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PREVALENCE OF LYMPH NODE INVOLVEMENT IN PATIENTS WITH ENDOMETRIAL CANCER, COLOMBIA 2009-2016: EXPLORATORY ANALYSIS OF ASSOCIATED FACTORS

Prevalencia del compromiso ganglionar en pacientes con cáncer de endometrio, colombia 2009-2016: análisis exploratorio de factores asociados

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ABSTRACT

Objective: To determine the prevalence of lymph node involvement in patients with endometrial cancer and to explore factors associated with lymph node invasion.

Materials and methods: Prevalence study with exploratory analysis. The study included patients with endometrial cancer who underwent total abdominal hysterectomy plus bilateral salpingo-oophorectomy and pelvic lymphadenectomy with or without para-aortic lymphadenectomy in seven oncology centers in Colombia between 2009 and 2016. Patients who had received prior radiotherapy or chemotherapy, with a histological diagnosis of neuroendocrine tumors, carcinosarcomas or synchronous or metachronous lesions were excluded. Non-probabilistic sampling. Sample size n=290. Measured variables: sociodemographic, clinical and histopathological, and pelvic or para-aortic lymph node involvement. The prevalence for the period is presented. The exploratory analysis was conducted using crude odds ratio (OR) and adjusted OR by means of a multivariate model (unconditional logistic regression).

Results: Overall, 467 cases were retrieved. Of them, 163 were excluded because of non-availability of all the variables. In total, 304 patients were studied. The prevalence of lymph node involvement was 15.8% (48/304). In the crude and adjusted analysis, factors associated with lymph node involvement were lymphovascular invasion (adjusted OR: 9.32; 95% CI 4.27-21.15) and myometrial invasion (adjusted OR: 3.95; 95% CI 1.29-14.98). **Conclusion**: Of the patients undergoing lymphadenectomy, 15%

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have lymph node involvement. Less invasive diagnostic options than radical surgery to ascertain lymph node invasion should be assessed.
Key words: Endometrial neoplasms; surgical pathology; lymph nodes.

RESUMEN

Objetivo: determinar la prevalencia del compromiso ganglionar de pacientes con cáncer de endometrio y hacer una exploración de los factores asociados a la invasión ganglionar.

Materiales y métodos: estudio de prevalencia con análisis exploratorio. Se incluyeron pacientes con cáncer de endometrio llevadas a histerectomía abdominal total más salpingooforectomía bilateral y linfadenectomía pélvica, con o sin linfadenectomía paraaórtica en siete centros de oncología de Colombia, en el periodo 2009-2016. Se excluyeron pacientes con radioterapia o quimioterapia previa, diagnóstico histológico de tumores neuroendocrinos, carcinosarcomas, tumores sincrónicos o metacrónicos. Muestreo no probabilístico. Tamaño muestral n = 290. Variables medidas: sociodemográficas, clínicas e histopatológicas y compromiso ganglionar pélvico o paraaórtico. Se presenta la prevalencia de periodo; el análisis exploratorio se realizó por medio de *odds ratio* (OR) crudo y el ajustado mediante un modelo multivariado (regresión logística no condicional).

Resultados: se obtuvieron 467 casos de los cuales se excluyeron 163 por no presentar la totalidad de las variables, se estudiaron 304 pacientes. La prevalencia del compromiso ganglionar fue del 15,8 % (48/304). Los factores asociados al compromiso ganglionar en el análisis crudo y ajustado fueron la invasión linfovascular (OR ajustado = 9,32; IC95%: 4,27-21,15) e invasión miometrial (OR ajustado = 3.95; IC 95 %: 1,29-14,98).

Conclusión: el 15% de las pacientes sometidas a linfadenectomía tienen compromiso ganglionar. Se deben evaluar alternativas diagnósticas menos invasivas que la cirugía radical para establecer la invasión ganglionar.

Palabras clave: neoplasias endometriales; patología quirúrgica; ganglios linfáticos.

