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RESEARCH ARTICLE

Radical hysterectomy in cancer cervix: experience after adoption of robotic surgery

Kavita Mahadevappa, Uttam D Bafna, Pallavi V Ramachandra, Naveen Prasanna

Corresponding author: Dr Naveen Prasanna, Associate Professor, Dept OBG, Karnataka Institute of Medical Sciences, Hubli, Karnataka, India; Email : prasananya10@gmail.com

ABSTRACT

Background: Radical hysterectomy type III with pelvic lymphadenectomy is the surgical management for early cancer cervix. This study aims to know the perioperative and pathological outcomes of radical hysterectomy with bilateral salpingo-ophorectomy and pelvic lymphadenectomy in early cancer cervix done by open, laparoscopic and robotic routes. **Methods:** This was a prospective study conducted in KIDWAI Cancer Institute, Bangalore, India from December 2016 to June 2019. Cancer cervix stage 1B to IIA undergoing radical hysterectomy were included in the study. Demographic profile of patients, duration of surgery, intraoperative and postoperative findings, complications, specimen details and pathology reports were analysed. Data analysis was carried out using Python 3.7 version. Pearson Chi square test and Kruskal-Wallis test were used. P value <0.05 was considered statistically significant. **Results**: There were 60 patients, 20 each in open radical hysterectomy (ORH), laparoscopic radical hysterectomy (LRH) and robotic radical hysterectomy (RRH) groups. Median duration of surgery (minutes) was more in RRH (196) compared to LRH (180) and ORH (180), (p=0.029). The intraoperative blood loss (ml) was least in LRH (100), RRH(200) and more in ORH (300), (p=0.0001). Median duration of stay (days) were ORH(5), LRH(4), RRH(4), (p=0.0001). There were no conversions to laparotomy in LRH or RRH group. There were no bowel, bladder or vascular injury in RRH group. The number of lymphnodes retrieved were similar in all the groups (15vs12vs12 with ORH, LRH, RRH). However parametrial and the vaginal length were significantly less in RRH (left parametrium 1cm and right parametrium 1cm, vaginal length 1cm). **Conclusion**: Robotic radical hysterectomy has lesser blood loss, shorter hospital stay and lesser Intraoperative and postoperative complications. The parametrial and vaginal margin length obtained were least in robotic radical hysterectomy. Surgical experience is of paramount importance along with route of surgery.

Keywords: Cervical cancer, laparoscopic surgery, radical hysterectomy, robotic surgery.

Cervical cancer is a global concern because it is the fourth most common cancer and fourth leading cause of cancer associated death in women. According to Globocan 2020 there were approximately 6,04,000 new cases of cervical cancer with 3,42,000 deaths annually. In India it is the second most common cause of cancer next to breast, with 1,23,907 new cases and around 77,348 deaths annually. Less than 20% of cases present in early stage which can be treated surgically [1]. Radical hysterectomy type III is the treatment of choice for IB1 to IIA stage of cancer cervix according to NCCN 2020 [2]. Laparotomy, laparoscopy or robotic technique is an acceptable approach to radical hysterectomy in early stage cancer cervix [3]. Minimal invasive technique including laparoscopy and robotic radical hysterectomy have shown less blood loss, shorter hospital stay, and less postoperative analgesic needs with lesser post operative morbidity and complications than laparotomy [4,5]. However newer techniques have a learning curve, which is defined as the time taken and/or the number of procedures an average surgeon needs to be able to perform a procedure independently with a reasonable outcome. Laparoscopy is also associated with prolonged learning curve and ergonomic

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challenges for surgeons whereas Robotic surgery offers shorter learning curve and better ergonomics [6, 7]. We have conducted this study to know the intraoperative, postoperative findings and complications and pathological outcomes of radical hysterectomy with pelvic lymphadenectomy in early cancer cervix done by open, laparoscopic and robotic route.

