Meta-Analysis the Prognosis of Surgical Treatment for Early-Stage Invasive Cervical Cancer

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Conflicts of Interest There are no conflicts to declare.

ABSTRACT

Background: The possible advantages of laparoscopic (LPR) and laparotomy (LPT) have not been systematically evaluated. The aim of this study was to systematically review the comparative efficacy between LPR and LPT to treatment cervical cancer, based on perioperative outcomes, complications and long-term outcomes.

Materials and methods: Our research was conducted by searching PubMed, EMBASE and the Cochrane Library database. All the original studies comparing LPR with LPT were included in the critical assessment. Software Revman 5.3 was used for meta-analysis. Average difference and standard deviation (SD) and 95% confidence interval (CI), ratio (ORs), 95% CI and aggregate risk ratio (HRs) and 95% confidence interval (CIs) were used to estimate the association strength between laparoscopic and laparotomy patients.

Results: A total of nine studies that compared LPR (n = 487) with LPT (n= 510) in patients with cervical cancer fulfilled quality criteria were selected for review and meta-analysis. LPR compared with LPT was associated with a significant reduction of intra operative blood loss (weighted mean difference =313.29 ml, 95% CI: -113.69 to 740.28; p=0.15). The mean blood loss was (555.8 \pm 304.4) ml in LPT group compared with (180.34 \pm 213.9) ml in LPR group. A reduced risk of postoperative complications was seen in LPR (9.72% LPR vs. 13.6% LPT; OR = 1.34; 95 % CI 0.83–2.15; p=0.23); wound infection rate (1.03% LPR vs 4.07% LPT, *p* = 0.009); fever morbidity (1.29% LPR vs 4.9% LPT, *p* = 0.004); wound dehiscence (1.55% LPR vs. 5.8% LPT, p = 0.003); The rates of wound infection, febrile morbidity and wound dehiscence were found in the patients of both groups and the results showed that the rate of LPT was higher in all the three complications as compared to the rates of LPR and the difference was statistically significant. The hospital stay was shorter (4.8 \pm 2 days) in LPR group compare to LPT group (13.77 \pm 4 days; 95% CI: 1.09 to 16.28; p=0.03). The mean operative time for the laparoscopic technique was (247.83 ± 200.45) min which was shorter than

the laparotomy group (233.72 \pm 139 min). The rate of intra operative complications was similar between two groups(LPR 8.97% versus LPT 6.12%; OR = 0.65; 95% CI 0.38-1.11; p=0.12); Bladder injury occurred in 4.076% of LPR patients and 1.28% of LPT patients (p = 0.03); Patients with LPT showed less bladder injuries as compared to patients with LPR. The incidence of urethral injury was 2.4% in LPR group and 0.5% in LPT group (p = 0.06); Urethral injuries were also observed to be more in patients with LPR and less in patients with LPT. Vascular injury occurred in 1.63% of patients with LPR and 0.5% of patients with LPT (p = 0.16); vascular injury occurred more in patients with LPR as compared to patients with LPT. There were not significant differences in 5-year OS (hazard ratio [HR]=1.02; 95% CI:0. 60 to 1.70; p=0.95) and progression free survival (hazard ratio [HR]=1.17; 95% CI: 0.64 to 2.14; p=0.61) between two groups. Neither have higher risks of recurrence [hazard ratio (HR) = 0.73; 95% confidence interval (CI) 0.29–1.83; p=0.50] in LPR vs. LPT.

Conclusions: LPR treatment for early invasive cervical cancer showed less blood loss and shorter hospital stay than patients receiving LPT. The incidence of intra operative complications was similar between the two groups, but the character was quiet different. There was no significant difference in the 5-year OS, PFS and recurrent risk between the two groups.

Keywords: CERVICAL CANCER; EARLY STAGE CERVICAL CANCER; CANCER OF CERVIX; LAPAROSCOPIC; LAPAROTOMY

1. Introduction

Cervical cancer is one of the most often diagnosed malignancies in females. It is the fourth most frequent type of cancer globally, behind breast cancer, colorectal cancer, and lung cancer. Cervical cancer is frequently diagnosed in women of reproductive age (44–55 years old) [1]. Cervical cancer is caused by persistent infection with high-risk human papilloma virus (HR-HPV) [2]. Cervical cancer is classified histologically into two distinct types: "squamous cell carcinoma" and "adenocarcinoma," with squamous cell carcinoma being the more frequent type [3]. HPV infections of the reproductive tract are the most often transmitted sexually transmitted infections. While the immune system is often powerful enough to eradicate HPV infection in the general population, HPVs can survive and advance cervical infected cells to the precancerous stage due to viral oncogenes integrated into the host genome and the ensuing genomic instability. Between faulty cervical cytology and early stage invasive cervical cancer, it takes 15 to 20 years. Although this stage involves the chronic growth of cervical precancerous lesions, it is a manageable stage of chronic illness, making it crucial for the prevention of early stage invasive cervical cancer [4].