INTRODUCTION

Endometrial carcinoma is the most common gynecological cancer in developed countries and the second gynecological neoplasm in developing countries after cervical cancer, with an age-adjusted incidence rate of 8.4 for every 100 thousand inhabitants in the world in 2018, and an age-adjusted mortality rate of 1.8 for every 100 thousand inhabitants (1). In 2011, the age-adjusted incidence rate in Colombia was 3.5 per 100 thousand inhabitants, with an age-adjusted mortality rate of 0.8 for every 100 thousand inhabitants (2).

This neoplasm is more frequent among postmenopausal women. Bleeding is the initial sign in 75% and diagnosis is confirmed by means of uterine dilation and curettage (D&C) or hysteroscopy. As for treatment, the International Federation of Obstetrics and Gynecology (FIGO) recommends staging the disease by means of total abdominal hysterectomy, bilateral salpingo-oophorectomy plus bilateral pelvic lymph node dissection and paraaortic lymphadenectomy and, actually recommends it as the treatment of choice. Final clinical and surgical staging is determined following these procedures. In cases of patient comorbidity or in very advanced stages in which surgery is contraindicated, the recommendation is to use palliative treatments such as hormone, chemo or radio therapy (3). Some researchers challenge the use of radical surgical treatment, as discussed below.

Prognostic factors may be divided into two large groups: uterine and extrauterine. The former includes histologic type and grade, myometrial and lymphovascular invasion (LVI), cervical compromise and DNA ploidy, S phase fraction determination and the presence of hormonal receptors. Extrauterine factors include adnexal or nodal compromise, and metastasis to the peritoneum and neighboring organs (4). These are currently consid-

ered as the main prognostic factors for disease stage and lymph node involvement (5,6).

The majority of patients are diagnosed with intrauterine compromise (stage I), with a 5-year survival of 90%. Lymph node involvement, or stage III in the 2009 FIGO classification, occurs in 8-34% of patients, where stage III C1 involves pelvic lymph nodes and stage III C2 involves para-aortic lymph nodes; their presence indicates the need for adjuvant therapy (7-9).

The role of pelvic or para-aortic lymphadenectomy as standard management for all patients is controversial because the majority of patients do not have lymph node involvement and this procedure is associated with morbidity in 8-50% of cases, with intraoperative complications such as vascular injuries, or postoperative complications such as infection, lymphedema and ileus, among others (10,11). For this reason, the recommendation from several authors is to perform that intervention when: a) there are factors indicating a high possibility of lymph node involvement, including serous papillary or clear cell histology, histologic grade III, myometrial invasion greater than 50%, lymphovascular invasion, tumor size greater than 2 cm, and cervical compromise (11,12); b) sentinel lymph node compromise is ruled out (13-15); c) diagnostic images suggest lymph node involvement (16,17) or preoperative positive tumor markers (18).

Several diagnostic models have been proposed which include some of the factors described above. The aim is to gain a clearer idea of the actual indication for performing pelvic or para-aortic lymphadenectomy. However, there is no unanimous agreement to date regarding the model of choice or the way to use it (19-21). The associated factors that could be part of a diagnostic model include LVI which, if present, is associated with lymph node metastases in 21% of cases; if it is absent, that association is found only in 2.1% of cases ($p<0.001$) (22). On the other hand, it has been reported that when myometrial invasion is greater than 50% (*odds ratio* [OR] = 5.3; 95% CI: 2.11-13.20), LVI (OR = 3.7; 95% CI: 1.49-9.07) and positive pelvic lymph nodes (OR = 24.2; 95% CI: 10.18-57.47) are found, para-aortic lymphadenectomy is advisable (23). The SEER (Surveillance, Epidemiology and End Results) analysis found that patients with histological grade 3 (OR=2.77; 95% CI: 2.32-3.31), myometrial invasion greater than 50% (OR = 4.77; 95% CI: 4.16-5.47) and tumor size greater than 2 cm have factors associated with lymph node involvement (24). Kazuai *et al.* used tumor volume in cm^3 and CA 125 levels, together with myometrial invasion and histologic grade, and found that their analysis is useful for predicting lymph node involvement ($p < 0.005$) (21).

