Systematic Review and Meta-Analysis

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Impact of hospital care volume on clinical outcomes of laparoscopic radical hysterectomy for cervical cancer

A systematic review and meta-analysis

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Abstract

Background: In cervical cancer, the impact of hospital volume of laparoscopic radical hysterectomy (LRH) has not been investigated systematically as in ovarian cancer.

The aim of this study was to investigate the impact of hospital care volume of LRH on treatment outcomes of patients with cervical cancer.

Methods: The PubMed, Embase, and Cochrane Library databases were searched with the terms "cervical cancer," "radical hysterectomy," and "laparoscopy." The selection criteria included studies presenting operative outcomes and/or perioperative complications of LRH from high-volume hospitals (HVHs) (≥15 cases/year) and low-volume hospitals (LVHs) (<15 cases/year). Fifty-nine studies including 4367 cases were selected. Linear regression analysis weighted by the average annual case number in each study was performed to evaluate differences between the groups.

Results: In HVH, a higher number of lymph nodes (24.5 vs 21.1; $P = .037$) were retrieved by LRH in older women (48.4 vs 44.5 years; $P = .010$) with tendencies of shorter operation time (224.4 vs 256.4 minutes; $P = .096$) and less blood loss (253.1 vs 322.2 mL; $P = .080$). Compared with LVH, HVH had fewer patients with stage IA disease (13.8 vs 24.4%; $P = .003$) and more patients with stage IIA disease (15.3 vs 7.1%; $P = .052$) with comparable 5-year overall survival (93.1 vs 88.6%; $P = .112$).

Conclusion: HVH is a prognostic factor for operative outcome and perioperative complications in patients with cervical cancer undergoing LRH. The exact effect of hospital volume on survival outcome needs to be evaluated.

Abbreviations: CIs = confidence intervals, DFS = disease-free survival, FIGO = International Federation of Gynecology and Obstetrics, HVH = high-volume hospitals, LARVH = laparoscopic-assisted radical vaginal hysterectomy, LNs = lymph nodes, LRH = laparoscopic radical hysterectomy, LVH = low-volume hospitals, OS = overall survival, TLRH = total laparoscopic radical hysterectomy.

Keywords: cervical cancer, high-volume hospitals, laparoscopic radical hysterectomy, survival

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BL and KK contributed equally to this work and are cofirst authors.

Ethical approval was not necessary because the type of this study was a systematic review and meta-analysis.

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1. Introduction

The incidence of cervical cancer is continuously decreasing in developed countries[1]; however, the mortality rate is still high.[2] Radical hysterectomy is the standard treatment for early cervical cancer, especially for International Federation of Gynecology and Obstetrics (FIGO) stages IA2 to IIA.[3] Radical hysterectomy requires wide dissection of the bladder and lower ureter, which is inevitably associated with a higher rate of complications such as lower urinary tract injuries than that for simple hysterectomy.[4,5]

In the management of ovarian cancer, high hospital, and/or surgeon volumes, specifically, a high number of cases performed by an individual hospital and/or surgeon have been recognized as predictive factors for receiving standard treatment and as prognostic factors for overall survival (OS) outcomes.[6,7] Since the introduction of laparoscopic radical hysterectomy (LRH) in the early 1990s for surgical treatment of cervical cancer, this minimally invasive procedure has now become well established, even when any surgeon lacks experience in open radical hysterectomy.[8–10] The learning curve for LRH in cervical cancer to achieve an acceptable level of surgical proficiency has been reported to be 40 cases.[11] In cervical cancer, high surgeon volume is a predictive marker for fewer postoperative complications, shorter hospitalization, and lower rates of transfusion after open radical hysterectomy.[12,13] However, the impact of hospital volume of LRH has not been investigated systematically as in ovarian cancer. Therefore, the objective of the present systematic analysis was to investigate the effect of hospital volume of LRH on treatment outcomes of patients with cervical cancer.

2. Materials and methods

2.1. Search strategy

In January 2017, PubMed, Cochrane Library, and Embase databases were searched for all pertinent studies without restriction on the year of publication. A combination of the following key words was used in the search: ("cervical cancer" AND "laparoscopy" AND "radical hysterectomy") and ("cervical cancer" AND "LRH") (see Appendix, Supplemental Content 1, http://links.lww.com/MD/C679, which demonstrates search strategy). Bibliographic references of selected clinical studies and review articles were also examined for additional relevant literature not covered by the database searches.