The World Health Organization (WHO) estimates that 80 percent of cervical cancer cases occur in underdeveloped nations, which account for only 5% of global medical resources [5]. Around 90% of cervical cancer fatalities occurred in low- and middle-income countries in 2016[6]. Cervical cancer mortality is higher in low-income nations due to a lack of screening and prevention, rather than a lack of treatment [7].

Today, a flawless preventative method for cervical cancer elimination has been devised. These preventative strategies include HPV vaccination and routine cervical cancer screening to detect precancerous lesions. The increased number of sexual partners, the onset of sexual activity at a young age, an impaired immune system, concurrent infection with other sexually transmitted diseases (such as chlamydia, gonorrhea, syphilis, and HIV), and smoking are all risk factors for persistent high-risk HPV infection [8]. Different surgical methods have been created for stage I B and II A cervical carcinoma. The most frequently recommended therapy for invasive cervical cancer is radical hysterectomy. The predictive value of surgical procedures was found to be between 80% and 90%.

The purpose of this study was to assess the surgical therapy of cervical cancer in its early stages. Our present research is to determine the prognosis of laparoscopic and conventional laparotomy for cervical cancer in its early stages.

1.1 Prevention of cervical cancer

1.1.1 Primary prevention (HPV VLP vaccine)

Human papilloma virus (HPV) virus-like particles (VLP) vaccine was introduced as the primary prevention for eradicating the cervical cancer. The vaccine is designed to fight HPV 16 and HPV 18. Vaccines contain only microbial "capsid proteins" and no "nucleic acid" microorganisms, so no virus imitation take place. There are three types of HPV vaccine.

The first "cervarix®" vaccine with viral type is used as an element of HPV 16 and 18. Both vaccines stimulate the immune system response and promote neutralizing antibodies. They are safer, more tolerable, and may stop at least 70% of all persistent "cervical cancer" incidents because 70% of "cervical cancer" is impure to HPV 16 and 18.

The second is the "Gardasil®" with viruses, such as those from human papilloma virus types 6 and 11, which produce low-risk species of "Kondyloma" and human papilloma virus 16 and 18.

The third "Gardasil®9," vaccine with viral types is used as an element of HPV types 31, 33, 45, 52, and 58 in addition to HPV 6, 11, 16, and 18. It protects against pre-cancer and cancer of cervix, vulva, and vagina; anal pre-cancer and genital warts. (National Cancer Institute 2018)

The last two vaccines target anogenital warts caused by HPV 6 and 11 in addition to the above-mentioned malignant and premalignant lesions. All the vaccines are recombinant vaccines composed of virus-like particles (VLPs) and are not infectious since they do not contain viral DNA. For girls and boys aged 9–14 years, a two-dose schedule (0.5 mL at 0 and 5–13 months) is recommended. If the second vaccine dose is administered earlier than 5 months after the first dose, a third dose is recommended. For those aged 15 years and above, and for immune compromised patients irrespective of age, the recommendation is for three doses (0.5 mL at 0, 1, 6 months). (World Health Organization)

^{1.1.2} Secondary prevention: cervical cancer screening

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Cervical cancer was once considered the leading cause of cancer in the United States. Until 1955-1992, the rate declined by 70% due to Pap smear screening and community-based understanding. It is said that the annual decrease is 3%, but the amount remains at a high level[1]. According to the latest estimates of the American cancer community, nearly 12,710 recent incident of insidious cancer will be detected in 2011, of these almost 4,290 mortalities would be estimated. (American Cancer Association 2010).