In Colombia, radical staging surgery is still performed without considering the existence or not of low or high-risk histophatological factors associated with lymph node involvement; moreover, few healthcare institutions have access to sentinel node assessment. As mentioned previously, staging surgery is associated with high morbidity. It is important to begin to study alternatives to improve the selection of patients who could benefit the most from pelvic and para-aortic lymphadenectomy. Among other things, this requires the evaluation of magnetic resonance and computed tomography and their performance in the diagnosis of lymph node compromise, as well as the validation of models developed in other countries to determine their diagnostic value or, alternatively, the development of our own models, taking into account the histophatological criteria described above together with tumor markers, in order to assess the operational characteristics at a local level. The first step towards the development of such a model is to determine the frequency of lymph node involvement in our country and the associated factors. There are only a few publications on this matter in the Colombian setting.

The objective of this study was to determine the prevalence of lymph node involvement in patients with endometrial cancer and to conduct an exploratory analysis of the associated factors.

MATERIALS AND METHODS

Design and population. Cross-sectional study. The study population included women with endometrial cancer diagnosed by endometrial biopsy and confirmed in the pathology specimen, who underwent abdominal hysterectomy plus bilateral salpingo-oophorectomy and pelvic or para-aortic lymphadenectomy in seven level III oncologic centers located in Barranquilla, Bogotá, Envigado and Bucaramanga (Clínica Bonnadona-Prevenir, Barranquilla; Unidad de Ginecología Oncológica Misión Médica, Barranquilla; Clínica Julio Enrique Medrano, Barranquilla; Clínica San Luis, Bucaramanga; Sociedad de Cirugía de Bogotá; Hospital de San José, Bogotá; Centro de Investigaciones Oncológicas Clínica San Diego, Bogotá; Hospital Manuel Uribe Ángel, Envigado), that serve patients affiliated to the state-subsidized and contributive regimes of the Colombian General Social Security System, between January 2009 and December 2016. Patients who had received radio or chemotherapy, or who had a histological diagnosis of neuroendocrine tumors, carcinosarcomas, synchronous or metachronous tumors, and patients with surgical lymph node dissection of less than 15 pelvic nodes or 10 para-aortic nodes in the pathology study were excluded. Convenience sampling was used in each institution. Sample size was calculated on the basis of population registries of the cities included in the study; 1,648 cases of endometrial cancer were estimated for the period between 2009 and 2016 (2). A prevalence of 8% of lymph node involvement was used, with a margin of error of 3%, design effect of 1 and confidence level of 95%. A number (n) of 264 cases was obtained with an adjusted attrition rate of 10%, for a total of 290 cases. The Epi Info software was used for calculating sample size.

Procedure. A secondary data source was used and data were collected by the gynecologic oncologists conducting the research in each of the institutions through the review of clinical records and pathology reports of the patients with a diagnosis of endometrial cancer (CIEO C54.0 o C54.1) between March and June 2018. The data were recorded in chronological order. Data from each institution were entered by each of the researchers in a form specifically designed for that purpose and were later entered into an Office Excel ® database and sent to the main epidemiological team in Barranquilla, which and filled general database up to sample size completion.

Measured variables. The measured variables were age (> or = < 60 years), body mass index (BMI > or = < 30), classification based on clinical-surgical stage (I-IV), type of surgery, histologic grade (grades II-III/I), histologic type (endometrioid, other), myometrial invasion (>, or =< de 50%), tumor size (>, or =< de 2 cm), presence of LVI or cervical compromise. Pelvic (stage IIIC1) or para-aortic (stage IIIC2) lymph node involvement was also determined based on pathology confirmation and defined as one or more than one lymph node with tumor involvement, regardless of the number, in a minimum count of 15 pelvic and 10 para-aortic lymph nodes removed.