Materials and methods

This was a prospective study conducted in KIDWAI Cancer Institute, Bangalore, India from December 2016 to June 2019. This Institute has been offering open radical hysterectomy for more than 30years, laparoscopic hysterectomy for more than 10years. Robotic surgeries were started from October 2016. Our study was approved by the Institutional Ethics Committee. All histopathologically confirmed cases of cancer cervix with clinical staging FIGO (International Federation of Gynaecology and Obstetrics) 2009, from IB to IIA were included in the study [8]. Written informed consent was taken from all the patients. Radical hysterectomy type III, (Piver and Rutledge classification) with BSO and PLND was done by open, laparoscopy and robotic route based on availability of slots in the respective operation theatre [9]. Open radical hysterectomy was done by Gynaecology-oncologist with a minimum of 5 years of experience in radical hysterectomy. The endoscopic surgeries were done by Gynaecology-oncologist with a minimum of 10 years of experience in radical hysterectomy. Patients with endocervical growth, tumour size of more than 4cms were given 2 cycles of neoadjuvant chemotherapy (NACT) with paclitaxel and carboplatin. Patients who responded to chemotherapy were taken up for surgery and nonresponders with progressive disease were sent for radiotherapy. Robotic surgery was done using da Vinci XI. Duration of surgery was taken from skin incision to skin closure. Docking time for robotic surgery was defined as time to advance the robotic column to the operating table, fastening the robotic arms to the inserted trocars and introducing the camera and instruments. Uterine manipulator was used for both robotic and laparoscopic surgery. Vault opening and suturing was done endoscopically. Gross measurements of the cervical tumour, parametrial tissue and vaginal cuff length were done before submitting the specimen for histopathology. Patients were followed up for 3 months postoperatively. Demographic profile of patients, duration of surgery Intraoperative and postoperative findings and complications, specimen details and pathology reports were analysed. Post operative adjuvant treatments based upon histopathology reports were analysed.

Statistical analysis - Data analysis was carried out using Python 3.7 version. Median scores were compared using Kruskal-Wallis test. The frequencies were compared using Pearson Chi square test. P value <0.05 were considered statistically significant.

Results

There were 60 patients who underwent radical hysterectomy with bilateral salpingo-ophorectomy and pelvic lymphnode dissection. The median ages of the patients were 49 years (range 31-77years). The median age at marriage was 18 years (range 14-21years). The median parity was 3 (range 1-6). Premenopausal were 27, and 33 were postmenopausal patients. Fifty seven out of 60 were below poverty line (BPL card holders issued by Government of Karnataka). Maximum number of patients were in stage1B1 [29 (48.3%)] followed by stage 1B2 [21 (35%)] and least in stage IIA [10(16.66%)]. Ectocervical growth were seen in 39(65%) and endocervical growth were seen in 21(35%) patients. All patients were HPV (Human papilloma virus) positive. HPV 16 were seen in 48(80%) and HPV 18 were seen in 12(20%) patients. Neoadjuvant chemotherapy (NACT) were given to 16 (26.6%) patients.

Table1: Intraoperative findings

Categories		ORH (n=20)	LRH (n=20)	RRH (n=20)	Chi square	P value
Duration of Surgery (mins)	Median Mean (Range)	180 174(150-240)	180 175 (150-240)	196 196 (150-330)	7.06	0.029
Estimated blood loss (ml)	Median Mean (Range)	300 280 (100-500)	100 140 (50-400)	200 200 (50-500)	15.21	0.0001
Duration of stay (days)	Median Mean (Range)	5 4.9(3-5)	4 3.6(3-5)	4 4(3-5)	20	0.001

ORH - Open radical hysterectomy, LRH - Laparoscopic radical hysterectomy, RRH - Robotic radical hysterectomy

There were 20 patients in each group of ORH (Open radical hysterectomy), LRH (Laparoscopic radical hysterectomy) and RRH (Robotic radical hysterectomy). There were no conversions to laparotomy in the LRH or RRH group. The median age was 48 in all the three groups and the BMI was 25, 24.5, 24 in ORH, LRH, RRH respectively (p=0.145). Intraoperative findings of surgery are compared as shown in table 1. Median duration of surgery was more in RRH when compared to LRH and ORH. The duration of surgery in RRH also includes docking time. The median docking time was 30 minutes and the mean was 28

minutes (range 20-40 minutes). The intraoperative blood loss was least in LRH and more in ORH. Median duration of stay was significantly more in ORH.

Table 2 shows the parameters of surgical specimen. The parametrial and the vaginal length size were significantly more in the ORH group and least in RRH group. The numbers of lymph nodes removed were also more in the ORH group (15) compared to RRH (12) and LRH (12), but this was not statistically significant.

Table 2: Parameters of specimens

Parameters		ORH (n=20)	LRH (n=20)	RRH (n=20)	P value
Left parametrium (cms)	Median	3	2	1	0.001
	Mean (Range)	2.9(0.8-4)	2.4(1-4)	1.6(0.5-3)	
Right parametrium (cms)	Median	3	2	1	0.0001
	Mean (Range)	2.9(1-4)	2.4(1-4)	1.5(0.5-3)	
Vagina (cms)	Median	3	2	1	0.001
	Mean (Range)	3.1(1-5)	1.9(1-3)	1.6(0.5-3)	
Lymph nodes (number)	Median	15	12	12	0.243
	Mean (Range)	15(5-30)	11(8-21)	12(6-20)	