Secondary prevention of cervical cancer is routine screening by using cytological testing and HPV testing. The function of cervical screening is to expose, observe and heal precancerous lesions. Planned screening courses aimed at identifying "cervical dysplasia" to stop cervical cancer have proven to reduce cancer incidence. According to Albrow, Kitchener, Gupta and Desai (2012), the planned screening process will also enhance early detection of cervical cancer and reduce the number of women, thus making diagnosis at a higher stage of infection, thereby reducing problematic cure and good endurance rates. Traditionally, cervical screening is actually carried out by observe the abnormal exfoliative cells(pap smear)invented by a pathologist named Papanicolau Nicolas,.. Recently, cytological testing has changed to liquid-based . Nowadays, human papilloma virus detection is essentially a screening course as a classification method for (ASCUS) and (CIN 1), as well as an evaluation of treatment after (CIN2-3/CIS), (AIS) and (CARG).

Shastri et al. (2013) were screened according to "visual examination". The investigator makes use of the "Acetic Acid" on the "Cervix" and if the areas of the acetic turn into white then the test is +ve (Positive).

Cervical cancer is more easily avoided by screening, especially for women having pre-cancerous cervical lesion "asymptomatic" that can be quickly and successfully cured before diagnosis. With the improvement of screening methods, the mortality rate of cervical cancer in developed countries has decreased. But in developing countries there is lack of these resources. But there are still almost 2,70,000 estimated deaths, of which 85% are from developing nations and the increased mortality is identified due to the lack of high-quality screening of precancerous lesion and treatment resources which are also deprived of good infrastructure.

When cervical cancers diagnosed and cured at the initial stage, almost 80% of patients diagnosed at the initial stage receive appropriate treatment. In developing countries, cervical cancer is mainly detected in the extremely delayed stage, because they do not have good screening and treatment technologies, in contrast to developed countries, which are incessantly able to diagnose and cure cervical cancer at its initial stage, usually in the precancerous stage. Several treatments used for the precancerous lesions, include cryotherapy, which involves the use of less fever, which can destroy irregular tissues. This technology does not require electricity, making it a cheap and affordable technology that can be used by low-income countries. "LEEP" (Loop electrosurgical excision process) is another approach, including the use of lean cables to remove affected areas. Although slightly costlier than cryotherapy, "LEEP" improves performance because it allows tissue removal for "biopsy" to allow additional examinations and reduce the tendency of advanced cervical cancer[1].

2 Materials and Method

2.1 Objective

The purpose of this study is to investigate the prognosis of surgical treatment for early-stage invasive cervical cancer.

2.2 Literature search strategy

Our study searched for "cervical cancer" and "laparoscopy" and "laparotomy" and their synonyms or abbreviations based on PubMed, EMBASE and Cochrane Library databases. No other search software or special functions are used. All eligible criteria articles are included in the systemic review.

2.3 Selection criteria

A total of 924 records were identified by the initial search strategy from PubMed, EMBASE, and Cochrane library. Of these, 893 ineligibles were removed. After a detail assessment of 31 records, 22 records more excluded due to following reasons; 1 has no quality-of-life study, 3 were Meta-analysis, 3 review papers, 2 has no postoperative outcomes and 13 had no relevant information or were conference abstracts. Finally, 9 included in the meta-analysis study.

The inclusion criteria for the eligibility of a study were as follows: (1) adult women diagnosed with earlystage invasive cervical cancer (2) women who had undergone LRH versus RH as primary treatment (3) patients who were classified as International Federation of Gynecology and Obstetrics (FIGO) stage IA1 with lymph vascular invasion to stage IIA.

The following studies were excluded from the analysis: (1) if radiation or concurrent chemo radiation therapy were used as primary treatment, (2) pregnant women with cervical cancer, (3) In case of multiple studies with the same or overlapping data published by the same researchers, (4) articles about animal or cell lines, (5) letters, reviews and conference abstracts.

2.4 Data abstraction

Extract the required information from the data collected in each study. Information includes: first author's surname, year of publication, sample size, participant's age, participant's characteristics, operation time, estimated blood loss, length of hospital stay, 5-year survival rate, disease-free survival rate. This meta-analysis procedure compares studies conducted in different parts of the world.