2.2. Selection criteria

The inclusion criteria for study selection were as follows: cervical cancer confirmed via permanent pathology; LRH or total laparoscopic radical hysterectomy (TLRH) or laparoscopic-assisted radical vaginal hysterectomy (LARVH); operative outcomes such as operation time, blood loss, number of lymph nodes (LNs) retrieved, and postoperative hospital stay; and/or intra- and postoperative complications. Articles on studies about neoadjuvant therapy, studies involving patients with endometrial cancers as the candidates for LRH, and studies including cases accompanied by other types of cancer; articles not in English; review articles; editorials; case reports; and letters were excluded. When multiple studies reported overlapping groups of patients, only 1 study with the largest number of events was included in the meta-analysis to avoid duplication of information.

2.3. Data extraction and outcomes of interest

Data retrieved from studies included the following details: hospital volume, surgeon volume, the name of the first author, publication year, data collection year, the number of total cases, the case number per year, study design, types of LRH, country, age, stage, histology, operation time, blood loss, number of LNs retrieved, postoperative hospital stay, intra- and postoperative complications, lymphovascular space invasion, tumor size, LN metastasis, parametrial invasion, surgical margin invasion, postoperative adjuvant therapy, postoperative radiotherapy, recurrence rate, and survival rates.

The eligible studies were classified as high-volume hospitals (HVHs) ($\geq$15 cases/year) and low-volume hospitals (LVHs) ($<$15 cases/year), based on the average annual case numbers of LRH performed in the hospitals. To evaluate the outcomes, each variable was compared with the hospital volumes.

The primary outcomes in the systematic analysis were operative outcomes, such as operation time, blood loss, the number of LNs retrieved, and postoperative hospital stay, and perioperative complications, such as intra- and postoperative complications. The secondary outcomes were as follows: prognostic factors such as lymphovascular space invasion, mass size, LN metastasis, parametrial invasion, and surgical margin invasion; postoperative adjuvant therapy, especially radiotherapy; and prognostic outcomes such as 5-year recurrence rate, OS, and disease-free survival (DFS). OS was defined as the length of time from surgery to death from any cause. DFS was defined as the length of time after the end of primary treatment for cancer wherein the patient survived without any signs or symptoms of cervical cancer.

2.4. Quality assessment

The quality of case–control studies was evaluated using the Newcastle–Ottawa Scale (see Table, Supplemental Content 2, http://links.lww.com/MD/C679, which demonstrates the quality of the included studies).[14,15] The risk of bias for interrupted time series studies was evaluated with the criteria suggested by the Cochrane Effective Practice and Organisation of Care (EPOC) Group (see Table, Supplemental Content 3, http://links.lww.com/MD/C679, which demonstrates the quality of the included studies).[16] The risk of bias of randomized controlled trials was evaluated with the Cochrane Collaboration tool (see Table, Supplemental Content 4, http://links.lww.com/MD/C680, which demonstrates how to evaluate the quality of the included studies).[17] The study qualities were independently evaluated by 2 authors (BL and KK) and any disagreements were resolved after discussion with all the other authors.

2.5. Statistics

Data expressed as a median were converted into mean by Hozo formula.[18] Linear regression analysis weighted by the average annual case number in each study was performed to overcome significant heterogeneity based on extracting data from the included studies with different study designs and to evaluate the differences between the groups using Stata/SE 14 (StataCorp LP, TX). All results were provided with 95% confidence intervals (95% CIs) and 2-sided P values. $P<.05$ was considered statistically significant. A P value between .05 and .1 was considered as having a tendency toward statistical significance. The open-source statistical software R version 3.3.2 (http://www.R-project.org) was used to illustrate differences in care between the HVHs and LVHs.

3. Results

3.1. Characteristics of included studies

Overall, 568 studies were identified and only 59 studies met the selection criteria (see Figure, Supplemental Content 5, http://links.lww.com/MD/C679, which demonstrates flow chart showing study selection). A total of 40 retrospective studies, 17 prospective studies, and 2 randomized controlled studies including 4367 cases were identified and classified as follows: HVH (13 studies, 2227 cases) and LVH (46 studies, 2140 cases). LRH, TLRH, and LARVH were performed in 27, 16, and 16 studies, respectively. Of the 59 eligible studies selected, 1 study, which was classified as a HVH,[26] included 2% of cases in which patients underwent neoadjuvant chemotherapy. Two studies classified as HVH and LVH, respectively,[25,50] also included 6% and 3.2% of cases with endometrial cancer. Three studies shared a few overlapping cases with another study published in collaboration with a different hospital.[21,27,29,30,42,63] One study was considered as 2 studies because it provided data separately according to surgeons' experience with LRH (Table 1).[19–75]

3.2. Comparisons between the high-volume and low-volume hospital care

Studies in the HVH group included patients older than those in the LVH group (age 48.4 vs 44.5 years; $P=.010$). The frequency of stage IA was lower in HVH than in LVH ($P=.003$). However, frequencies of stages IB1 and IB2 were not different between the groups. The frequency of stage IIA showed a higher tendency in the HVH group than in the LVH group (13.8 vs 24.4; $P=.052$) (Table 2 and see Table, Supplemental Content 6, http://links.lww.com/MD/C679, which demonstrates clinical outcomes of the included studies). Cases diagnosed as stage IA1 were fewer in the HVH group than in the LVH group (about 10 vs 68 cases, respectively). Of these, there were 6 cases in the HVH group and 19 cases in the LVH group with stage IA1 presenting lymphovascular space invasion; 4 cases in the HVH group and 49 cases in the LVH group were stage IA1 disease with or without lymphovascular space invasion. However, cases diagnosed as stage IIB or above were more numerous in the HVH group than in the LVH group (114 vs about 14 cases, respectively) (Table 1).

