

How to cite this article: Alin P, Stelian P, Felix B, Mircea S, Ciprian D, et al. Disease-Free Survival after Wertheim-Meigs Radical Hysterectomy Vs. Robotic-Assisted Radical Hysterectomy for Early-Stage Cervical Squamous Cell Carcinoma. J Gynecol Women's Health. 2021: 22(2): 556085. DOI: 10.19080/JGWH.2021.21.556085