Analysis. Descriptive statistics were applied to summarize the information on continuous variables using relevant central trend and scatter and taking into account the type of distribution (normal or not). For qualitative variables, the information was summarized using proportions. Prevalence during the study period of overall lymph node involvement and by site of compromise (pelvic and para-aortic) is presented.

Crude OR and the respective 95% confidence interval were used to explore the association between the occurrence of lymph node involvement (dependent variable) and clinical, anthropometric and histopathological factors (independent or exposure variables) (25). This was followed by a multivariate analysis by means of multiple binomial logistic regression using the stepwise method of successive backward steps, which allowed to rule out those variables that did not provide significant information. Initially, a model which included all the variables, regardless of the *p* value derived from

the bivariate analysis, was used. For the selection of the best model, the Akaike information criterion (AIC) was applied for goodness and adjustment. AIC compares the different regression models and selects the one that best explains the response variable. The model retained variables with a *p* value greater than the established significance, because when they are eliminated, the model loses information. Adjusted OR ($_{a}$OR), standard error and z value (Wald statistics) were derived from this process. The SPSS v 25 software (Released 2017. Armonk, NY: IBM Corp.) licensed to Universidad del Norte was used for the analysis.

Ethical considerations. This research was considered free of risk. Data confidentiality was ensured and no informed consent was required given that the study was based on clinical records. It was endorsed by the ethics committee of Universidad del Norte, as stated in minutes No. 175 of June 28, 2018. Approval was also obtained from the ethics committees of the participating centers.

RESULTS

There were 1,648 cases of endometrial cancer in the participating cities during the study period. In the participating centers, 467 patients with that diagnosis were identified and, of them, 304 that met the inclusion criteria were included; 163 patients (40%) were excluded because of absent variables in the clinical records and pathology reports (Figure 1).

The general characteristics of the population were: 49.3% (150 patients) over 60 years of age; 33.8% (103 pacientes) had a BMI > 30; median tumor size was 2.5 cm (range 0.1 to 13); the most frequent histological type was endometrioid in 84.5% (257 patients); histological grade II was the most common, found in 47.7% (145 patients); myometrial invasion greater than 50% was found in 55.2% (168 patients); LVI was detected in 19.7% (60 patients); cervical compromise occurred in 19% (58 patients). Tumor staging, the type of surgery performed, the type of tumor and the characteristics of the population are shown in Table 1.

Total abdominal hysterectomy plus bilateral salpingo-oophorectomy plus pelvic lymphadenectomy were performed in 173 patients (56.9%) while 131 patients (43.1%) underwent total abdominal hysterectomy plus bilateral salpingo-oophorectomy plus pelvic and para-aortic lymphadenectomy. The variables and final staging are detailed in Table 1.

Thus, the prevalence of lymph node compromise during the study period was 15.8% (48/304). The prevalence of pelvic lymph node involvement (stage III C1) was 11.1% (34/304), corresponding to 70.8% of the patients with nodal disease. The prevalence of para-aortic involvement (stage III C2) was 4.6% (14/304), corresponding to 29.2% of patients with nodal disease, with 10 cases of pelvic and para-aortic involvement and 4 cases of para-aortic involvement alone.

In terms of the exploratory bivariate analysis of variables associated with lymph node compromise, association was found with LVI (OR = 18.65; 95% CI: 9.00-38.68), myometrial invasion (OR = 11.70; 95% CI: 4.08-33.54), histologic type (OR = 2.42; 95% CI: 1.16-5.04), histologic grade (OR = 6.6; 95% CI: 2.30-18.90), and cervical compromise (OR = 5.80; 95% CI: 2.97-11.34) (Table 2).