In HVH compared with LVH, there was a tendency for shorter operation time (224.4 vs 256.5 minutes; $P=.096$) and less blood loss (253.1 vs 322.2; $P=.080$). The number of LNs retrieved (24.5 vs 21.1) was higher in the HVH than in the LVH group ($P=.037$). However, the length of postoperative hospital stay (6.5 vs 7.0 days) showed no difference between the HVH and LVH groups ($P=.715$) Moreover, intra- and postoperative complications, lymphovascular space invasion, LN metastasis, and parametrial invasion were not different between the HVH and LVH groups. Although not statistically significant, the frequency of surgical margin invasion was lower in the HVH than in the LVH group ($P=.123$). Mean mass size ranged from 0 to 3.3 cm in 5 studies in the HVH group and from 1.2 to 4.4 cm in 14 studies in the LVH group (data not shown). Postoperative adjuvant therapy and radiotherapy, and the 5-year recurrence and DFS rates were not different according to hospital surgical volumes. Although not statistically significant, the 5-year OS was higher in HVH cases than in LVH cases ($p=0.112$) (Figs. 1 and 2, and see Table, Supplemental Content 6, http://links.lww.com/MD/C679, which demonstrates clinical outcomes of the included studies).

Table 1

Characteristics of the included studies (n=59).

Study	Publication year	Data collection year	No. of cases	No. of cases/ year	Study design	Types of LRH	Country	Age, y (mean)	Stage, n (%)						Histology, n (%)			
									IA1	IA2	IB1	IB2	IIA	IIB or more	Squamous cell	Adeno-carcinoma	Adeno-squamous	Others
HVH (n=13)																		
Yang et al[19]	2015	5/2008–8/2013	403	75.6	Retrospective	LRH	China	44	IA: 29 (7.2)		304 (75.4)	24 (6.0)	45 (11.2)	IIB: 1 (0.2)	336 (83.4)	49 (12.2)	10 (2.5)	12 (2.9)
Puntambekar et al[20]	2007	9/2002–12/2006	248	57.2	Retrospective	TLRH	India	61		32 (12.9)	216 (87.1)				183 (73.4)	52 (21)	13 (5.2)	
Park and Nam[21]	2014	1/2007–11/2011	260	52.9	Retrospective	LRH	Korea	48		16 (6.2)	165 (63.5)	48 (18.5)	31 (11.9)		188 (72.3)	64 (24.6)		8 (3.1)
Xu et al[22]	2007	2000-2005	317	52.8	Prospective	LRH	China	55.6		82 (25.9)	73 (23.0)	52 (16.4)	65 (20.5)	58 (18.3)				
Spirtos et al[23]	2002	7/1994–12/1996	78	31.2	Retrospective	LRH	USA	41.5		26 (33.3)	IB: 52 (66.7)				68 (87.2)	8 (10.3)	2 (2.6)	
Hou et al[24]	2011	5/2009–7/2010	33	26.4	Prospective	LARVH	China	47.6	IA: 4 (12)		IB: 10 (30.3)		15 (45.5)	IIB: 4 (12)	25 (75.8)	6 (18.2)	1 (3)	1 (3)
Pareja et al[25]	2012	12/2008–10/2010	50	26.1	Retrospective	LRH	Colombia	44.5		IA2-IB2: 47 (94)					30 (61)	15 (31)	Endometrial cancer: 3 (6)	
Lanowska et al[26]	2014	8/1994–4/2002	200	25.8	Prospective	LARVH	Germany	44	6 (3.0), LVSI (+)	21 (10.5)	89 (44.5)	26 (13.0)	11 (5.5)	IIB:45 (22.5), III: 1 (0.5), IV: 1 (0.5)	150 (75.0)	47 (23.5)		3 (1.5)
Nam et al[27]	2012	10/1997–4/2008	263	24.9	Retrospective	LRH	Korea	46.4		36 (13.7)	197 (74.9)	25 (9.5)	5 (1.9)		214 (81.4)	41 (15.6)	8 (3)	
Wang et al[28]	2016	2002-2012	203	20.3	Retrospective	LRH	China	45.2		13 (6.4)	109 (53.7)	28 (13.8)	53 (26.1)		172 (84.7)	24 (11.8)	7 (3.5)	
Pellegrino et al [29]	2008	2/2003–12/2005	56	19.2	Prospective	TLRH	Italy	43	4 (7)	4 (7)	44 (78)		2 (4)	IIB: 2 (4)	33 (59)	16 (29)	6 (12)	
Pellegrino et al [30]	2009	9/2001–10/2007	101	16.4	Prospective	TLRH	Italy	44			101 (100)				55 (54.5)	38 (37.6)	5 (5)	3 (3)
Tan et al[31]	1998	1998	15	15	Retrospective	LARVH	New Zealand	44.5		1 (6.7)	IB: 14 (93.3)				11 (73.3)	4 (26.7)		
LVH (n=46)																		
Yan et al[32]	2012	1/2000–3/2010	148	14.4	Prospective	LRH	China	42			148 (100)				130 (87.8)	17 (11.5)	1 (0.7)	
Malur et al[33]	2001	4/1994–5/1999	70	13.5	Retrospective	LARVH	Germany	47.5	3 (4.3)	13 (18.6)	IB: 41 (58.6)		3 (4.3)	IIB:9 (12.9), III:1 (1.4)	53 (75.7)	16 (22.9)		1 (1.4)
Lim et al[34]	2013	11/2009–2/2011	18	13.5	Prospective	TLRH	Singapore	47.8	2 (11.1)		13 (72.2)	3 (16.7)			6 (33.3)	9 (50.0)	2 (11.1)	1 (5.6)