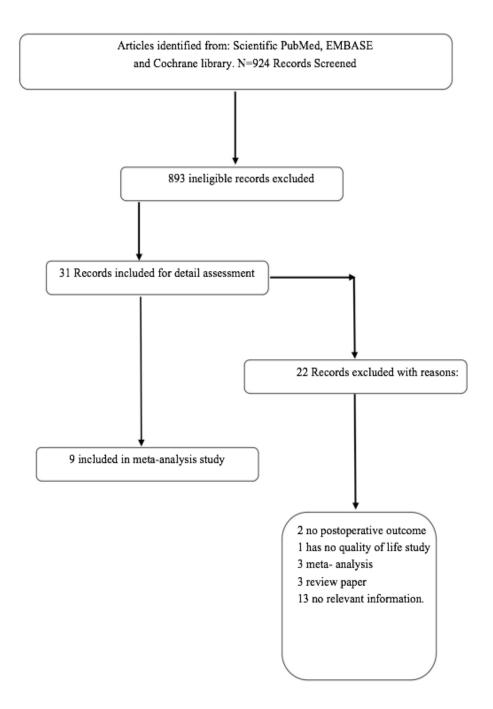


Figure 2-1Flow chart

Author, Year	Numbers	Туре	Age, years	BMI (kg/m2)	Operation duration/ min	Estimated blood loss/mL	Hospital stay/ days	5 years survival rate	Disease Free Survival rate
Magrina (2008)[2]	35	LPT	50.9 ± 8.6	27.3 ± 5.8	166.8 ± 33.2	443.6 ± 253.2	3.6 ± 1.2	81%	90%
	31	LPR	54.9 ± 14.3	26.8 ± 4.6	220.4 ± 37.5	208.4 ± 105.4	2.4 ± 1.5	87%	77%
Taylor (2011)[3]	18	LPT	51.0 ± 11.0	38.3 ± 17.0	119.0 ± 340.0	1400.0 ± 100.0	24.0 ± 3.0	89%	N/A
	9	LPR	$62.0{\pm}21.0$	36.1 ± 20.6	148.0 ± 313.0	300.0 ± 50.0	2.0 ± 4.0	95%	N/A
Estape (2009)[4]	10	LPT	58.0 ± 7.4	32.4 ± 3.3	120.0 ± 240.0	200.0 ± 450.0	6.9 ± 2.1	N/A	N/A
	18	LPR	52.8±14.2	22.0 ± 1.3	M=65.0	173.0 ± 156.0	3.1 ± 4.0	N/A	N/A
Lowe (2009)[5]	13	LPT	55.0±6.4	29.0 ± 2.5	232.0 ± 453.0	50.0 ± 400.0	N/A	N/A	77%
	19	LPR	50.0±8.4	39.0	$230.0{\pm}~600.0$	50.0 ± 34.0	N/A	N/A	69%
Spirtos,Eisenkop	51	LPT	49.0	32.9 ± 1.3	M=46.0	M= 85.0	N/A	N/A	N/A
(2002)[6]	50	LPR	38.0	28.2 ± 4.4	114.0 ± 540.0	278.0 ± 234.0	N/A	N/A	N/A
Eun-Ju Lee (2011)[7]	48	LPT	50.2	23.9	326.8 ± 53.8	836.0 ± 315.8	18.8 ± 6.7	N/A	93%
	24	LPR	48.4	23.4	334.8 ± 52.4	414.3 ± 69.2	10.7 ± 2.8	N/A	90%
JH.Nam (2011)[8]	263	LPT	46.5	23.2	247.2	541.8	20.7	96%	96%
	263	LPR	46.4	23.9	246.8	379.6	12.5	95 %	95%
Persson, and Bossmar	32	LPT	64.0 ± 2.4	49.0 ± 4.3	M=48.0	100.0 ± 500.0	3.4	N/A	82%
(2009)[9]	38	LPR	57.8 ± 5.0	32.0 ± 4.1	172.0 ± 312.0	50.0 ± 550.0	4.4	N/A	N/A
Yan (2009)[10]	40	LPT	55.0	N/A	M=42.0	M=95.0	N/A	76%	N/A
	35	LPR	48.0	N/A	N/A	100.0	N/A	67%	N/A

Table 2-1 Characteristics of inclusion studies

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2.5 Statistical Analysis

All statistical tests were performed using the Cochrane collaboration's Revman 5.3 and Stata software. Continuous data are expressed as mean differences with standard deviations (SD). Meta-analysis is a quantitative study. Result for comparisons of continuous outcomes are expressed as risk differences with 95% confidence intervals (CI). A meta-analysis was planned if the included studies was determined by the chisquare-based Q test and the I² statistics. A *p*-value less than 0.05(p < 0.05) for the Q test together with I² value greater than 50%(I²>50%) was considered a measure of severe heterogeneity. Therefore, the study was calculated using the Random-effect model otherwise, fixed-effect model was used. All p-values were two-sided, and A p-value less than 0.05(p < 0.05) was considered to be statistically significant and a p-value greater than 0.10(p>0.10) for the Q test was not significant. Dichotomous variables, were expressed as Odds ratios (ORs) with 95% CIs for each study. the study was calculated using the fixed-effect model (the Mantel-Haenszel method). Next, Begg's funnel plot and Egger's test were used to evaluate publication bias in our included studies a p value greater than 0.05 (p>0.05) considered to be statistically not significant. This is done in order to compare the results obtained from different research studies done in the past regarding the prognostic value of the surgical treatment for the early-stage cervical cancer. The factors, which are focused in this, research study included: the histological areas, the mean age of the participants, in early-stage cervical cancer treatment with surgical procedure Laparotomy and Laparoscopic.