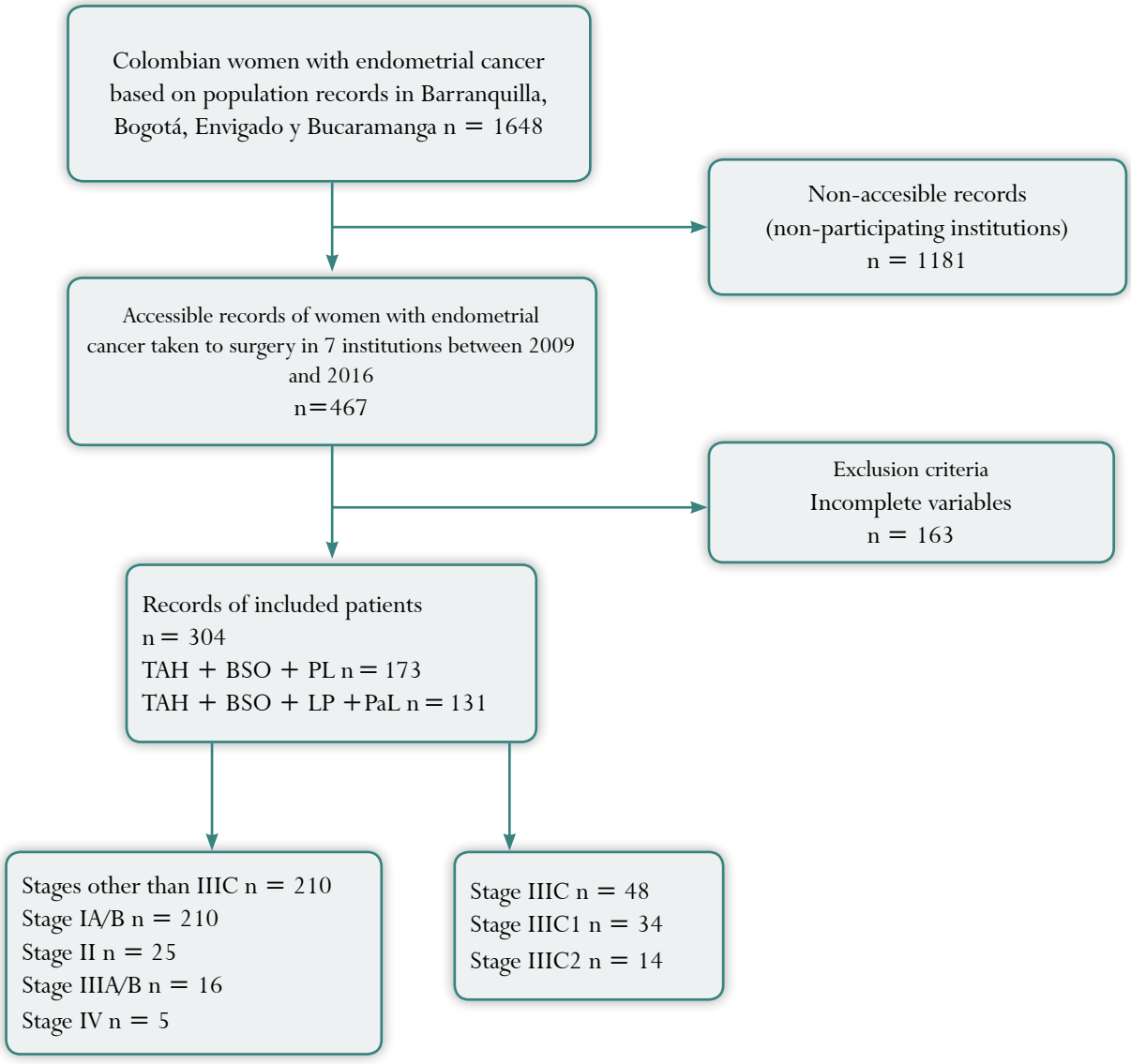
The multivariate logistic regression showed that lymph node involvement was associated with LVI ($_{a}$OR = 9.32; 95% CI: 4.27-21.15) and myometrial involvement ($_{a}$OR = 3.95; 95% CI: 1.29-14.98) as histopathological factors (Table 3).