(continued)

Table 1

(continued).

Study	Publication year	Data collection year	No. of cases	No. of cases/ year	Study design	Types of LRH	Country	Age, y (mean)	Stage, n (%)						Histology, n (%)			
									IA1	IA2	IB1	IB2	IIA	IIB or more	Squamous cell	Adeno-carcinoma	Adeno-squamous	Others
Hong et al[35]	2012	3/2003–12/2011	118	13.4	Retrospective	LRH	Korea	49		6 (5.0)	66 (55.9)	41 (34.7)	5 (4.4)		88 (74.5)	27 (22.8)	3 (2.7)	
Kim et al (K.T.J.)[36]	2014	1/2008–5/2013	69	12.7	Retrospective	LRH	Korea	42			66 (65.65)		3 (4.35)		37 (53.62)	25 (36.23)	3 (4.35)	4 (5.8)
Li et al[37]	2007	8/1998–12/2005	90	12.1	Retrospective	LRH	China	42					18 (20)		81 (90)	5 (5.6)	2 (2.2)	2 (2.2)
Lee et al (L.C.L.)[38]	2010	6/1994–12/2005	139	12.0	Prospective	LRH	Taiwan	48.1	IA: 60 (43.2)		75 (54.0)	1 (0.7)	3 (2.2)		119 (85.6)	11 (7.9)	7 (5.0)	2 (1.4)
Frumovitz et al[39]	2007	1/2004–12/2006	35	11.7	Retrospective	TLRH	USA	41.8	2 (5.7)	5 (14.3)	28 (80)				15	17	3	
Sardi et al[40]	1999	6/1993–12/1997	47	10.3	Retrospective	LRH	Argentina	44		10 (21.3)	30 (63.8)	5 (10.6)	1 (2.1)	IIB: 1 (2.1)				
Laterza et al[41]	2016	1997-2014	82	10.3	Retrospective	LRH	Italy	43	21 (25.6)	5 (6)	53 (64.6)		3 (3.6)					
Tinelli et al[42]	2011	1/2003–5/2010	76	10.3	Retrospective	TLRH	Italy and USA	41.9	6 (7.9), LVSI (+)	23 (30.3)	40 (52.6)	3 (3.9)	4 (5.3)		65 (85.5)	8 (10.5)	3 (3.9)	
Hwang et al[11]	2012	8/2004–4/2011	70	10.1	Retrospective	LRH	Korea	45.6	IA: 19 (27.1)		49 (70.0)	0 (0)	2 (2.9)		49 (70.0)	16 (22.9)	4 (5.7)	1 (1.4)
Steed et al[43]	2004	11/1996–12/2003	71	10.1	Prospective	LARVH	Canada	43	14 (19.7)	10 (14.1)	46 (64.8)	1 (1.4)			31 (44)	40 (56)		
Mendivil et al[44]	2016	1/2009–12/2013	49	9.8	Retrospective	LRH	USA	47.8		4 (8.2)	18 (36.7)	15 (30.6)	9 (18.4)	IIB: 3 (6.1)	38 (77.6)	9 (18.4)	1 (2)	1 (2)
Abu-Rustum et al[45]	2003	12/2000–12/2002	19	9.1	Retrospective	LRH	USA	42.6	2 (10.5)	6 (31.6)	11 (58)				10 (52.6)	7 (36.8)	2 (10.5)	
Renaud et al[46]	2000	2/1993–6/1999	57	8.9	Retrospective	LARVH	Canada	37		3 (5)	53 (93)		1 (2)		36 (63)	21 (37)		
Simsek et al[47]	2011	2007-2010	35	8.8	Prospective	TLRH	Turkey	49.2	I-IIA: 35 (100)						26 (74.2)	Nonsquamous: 9 (25.7)		
Kim and Moon[48]	1998	2/1994–2/1996	18	8.6	Prospective	LRH	Korea	48		6 (33.3)	12 (66.7)				15 (83.3)	3 (16.7)		
Marchiole et al[49]	2007	12/1986–12/2003	139	8.1	Prospective	LARVH	France	47	8 (5.8), LVSI (+)	17 (12.2)	IB: 106 (76.3)	8 (5.8)			102 (73.4)	Adenocarcinoma or adenosquamous: 33 (23.7)		4 (2.9)
Soliman et al[50]	2011	1/2007–11/2010	31	7.9	Retrospective	TLRH	USA	44.2	2 (6.5)	8 (25.8)	20 (64.5)				16 (51.6)	12 (38.7)	1 (3.2) 2 (6.5) Endometrial cancer: 1 (3.2)	
Yu et al[51]	2013	12/2003–12/2008	40	7.9	Retrospective	LARVH	China	44.9		12 (30)	17 (42.5)	9 (22.5)	2 (5)		28 (70)	12 (30)		
Estape et al[52]	2009	4/2006–8/2008	17	7.0	Prospective	TLRH	USA	52.8		2 (11.8)	14 (82.4)	1 (5.9)			11 (64.7)	6 (35.3)		