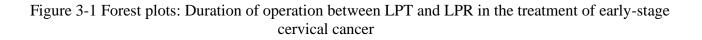
3 Results

3.1 Short-term outcomes about LPT and LPR in treatment of invasive cervical cancer

3.1.1 Duration of operation time

The mean duration of surgery was described in four studies. The duration of operation was found in LPT and LPR (Fig. 3-1 weighted mean difference = - 31.79 minutes; 95% CI: -69.90 to 6.32; p = 0.10). The average operation time of laparoscopic technique was (247.83 ±200.45) minutes, and the LPT was shortened to (233.72 ± 139.4) minutes. In most studies, LPR procedure were found to be longer than LPT.

		LPT			LPR			Mean Difference		Mean D	ifference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Rando	m, 95% CI	
Eun-Ju Lee 2010	326.8	53.8	48	334.8	52.4	24	45.4%	-8.00 [-33.91, 17.91]				
Lowe 2009	232	453	13	230	600	19	1.1%	2.00 [-363.27, 367.27]	←		•	
Magrina 2008	166.8	33.2	35	220.4	37.5	31	51.4%	-53.60 [-70.78, -36.42]	-			
Taylor 2011	119	340	18	148	313	9	2.1%	-29.00 [-286.85, 228.85]	•	•		
Total (95% CI)			114			83	100.0%	-31.79 [-69.90, 6.32]			-	
Heterogeneity: Tau ² = 658.17; Chi ² = 8.32, df = 3 (P = 0.04); i^2 = 64% Test for overall effect: Z = 1.63 (P = 0.10)										-50 Favours LPT	0 50 Favours LPR	100



3.1.2 Estimated blood loss

In six studies, blood loss was reduced in the LPT and LPR groups. Blood loss was observed in LPT and LPR (fig 3-2 weighted mean difference = 313.29 ml, (95% CI: -113.69 to 740.28; p = 0.15). The average blood loss in LPT was (555.8 ± 304.4) ml (180.34±213.9) ml in LPR. It shows that LPR has less blood loss than LPT.

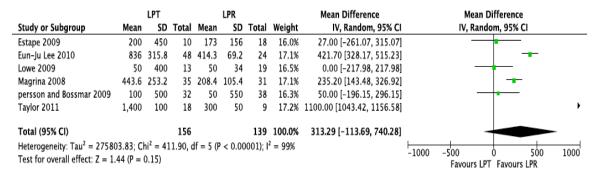


Figure 3-2 Forest plots: Estimated blood loss between LPT and LPR in the treatment of early-stage cervical cancer

3.1.3 Hospital stays

In four studies of LPT and LPR, the average length of hospitalization was observed (Fig. 3-3, weighted average difference = 8.68 days, (95% CI: 1.09 to 16.28; p = 0.03). The shorter length of hospitalization (4.8 ± 2) days for LPR patients meant that the length of stay of LPT (13.77 ± 4) days was longer. In laparoscopic surgery, hospitalization time is shorter than that of laparotomy.

		LPT			LPR			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	r IV, Random, 95% Cl
Magrina 2008	3.6	1.2	35	2.4	1.5	31	25.5%	1.20 [0.54, 1.86]	2008	3
Estape 2009	6.9	2.1	10	3.1	4	18	25.0%	3.80 [1.54, 6.06]	2009)
Eun-Ju Lee 2010	18.8	6.7	48	10.7	2.8	24	25.0%	8.10 [5.90, 10.30]	2010)
Taylor 2011	24	3	18	2	4	9	24.6%	22.00 [19.04, 24.96]	2011	
Total (95% CI)			111			82	100.0%	8.68 [1.09, 16.28]		•
Heterogeneity: Tau ² Test for overall effect					= 3 ((P < 0.0	0001); I ²	= 99%		-100 -50 0 50 100 Favours LPT Favours LPR