DISCUSSION

This study showed a prevalence of lymph node involvement of 15.8%, with LVI and myometrial compromise greater than 50% being the factors associated with lymph node involvement. The prevalence of pelvic and para-aortic lymph node involvement is 11.1% and 4.6%, respectively.

The prevalence found in our study is higher than the one reported by Chi *et al.,* who found pelvic lymph node involvement in 9% of cases (26). The SEER (Surveillance, Epidemiology and End Results) analysis found evidence of lymph

Figure 1.
Flow diagram of the study population of women with endometrial cancer in 7 centers in Colombia, 2009-2016



TAH: total abdominal hysterectomy.
BSO: bilateral salpingo-oophorectomy.
PL: pelvic lymphadenectomy.
PaL: para-aortic lymphadenectomy.

Source: Authors.

Table 1.
General characteristics of the population of patients with endometrial cancer in 7 hospital centers in Colombia, 2009-2016

Characteristics	N=304
Age (years), median (IQR*)	60.0 (14)
< 60 years N (%)	150 (49.3)
> 60 years	154 (50,6)
BMI (kg/m2), median (IQR)	28.5 (3.2)
<30 N (%)	201 (66.1)
>=30	103 (33.8)
Clinical stage N (%)	
IA	118 (38.8)
IB	92 (30.2)
II	25 (8.2)
III A	9 (2.9)
III B	7 (2.3)
III C	48(15.8)
V	5 (1.6)
Surgery N (%)	
TAH+BSO+PL†	173 (56.9)
TAH+BSO+PL+PaL‡	131 (43.0)
Histologic type N (%) Endometrioid Serous papillary	257 (84.5)
Clear cells	17 (5.5)
Others	9 (2.9)
	21 (6.9)
Histologic grade N (%)	
I	106 (34.8)
II	145 (47.7)
III	53 (17.4)
Myometrial invasion N (%)	
Mayor del 50 %	168 (55.2)
Less than 50 %	136 (44.7)
LVI§ N (%)	
Yes	60 (19.7)
No	244 (80.2)
Cervical compromise N (%)	
Yes	58 (19)
No	246 (80.9)
Tumor size (cm), median (IQR)	2.5 (2.7)
<2cm N (%)	118 (38.8)
>2cm	186 (61,18)

* IQR: inter-quartile range.
† TAH+BSO+PL: abdominal hysterectomy plus bilateral salpingo-oophorectomy + pelvic lymphadenectomy
‡ TAH+BSO+PL+PaL: abdominal hysterectomy plus bilateral salpingo-oophorectomy + pelvic lymphadenectomy plus para-aortic lymphadenectomy. § LVI: lymphovascular invasion.

Table 2.
Distribution of sociodemographic, anthropometric and histopathological characteristics according to lymph node involvement in patients with endometrial cancer, in 7 hospital centers in Colombia, 2009-2016 (N = 304)

Characteristic	Lymph node involvement		OR (95% CI)
	Yes n=48	NO n=256	
Histologic type			
Non-endometrioid	13	34	2.42 (1.16-5.04)
Endometrioid*	35	222	
Histologic grade			
II-III	44	170	6.6 (2.30-18.90)
I*	4	102	
Myometrial invasion			
More than 50%	44	124	11.70 (4.08-33.54)
Less than 50%*	4	132	
LVI†			
Yes	33	27	18.65 (9.00-38.68)
No*	15	229	
Cervical compromise			
Yes	23	35	5.80 (2.97-11.34)
No*	25	221	
Age			
Over 60 years	20	130	0.69 (0.37-1.29)
Under 60 years*	28	126	
Tumor size			
Greater than 2 cm	42	144	5.44 (2.23-13.26)
Smaller than 2 cm*	6	112	
BMI‡			
More than 30	19	84	1.34 (0.71-2.53)
Less than 30*	29	172	