Gil-Moreno et al[53]	2005	9/1999–7/2003	27	6.9	Retrospective	TLRH	Spain	45.1		4 (15)	IB: 23 (85)				20 (74)	6 (22)	1 (4)	
Yin et al[54]	2014	6/2010–8/2013	22	6.8	Prospective	LRH	Korea	44		1 (4.5)	13 (59.1)	3 (13.6)	5 (22.7)		19 (36.4)	2 (9)		1 (4.5)
Nezhat et al [55]	2006	1/2004–2/2005	7	6.5	Retrospective	TLRH	USA	40		3 (42.9)	3 (42.9)				2 (28.6)	4 (57.1)		
Jackson et al[56]	2004	1996-2003	50	6.3	Retrospective	LARVH	UK	45.7		2 (4)	47 (94)		1 (2)		33 (66)	17 (34)		
Pahisa et al[57]	2010	1/1997–12/2007	67	6.1	Prospective	LARVH	Spain	51		3 (4.5)	61 (91)		3 (4.5)		54 (80.6)	13 (19.4)		
Mehra et al[58]	2010	1994-2002	51	5.7	Prospective	LARVH	UK	39			51 (100)				30 (58.8)	21 (41.2)		
Kong et al[59]	2014	2/2006–3/2013	40	5.6	Retrospective	LRH	Korea	45			22 (55.0)	12 (30.0)	6 (15.0)		30 (75.0)	7 (17.5)	3 (7.5)	
Sobiczewski et al[60]	2009	1/2001–12/2004	22	5.5	Retrospective	TLRH	Poland	45.4	IA: 7 (31)		15 (68.2)				20 (91)	2 (9)		
Toptas et al[61]	2014	2007-2010	22	5.5	Retrospective	TLRH	Turkey	46.5		9 (40.9)	13 (59.1)				18 (81.8)	1 (4.6)	3 (13.6)	
Mogan et al[62]	2007	1/2000–6/2005	30	5.5	Retrospective	LARVH	Ireland	35	IA: 9 (30)		IB: 21 (70)				24 (80)	6 (20)		
Malzoni et al[63]	2009	1/1995–5/2007	65	5.2	Retrospective	TLRH	Italy	40.5	5 (7.7), LVSI (+)	21 (32.2)	39 (60)				56 (86.2)	7 (10.8)	2 (3.1)	
Ditto et al[64]	2015	2/2002–10/2013	60	5.1	Retrospective	LRH	Italy	46		13 (22)	47 (88)							
Nezhat et al [65]	1993	6/1989–12/1992	18	5.0	Retrospective	LRH	USA	36.5		10 (55.6)	IB: 7 (38.9)		1 (5.6)					
Sert et al[66]	2011	4/2004–8/2005	7	4.9	Retrospective	TLRH	Norway	45	2 (28.6)		5 (71.4)							
Suh et al [67]	2015	2003–2011	40	4.4	Retrospective	LRH	Korea	48.2		IA2-IB1:39 (97.5)		IB2-IIA: 1 (2.5)			Squamous cell carcinoma, adenocarcinoma, or adenosquamous: 40 (100) adenosquamous:carcinoma			
Zakashansky et al[68]	2007	2000–2006	30	4.3	Prospective	TLRH	USA	48.3	1 (3.33)	8 (26.7)	17 (56.7)	2 (6.7)	2 (6.7)		19 (63.3)	8 (26.7)	2 (6.7)	1 (3.3)
Naik et al[69]	2010	20 mo	7	4.2	RCT	LARVH	UK	38.5			7 (100)				6 (85.7)	1 (14.3)		
Papacharalabous et al[70]	2009	1/2003–6/2006	14	4	Retrospective	LARVH	UK	38.6		IA2-IB: 14 (100)								
Sharma et al[71]	2006	1999–2005	27	3.9	Retrospective	LARVH	UK	43.4			27 (100)				18 (66.7)	9 (33.3)		
Chen et al[72]	2014	2005–2013	32	3.6	Retrospective	LRH	Taiwan	51.2	I: 27 (84.4)				II: 5 (15.6)		26 (81.3)	5 (15.6)		
Lee et al (L.E.J.)[73]	2011	1/1994–12/2001	24	3	Retrospective	LRH	Korea	48.4		5 (20.8)	13 (54.2)	2 (8.3)	4 (16.7)		19 (79.2)	4 (16.7)	1 (4.1)	
Campos et al[74]	2013	1999–2004	16	2.7	RCT	LRH	Brazil	36.2		IA2-IIA: 16 (100)					12 (75)	4 (25)		
Suh et al [67]	2015	2003–2011	15	1.7	Retrospective	LRH	Korea	50.1		IA2-IB1:11 (73.3)		IB2-IIA: (26.7)			Squamous cell carcinoma, adeno-carcinoma, or adenosquamous: 15 (100)			
Taylor et al[75]	2011	7/2003–4/2009	9	1.5	Retrospective	LARVH	USA	41.4		3 (33.3)	6 (66.7)				5 (55.6)	4 (44.4)		