ORH - Open radical hysterectomy, LRH - Laparoscopic radical hysterectomy, RRH - Robotic radical hysterectomy

Table 3: Perioperative complications

Complications	ORH (n=20)	LRH (n=20)	RRH (n=20)
Vascular injury	1	0	0
Fever	3	0	0
Wound infection	4	0	0
Urinary tract infection	1	0	0
Vesicovaginal fistula	2	1	0
Ureterovaginal fistula	1	1	0
Vaginal cuff separation	0	0	1
Deep vein thrombosis	0	0	0
Lymphedema	0	0	0

ORH - Open radical hysterectomy, LRH - Laparoscopic radical hysterectomy, RRH - Robotic radical hysterectomy.

Table 4: Postoperative adjuvant therapy across the groups

Categories	ORH (n=20)	LRH (n=20)	RRH (n=20)
Observation	9	11	12
Radiotherapy	2	2	2
Chemotherapy	3	5	3
Radiotherapy + Chemotherapy	6	2	3

Chi square value = 3.528, p value=0.740

ORH - Open radical hysterectomy, LRH - Laparoscopic radical hysterectomy, RRH - Robotic radical hysterectomy.

Table 3, shows the incidence of perioperative complications in the three groups. Total complications were more in ORH [12(60%)] than in RRH [1(5%)] and LRH [2(10%)] group. There was one vascular injury of internal iliac vein in ORH. There were no bowel and bladder injury identified intraoperatively in neither of the groups. However 2 patients in ORH group and one patient in LRH group developed VVF (vesico-vaginal fistula) postoperatively but none of RRH group developed fistula. One patient in the ORH group and one patient of LRH group developed UVF (uretero-vaginal fistula). One patient of RRH came with lymphorrhoea and had developed vaginal cuff separation, which was managed conservatively.

The final pathology report showed squamous cell carcinoma in 46 patients, adencarcinoma in 9 patients and adenosquamous carcinoma in 5 patients. For adjuvant treatment, patients were categorized into high-risk, intermediate-risk and low-risk disease. High-risk factors were lymph node metastasis (6/60), parametrial invasion (4/60) and positive vaginal margin (2/60). Patients having any one of the above factors were considered high risk disease. Intermediate-risk factors were tumor size more than 4 cm (24/60), lymphovascular invasion (11/60), and deep stromal invasion (22/60). Patients having any 2 of the above risk factors were considered intermediate risk disease, whereas patients having only one intermediate risk factor or no risk factor were considered low risk disease. There were 11 patients with high risk disease, 8 patients in intermediate risk disease and rest 41 were low risk disease. Patients with high risk disease were given radiotherapy with chemotherapy. Patients with intermediate risk disease were given only radiotherapy and the patients with low risk disease were followed up without any adjuvant therapy. All patients of NACT were given 2 cycles of chemotherapy postoperatively and the patients of high risk and intermediate risk received additional radiotherapy. The comparison of adjuvant treatment in various groups is shown in table 4. There was no statistical difference seen across the group.

Discussion

The first robot assisted laparoscopic radical hysterectomy was reported by Bilal M Sert [10]. Since then many studies have been conducted all over the world. One such retrospective systematic review for radical hysterectomy in early stage cervical cancer was conducted by Sherif AM et al in 2015, which included meta-analysis of 26 nonrandomized studies enrolling 4013 women (1013 radical robotic hysterectomy (RRH), 710 laparoscopic radical hysterectomy (LRH) and 2290 abdominal radical hysterectomy) suggested that robotic radical hysterectomy may be superior to abdominal radical hysterectomy with lower estimated blood

loss, shorter hospital stay, less febrile morbidity and wound related complications and concluded, robotic radical hysterectomy and LRH appear equivalent in intraoperative and short-term postoperative outcomes [11]. However there were no Indian studies in this meta-analysis.

Very few institutes in India offer robotic surgery and our institute is privileged to be one of the government institute offering robotic surgery. There were 20 patients in each group. There was no difference in the BMI of patients across the groups. Intraoperative findings showed significantly lesser blood loss and shorter duration of stay in RRH but the duration of surgery was more in RRH which was not statistically significant. A similar study comparing all the three surgical approaches, done by Pamela T et al at MD Anderson cancer centre, Texas, had a total of 95 radical hysterectomy: 30 open (RAH), 31 laparoscopic (LRH) and 34 robotic (RRH) [12]. There were no differences in the age, BMI, between the groups. Out of this 95 cases, 8 were endometrial cancer, cancer cervix 1A1(8), 1A2(17), 1B1(60) and only 2 cases were 1B2/IIA. Estimated blood loss was significantly lower in LRH and RRH compared with RAH (100vs100vs350ml, $p<0.001$). Median length of stay was significantly shorter in RRH (1 days) vs LRH or RAH (2 vs 4 days, $p<0.01$) similar to our study. In this study operative time was significantly shorter in the RAH compared to LRH and RRH (265min vs 338 vs 328mins, p value 0.002). Our study also showed slightly more operative time in RRH, but was not statistically significant. In our study there were no conversion rates in RRH or LRH. There were no intraoperative complications like vessel injury, bowel injury, and bladder injury in the RRH group.