Figure 3-3 Forest plots: Hospital stay between LPT and LPR in the treatment of early-stage cervical cancer

References	Approach	Number	Bladder injury	Urethral injury	Vascular injury
Lowe et al.	LPT	13	0	0	0
	LPR	19	1	1	0
Yan et al.	LPT	40	1	0	0
	LPR	35	1	1	1
Estape et al.	LPT	10	0	0	0
	LPR	18	1	0	1
Eun-Ju Lee et al.	LPT	48	1	1	1
	LPR	24	3	2	1

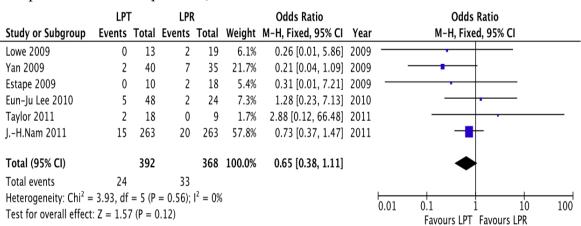
Table 3-1 Intraoperative complications

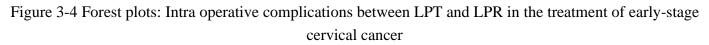
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Taylor et al.	LPT	18	1	0	0
	LPR	09	0	0	0
J-H Nam et al.	LPT	263	2	1	1
	LPR	263	9	5	3
Total	LPT	392	5	2	2
	LPR	368	15	9	6
pvalue			0.03	0.06	0.16

3.1.4 Intra operative complications

In nine studies, 6 studies were selected as the incidence of intra operative complications, similar between the two groups (fig 3-4 LPR 8.97% versus LPT 6.12%; OR = 0.65; 95% CI 0.38-1.11; p= 0.12). Bladder injury occurred in 4.076% of LPR patients and 1.28% of LPT patients (p = 0.03). The incidence of urethral injury was 2.4% in LPR group and 0.5% in LPT group (p = 0.06). Vascular injury occurred in 1.63% of patients with LPR and 0.5% of patients with LPT (p = 0.16) as shown in Table 3-1





3.1.5 Postoperative complications

Of a total of nine studies, five studies show postoperative complications. The incidence of postoperative complications was lower in LPR than LPT groups (LPR 9.72% vs LPT 13.6%; OR = 1.34; 95% CI 0.83-2.15; p = 0.23); wound infection rate (1.03% LPR vs 4.07% LPT, p = 0.009); fever morbidity (1.29% LPR vs 4.9% LPT, p = 0.004); wound dehiscence (1.55% LPR vs. 5.8% LPT, p = 0.003) was higher in LPT group than in LPR group, and the difference was statistically significant.

	LPT	Г	LPR	ł		Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	Year	M-H, Fixed, 95% Cl
Lowe 2009	8	13	3	19	3.2%	8.53 [1.62, 45.06]	2009	
Yan 2009	7	40	10	35	29.7%	0.53 [0.18, 1.59]	2009	
Eun-Ju Lee 2010	17	48	4	24	11.6%	2.74 [0.80, 9.34]	2010	
JH.Nam 2011	15	263	17	263	54.0%	0.88 [0.43, 1.79]	2011	
Taylor 2011	5	18	0	9	1.6%	7.74 [0.38, 157.31]	2011	`
Total (95% CI)		382		350	100.0%	1.34 [0.83, 2.15]		•
Total events	52		34					
Heterogeneity: Chi ² =	11.47, d	f = 4 (P = 0.02)	; l ² = 6	5%			0.01 0.1 1 10 100
Test for overall effect	: Z = 1.2	1 (P = 0).23)					Favours LPT Favours LPR

Figure 3-5 Forest plots: postoperative complications between LPT and LPR in the treatment of early stage cervical cancer

3.2 Long-term outcomes

3.2.1 Disease free survival rate

Four of the nine studies reported disease-free survival. Disease-free survival (hazard ratio [HR] = 1.17; 95% CI: 0.64 to 2.14; p = 0.61) where p value is not significant as shown in figure 3-6.