HVH = high-volume hospitals, LARVH = laparoscopic-assisted radical vaginal hysterectomy, LRH = laparoscopic radical hysterectomy, LVH = low-volume hospitals, LVSI = lymphovascular space invasion, RCT = randomized controlled trials, TLRH = total laparoscopic radical hysterectomy.

Table 2

Patient selection.

	HVH (n = 13)			LVH (n = 46)			
	No. of studies	Mean	95% CI	No. of studies	Mean	95% CI	*P*
Age, y (mean)	13	48.4	46.5–50.3	46	44.5	42.3–46.7	.010
Stage IA (%)	11	13.8	9.5–18.0	33	24.4	19.2–29.7	.003
Stage IB1 (%)	9	65.2	56.9–73.6	36	70.3	61.0–79.5	.421
Stage IB2 (%)	7	11.6	6.8–16.4	14	13.7	6.6–20.8	.619
Stage IIA (%)	8	15.3	10.2–20.3	20	7.1	0.5–13.6	.052

Weighted linear regression analysis evaluating differences in care between the high-volume and low-volume hospitals.
HVH = high-volume hospitals, LVH = low-volume hospitals.

4. Discussion

4.1. Main findings

In the present study, hospital volume was a prognostic factor for operative outcomes in patients with cervical cancer undergoing LRH. A higher number of retrieved LNs, shorter operation time, less blood loss, and comparable perioperative complications and survival outcomes were observed in the HVH group consisting of fewer stage IA and more stage IIA cases.

4.2. Interpretation

4.2.1. Operative outcomes. The impact of hospital volume has not been evaluated for LRH as in open radical hysterectomy and cytoreductive surgery for ovarian cancer.[6,7,12,13] The effect of