* Reference group.
† LVI: lymphovascular invasion.
‡ BMI: body mass index.
Source: Databases of participating centers.

node involvement in 5.3% of cases, with 1.4% in patients with low-risk factors, and 6.4% in cases of high-risk factors (24). Creasman *et al.* found pelvic lymph node involvement in 9% of patients (8). On the other hand, our findings are lower than those reported by Mariani *et al.* at 29% (27) and Ortoft *et al.* at 28%, (28). Finally, our results are similar to those of Wakayama *et al.* who report a prevalence of 13.2% (29).

In terms of para-aortic lymph node involvement, our findings are similar to those reported by Creasman *et al.* and Kumar *et al.* who found evidence of such a finding in 6% and 4% of cases, respectively, but lower than those reported by Mariani *et al.* who found evidence of para-aortic lymph node involvement with no pelvic lymph node involvement in 9% of cases (27). In our study, the prevalence of para-aortic compromise may be underestimated, considering that only 43% of the patients underwent para-aortic lymphadenectomy. The reason why lymph node dissection was not performed in that region could not be found in the records.

In the exploratory analysis, our findings regarding myometrial invasion and LVI are similar to those of other studies. Wakayama *et al.* (29) found that only LVI was associated with lymph node involvement (OR = 14.36; 95% CI: 4.3-57.6; p < 0.0001). Kumar *et al.* (23) determined that LVI (OR=3.68; 95% CI: 1.49-9.07) and myometrial compromise greater than 50% (OR=5.27; 95% CI: 2.11-13.20) were the only independent factors that could predict para-aortic lymph node involvement. On the other hand, the SEER analysis found nodal metastasis in 61.8% of the patients with myometrial invasion greater than 50%, with a *p* value =<0.001 (24). Jorge *et al.* found nodal metastasis in 21% of patients with LVI (p < 0.001) (22).

Strengths of this study include sample size and the fact that it is the first multi-center study carried out in our country to explore the association of lymph node involvement with sociodemographic, anthropometric and histopathological factors in patients with endometrial cancer. Limitations include the fact that information obtained through non-probabilistic sampling can only be applied to the studied population and, consequently, the results cannot be extrapolated to all women with

Table 3.
Anthropometric and histopathological variables associated with lymph node involvement in patients with endometrial cancer, Colombia 2009-2016. Logistic regression model

	OR	95% CI
BMI*	1.70	0.75-3.87
Histologic grade (II and III)	3.04	1.01-11.42
LVI†	9.32	4.27-21.15
Myometrial invasion (> 50%)	3.95	1.29-14.98
Tumor size (> 2 cm)	1.63	0.49-6.52
Cervical compromise (SI)	2.21	0.97-5.02

* BMI: body mass index.
† ILV: lymphovascular invasion
Source: Databases of participating centers.

endometrial cancer. As mentioned previously, the unavailability of para-aortic lymph node pathology influences the estimated prevalence. Another limitation is lack of access to central pathology review which prevents standardization of the histopathological reports. Therefore, misclassification bias is a possibility which could not be addressed although all the histopathological reports were assessed by a meeting of the pathology specialists of the participating centers.

CONCLUSIONS

The prevalence of lymph node involvement during the study period was 15%, lymphovasculaar invasion and myometrial compromise greater than 50% being the main associated factors. Less invasive alternatives to determine lymph node involvement should be evaluated, such as imaging studies or diagnostic models based on biochemical, molecular and histopathological factors pre-operatively in order to diagnose compromise and assess risks and benefits of performing radical staging surgery on a routine basis.