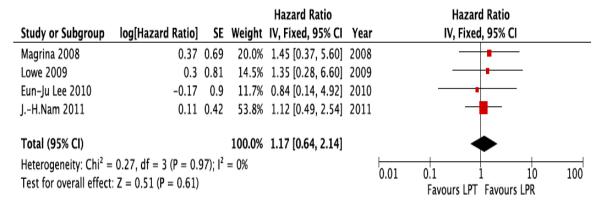


Figure 3-6 Forest plots: Disease free survival rate between LPT and LPR in the treatment of early-stage cervical cancer

3.2.2 5 years' survival rate

Of a total nine studies, only four studies reported a 5-year survival rate. Five-year overall survival rate (hazard ratio [HR] = 1.02; 95% CI: 0.60-1.70; p= 0.95) where p value is not significant as shown in figure 3-7.

				Hazard Ratio		Hazard Ratio
Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV, Fixed, 95% CI	Year	r IV, Fixed, 95% Cl
Magrina 2008	-0.244	0.6	19.4%	0.78 [0.24, 2.54]	2008	
Yan 2009	0.086	0.437	36.6%	1.09 [0.46, 2.57]	2009)
JH.Nam 2011	0.114	0.421	39.4%	1.12 [0.49, 2.56]	2011	
Taylor 2011	-0.301	1.23	4.6%	0.74 [0.07, 8.25]	2011	
Total (95% CI)			100.0%	1.02 [0.60, 1.70]		•
Heterogeneity: Chi ² = Test for overall effect				0.01 0.1 1 10 100 Favours LPT Favours LPR		

Figure 3-7 Forest plots: 5 years' survival rate between LPT and LPR in the treatment of early-stage cervical

3.2.3 Recurrence rate

Of a total nine studies, only four studies reported recurrence. Compared with LPT (n = 394), LPR (n = 375) had no higher recurrence risk [hazard ratio (HR) = 0.73; 95% confidence interval (CI) 0.29-1.83; p = 0.50] where p value is not significant as shown in figure 3-8.

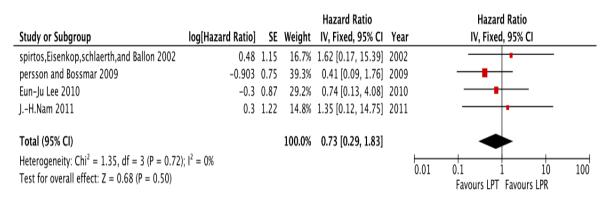


Figure 3-8 Forest plots: Recurrence rate between LPT and LPR in the treatment of early-stage cervical cancer

3.3 Publication bias

Begg test and Egger test were carried out to detect publication bias. The results showed that there was no significant evidence of publication bias (p > 0.05) (Figures 3-9(a) and 3-9(b)).

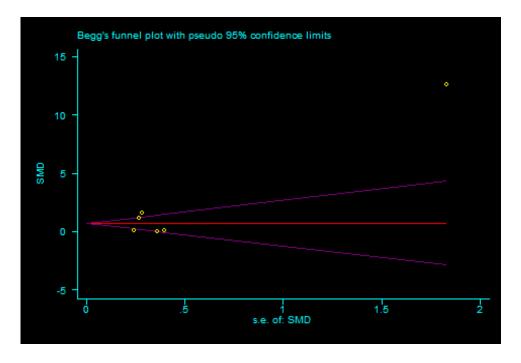


Figure 3-9 (a) Begg's funnel plot with pseudo 95% confidence limit.

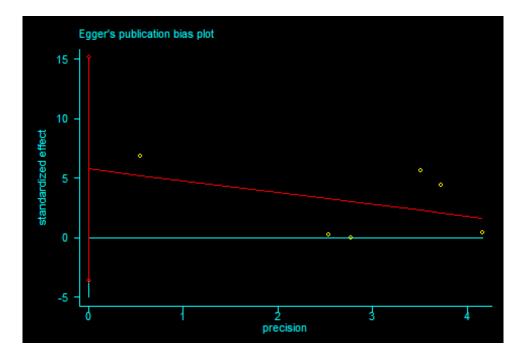


Figure 3-9(b) Egger's publication bias plot.

4 Discussion

The current study aimed to investigate the prognosis of surgical treatment for the early stage invasive cervical carcinoma. Short-term outcomes included the mean duration of operation time, the estimated blood loss, the duration of hospital stay, intra operative complications and postoperative complications for patients undergoing procedures of laparoscopic surgery and laparotomy operation.