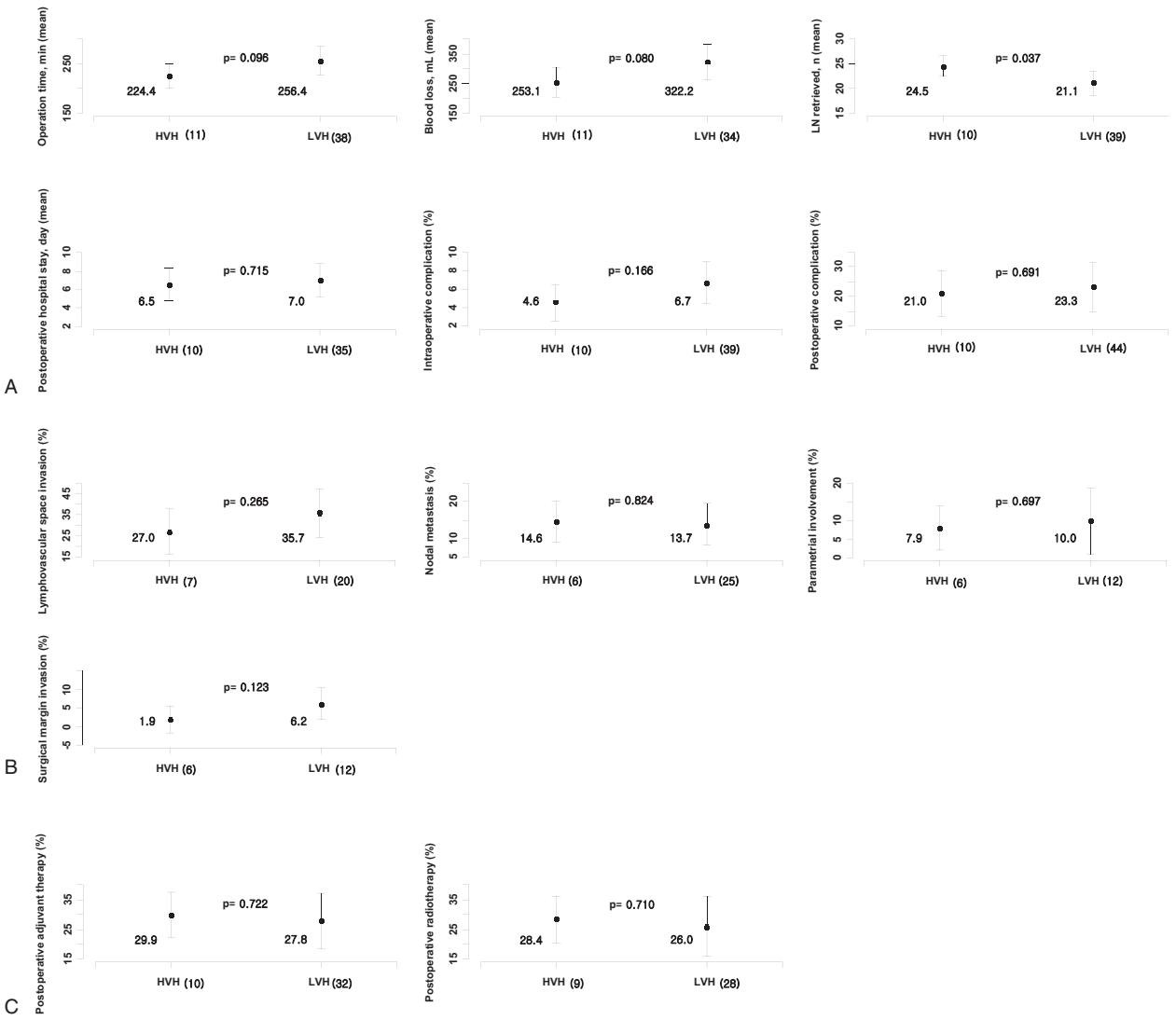

Figure 1. Weighted linear regression analysis to evaluate differences between the high-volume and low-volume hospital care. (A) Operative outcomes and perioperative complications. (B) Prognostic factors: pathologic outcomes. (C) Postoperative treatments. y-axis represents mean or percentage according to each variable and is expressed as mean ± 95% CI. Mean value of mean or percentage according to each variable is provided. Number in parenthesis represents number of studies providing data for each variable. HVH = high-volume hospitals, LN = lymph node, LVH = low-volume hospitals.

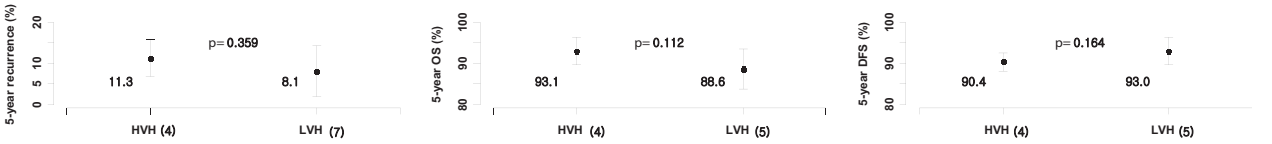

Figure 2. Recurrence and survivals: Weighted linear regression analysis to evaluate differences between the high-volume and low-volume hospital care. The y-axis represents mean or percentage according to each variable and is expressed as mean ± 95% CI. Mean value of mean or percentage according to each variable is provided. Number in parenthesis represents number of studies providing data for each variable. DFS = disease-free survival, HVH = high-volume hospitals, LVH = low-volume hospitals, OS = overall survival.