There were no postoperative complications like VVF and UVF noted in RRH, however 1 case of vaginal cuff separation was noted in RRH. Whereas in a study conducted by Pamela et al, showed conversion rates which were higher in the LRH (16%) compared to RRH (3%) although not significant ($p=0.10$). There were 2 cases of ureteral injury and. 2 cases of cuff complication in RRH. In their laparoscopy group there were 2 cases of ureteral injury and 1 vascular injury. But no bowel, bladder or cuff complication in open case. Whereas in our study open cases had 1 vascular injury and 2 VVF. Pathological findings in our study showed lymphnode retrieval in ORH (15), LRH (12), RRH (12), the difference was not statistically significant. The surgical margins of both left and right parametrium was 3 vs 2 vs 1cm with ORH vs LRH vs RRH and vagina was 3 vs 2 vs 1cm with ORH vs LRH vs RRH, which was statistically significant.

However unlike our study, Pamela et al showed pathological findings like size of parametrium, length of vaginal cuff and pelvic lymph nodes were similar in all the groups. Mean pelvic lymphnodes were 19 vs 14 vs 17 with ORH vs LRH vs RRH, the median length of the vaginal cuff 1.5 vs 1.5 vs 1.5 cms with ORH vs LRH vs RRH and left parametrium 3.5 vs 3.3 vs 3.5 cms with ORH vs LRH vs RRH and right parametrium 3.6 vs 3.0 vs 3.5 cms with ORH vs LRH vs RRH. The lesser surgical margins in our study could be explained by the fact that our study had more than 50% of 1B2-IIA cases, whereas in their study only 2% cases were 1B2-IIA. It was also observed that robotic operated specimens had more charred edges reducing the margin in our study, however there were only 4 out of 60 cases with parametrial invasion (2 open and 2 Laparoscopy) and 2 out of 60 cases with positive vaginal margin(both in open cases). So none of margin positive cases were of robotic group. According to Ga Won Yim et al, who did a learning curve analysis of robot-assisted radical hysterectomy for cervical cancer concluded that the surgical performance improvement can be achieved after 28 cases [13]. Our study showed a better intraoperative outcome and less postoperative complications in RRH, however the surgical margins were lesser in RRH, which could be because of more number of cancer cases [24(40%)] had lesion size of more than 4cms and charring of the margins could be due to early phase of learning curve.

The scenario of minimal invasive surgery in cancer cervix changed when the LACC trial (Laparoscopic Approach to Cervical Cancer) was published by Pedro T Ramirez et al, which compared minimal invasive versus abdominal radical hysterectomy for early cervical cancer [14]. There were total of 631 patients, out of which 319 patients underwent minimally invasive surgery, and 312 patients underwent open surgery showed minimally invasive route was associated lower overall survival, lower rates of disease free survival, with higher rates of recurrence than the open approach in early-stage cervical cancer patients [14]. In our study minimal invasive surgery had a better short term perioperative outcome but the surgical margins were lesser than that of open surgery. However there was no difference in the disease risk or postoperative adjuvant treatment across the groups. These patients need to be followed up to see the long term outcomes like overall survival and disease free survival.

Conclusion

Robotic radical hysterectomy has lesser blood loss, shorter hospital stay and lesser intraoperative and postoperative complications. The parametrial and vaginal margin length obtained were least in Robotic radical hysterectomy. Surgical experience is of paramount importance along with route of surgery.

Conflict of interest: None. **Disclaimer:** Nil.

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Kavita Mahadevappa [1], Uttam D Bafna [2], Pallavi V Ramachandra [3], Naveen Prasanna [4]

[1] Associate Professor, Dept OBG, Karnataka Institute of Medical Sciences, Hubli, Karnataka, India; [2] Professor, Dept. Gynae-Oncology, KIDWAI Cancer Institute, Bangalore, Karnataka, India; [3] Professor, Dept. Gynae-Oncology, KIDWAI Cancer Institute, Bangalore, Karnataka, India; [4] Associate Professor, Dept OBG, Karnataka Institute of Medical Sciences, Hubli, Karnataka, India.