This study observed the mean duration of operation time in four studies. The mean operation time was observed in both groups of patients. The mean calculated from the results exhibited that the mean duration of surgical procedure shortened in case of LPT. These findings of current study are aligned with the results Wang, Yan-zhou, et al.[11]. It has been observed that LPR has a longer mean duration. Hence, the study showed LPR operations have increased duration of surgery time in contrast to LPT. This finding also finds its support from Hertel, H., et al.[12]. Six studies were observed in current study for estimating the blood loss in both surgical procedures. Mean blood loss was calculated following the LPT surgery and LPR surgery. The results exhibited that patients undergoing procedures of LPR has less blood loss then patients undergone LPT procedure. The mean hospital stay of the patients undergoing LPR and LPT in six studies. The results showed a shorter mean hospital stay in patients with LPR whereas a longer mean hospital stay was seen in patients with LPT. These results are much aligned with the results of (Sood, A.K., et al).[13]. The findings about the laparotomy operations showed that patients with laparotomy operation have a longer hospital stay then patients with laparoscopic operation. The study performed by Walker, J.L., et al^[14] also demonstrated somehow similar findings. For the rate of intra-operative complications in patients with LPT and LPR, 6 studies of the total 9 studies were selected. Rate of intra-operative complications was found to be same in both groups. Patients with LPT showed less bladder injuries as compared to patients with LPR. Urethral injuries were also observed to be more in patients with LPR and less in patients with LPT. Similarly, vascular injury occurred more in patients with LPR as compared to patients with LPT. Some similar results have also been presented regarding urethral injuries in surgical treatments by past research e.g. [15, 16].5 studies were selected to assess the rate of postoperative complications between the two groups of patients. Patients who have undergone LPR operative

procedures exhibited decreased rate of post-operative complications as compared to the patients' undergone LPT surgical procedures that exhibited greater rate of post-operative complications. The studies of Lagasse, Creasman [17] and Walker, Piedmonte [14] also revealed post-operative complications in surgical treatment of cervical cancer. The rates of wound infection, febrile morbidity and wound dehiscence were found in the patients of both groups and the results showed that the rate of LPT was higher in all the three complications as compared to the rates of LPR. The results showed significant presence of post-operative complications in patients with LPT.

The current study attempted to find the long-term outcomes in terms of the disease-free survival rate and 5-year survival rate was observed in the patients with LPT and LPR. In this study, 4 out of 9 studies exhibited the disease-free survival in the patients. Hazard ratio was calculated to assess disease free survival in patients. But the results were not significant in this case. These results about hazard ratio are also aligned with the past studies as Rydzewska, Tierney [18] also reported supportive findings. Compared with LPT and LPR did not have higher risks of recurrence. Thus, the results found in current study find their significant support from previous research work.

5 Conclusion

Our meta-analysis shows that LPR is a safe and feasible method for treatment of early-stage cervical cancer. Through our meta-analysis, it is clear that the advantages of this approach are reduced blood loss, shorter hospital stay, lower incidence of post operative complications, faster functional recovery and longer operation time. Other outcomes included similar intra operative complications in both groups. Compared with LPR and LPT, the recurrence rate of the two surgical techniques has no significant difference, and the 5-year survival rate and disease-free survival rate were similar. Further prospective RCT studies are needed to assess long-term survival outcomes.

5.1 Implications

This research study implies in increasing the information regarding the better treatment of the early-stage invasive cervical cancer. The meta-analysis is done in order to compare the research studies done in the past regarding the surgical treatment of the cervical cancer thus improving the methods used for the treatment of the patients suffering from the invasive cervical cancer. This research study helps in increasing the literation review regarding the prognosis of the surgical treatment for the early-stage invasive cervical cancer. The surgical methods are proved to be very effective for the treatment of early-stage invasive cervical cancer. Many research studies have been conducted in order to compare the outcomes of both laparoscopic method and the radical hysterectomy in case of the cervical cancer.

5.2 Limitations

Data collected from different studies for meta-analysis did not show authentic results. It takes a lot of time to collect the required data. The number of participants in this study is limited. The research results were selected from different regions of the world. This study only focused on the recommended surgical treatment for early

invasive cervical cancer. Other therapies for this purpose have not been properly discussed.

5.3 Future research indications

This research study plays an important role in determining better treatment of the early-stage invasive cervical cancer. Different stages of the cervical cancer are also included in this research study. A radical hysterectomy is a method, which is used, in the early stages of the cervical cancer. The cervix and the uterus are usually removed and the lymph nodes of the pelvic are also removed in this procedure. The radical hysterectomy is used for the treatment of the women suffering from the cervical cancer in early stages. Thus, from this research study it was concluded that the laparoscopic method shows high rate of survival than the invasive radical hysterectomy as well as the open abdominal radical hysterectomy.

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