hospital volume on outcomes of cancer operation is related to a surgeon's skill and experience defined by surgical volumes, as well as hospital infrastructure and the supporting team dedicated to surgical care. Therefore, a measure of hospital volumes of surgical procedures is the most comprehensive factor affecting the outcome of surgery for cancer patients.[76] However, there have been few studies evaluating the influence of hospital volume on operative outcomes or morbidity after radical hysterectomy.[12,13,77,78] In retrospective analyses of 903 esophageal resections for esophageal carcinoma patients and 1894 primary ovarian cancer operations, HVH was associated with a shorter length of hospital stay.[77,78] In the present meta-analysis in which LRH was performed in cervical cancer patients, HVH showed higher LN retrieval rates with a tendency for a shorter operation time, less blood loss, and similar lengths of postoperative hospital stay. These findings support the results of 2 previous retrospective studies analyzing radical hysterectomy performed in 407 and 1536 cervical cancer patients, respectively, which showed favorable or comparable operative outcomes in HVH.[12,13] In addition, operative outcomes of HVH performing LRH are comparable to those of HVH performing radical hysterectomies despite the technical differences with regard to the use of laparoscopy.[12,13]

A previous retrospective study reported that HVH is associated with a higher cytoreduction rate in primary ovarian cancer operations.[78] Accordingly, the present study also showed a higher surgical adequacy with LRH in HVH based on the higher LN retrieval rate and lower surgical margin invasion rate.

4.2.2. Perioperative complications. Radical hysterectomy necessitates en bloc resection of the parametria and upper vagina in addition to extrafascial hysterectomy, which is surgically associated with dissection of the ureter and bladder, resulting in a higher rate of lower urinary tract injury than conventional hysterectomy for benign disease.[3] Therefore, perioperative complications may potentially reflect the skill of the surgeon performing LRH. Moreover, hospital volumes may more accurately reflect the impact of perioperative complications associated with radical hysterectomy because it includes assessment of the capacity of the individual surgeon and of support systems of the institution.[76] A previous retrospective study reported that HVH was associated with lower perioperative complications in esophageal carcinoma surgery, which is considered one of the most complex surgical procedures.[77] In 2 retrospective studies in which cervical cancer patients underwent radical hysterectomy, hospital volume had no influence on perioperative complications.[12,13] In the present analysis, perioperative complications did not depend on hospital case volumes of LRH performed, which was in accordance with previous studies on radical hysterectomy.[12,13] In the present study, the HVH group, because of the inclusion of cases with a higher FIGO stage, might involve a higher incidence of more extensive radical hysterectomies than the LVH group. This may induce a higher number of LN retrievals and a lower rate of positive surgical margin as pathological outcomes. However, HVH showed comparable intraoperative and postoperative complication rates to those of LVH.

4.2.3. Survival: prognostic factors and outcomes. Hospital volume has been reported to be a prognostic factor in the oncologic management of esophageal and ovarian cancer.[6,7,77,78] Common cancers including ovarian cancers showed a positive hospital and/or surgeon volume relationship with survival outcome in initial cancer treatment for particularly complex surgical procedures.[6,79,80] The current study in which HVH included cases with relatively more advanced stages, survival outcome was favorable in HVH, although the difference did not reach statistical significance.

4.2.4. Patients selection. Given the greater radicality of traditional radical hysterectomy, greater skill is required by surgeons when compared with the modified radical hysterectomy performed currently.[3] In the present meta-analysis, the HVH group included fewer stage IA cases and more stage IIA and advanced stage cases than the LVH group suggesting that more radical hysterectomies than modified radical hysterectomies might be performed in HVH. On the basis of the stage information between the 2 groups, poor survival outcomes might be expected in HVH because LVH (13.8 vs 24.4%; $P = .003$) included more stage IA1 cases and especially more cases without lymphovascular space invasion. In patients with more advanced stage disease and older age (48.4 vs 44.5 years; $P = .010$), the survival outcome was comparable between the 2 groups.

4.3. Strengths and limitations

The present meta-analysis has the following limitations. First, a relatively small number of studies from HVH were included although their patient numbers were similar to those included in LVH. Recurrence rate and survival rates might be influenced by different follow-up strategies in terms of follow-up intervals and surveillance modalities. Furthermore, comparable data from the different studies were not extracted consistently because numerous studies provided only limited information. Despite these limitations, the effect of the hospital volume on treatment outcomes has been thoroughly investigated.

5. Conclusion

On the basis of the present systematic review and meta-analysis, HVH may be considered one of favorable prognostic factors for operative outcome and perioperative complication rates in patients with cervical cancer undergoing LRH. Although there are comparable survival outcomes in LVH and HVH, with a

higher number of patients with poorer prognosis in the latter, the real benefit of hospital volume should be investigated in a well-designed study.

Author contributions

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