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REFERENCES

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. Cancer J Clin. 2018;68(6):394-424. https://doi.org/10.3322/caac.21492
2. Pardo C, Cendales R. Incidencia, mortalidad y prevalencia de cáncer en Colombia, 2007-2011. Bogotá: Instituto Nacional de Cancerología; 2015. p. 148.
3. Pecorelli S. Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. Int J Gynaecol Obstet. 2009;105:103-4. https://doi.org/10.1016/j.ijgo.2009.02.012
4. Prat J. Prognostic parameters of endometrial carcinoma. Hum Pathol. 2004;35(6):649-62. https://doi.org/10.1016/j.humpath.2004.02.007
5. Milam MR, Java J, Walker JL, Metzinger DS, Parker LP, Coleman RL; Gynecologic Oncology Group. Nodal metastasis risk in endometrioid endometrial cancer. Obstet Gynecol. 2012;119(2Pt 1):286-92. https://doi.org/10.1097/AOG.0b013e318240de51
6. Dinkelspiel HE, Wright JD, Lewin SN, Herzog TJ. Contemporary clinical management of endometrial cancer. Obstet Gynecol Int. 2013;2013:583891. https://doi.org/10.1155/2013/583891
7. ASTEC study group, Kitchener H, Swart AM, Qian Q, Amos C, Parmar MK. Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): A randomised study. Lancet. 2009;373(9658):125-36. https://doi.org/10.1016/S0140-6736(08)61766-3
8. Creasman WT, Morrow CP, Bundy BN, Homesley HD, Graham JE, Heller PB. Surgical pathologic spread patterns of endometrial cancer. A Gynecologic Oncology Group Study. Cancer. 1987;60(8 Suppl):2035-41. https://doi.org/10.1002/1097-0142 (19901015)60:8+<2035::AID-CNCR 2820 601515>3.0.CO;2-8
9. Todoa Y, Yamamotob R, Minobea S, Suzukia Y, Takeshia U, Nakatania M, et al. Risk factors for postoperative lower extremity lymphedema in endometrial cancer survivors who had treatment including lymphadenectomy. Gynecol Oncol. 2010;119:60-64. https://doi.org/10.1016/j.ygyno.2010.06.018
10. Abu-Rustum NR, Alektiar K, Iasonos A, et al. The incidence of symptomatic lower-extremity lymphedema following treatment of uterine corpus malignancies: A 12-year experience at Memorial Sloan-Kettering Cancer Center. Gynecol Oncol. 2006;103:714. https://doi.org/10.1016/j.ygyno.2006.03.055
11. Mariani A, Webb MJ, Keeney GL, Haddock MG, Aletti G, Podratz KC. Stage IIIC endometrioid corpus cancer includes distinct subgroups. Gynecol Oncol. 2002;87(1):112-7. https://doi.org/10.1006/gyno.2002.6789

12. Zhang H, Zuo Z, Wang Y, Wang L, Zhu Z. A cohort study evaluating paraaortic lymphadenectomy in endometrial cancer. Oncol Lett. 2012;4(6):1361-5. https://doi.org/10.3892/ol.2012.919
13. Kang S, Yoo HJ, Hwang JH, Lim MC, Seo SS, Park SY, et al. Sentinel lymph node biopsy in endometrial cancer: Meta-analysis of 26 studies. Gynecol Oncol. 2011;123:522-7. https://doi.org/10.1016/j.ygyno.2011.08.034
14. Robison K, Holman LL, Moore RG. Update on sentinel lymph node evaluation in gynecologic malignancies. Curr Opin Obstet Gynecol. 2011;23:8-12. https://doi.org/10.1097/GCO.0b013e32834156fb
15. Bogani G, Dowdy SC, Cliby WA, Ghezzi F, Rossetti D, Mariani A. Role of pelvic and para-aortic lymphadenectomy in endometrial cancer: Current evidence. J Obstet Gynaecol Res. 2014;40(2):301-11. https://doi.org/10.1111/jog.12344
16. Kitajima K, Murakami K, Yamasaki E, et al. Accuracy of integrated FDG- PET/contrast-enhanced CT in detecting pelvic and paraaortic lymph node metastasis in patients with uterine cancer. Eur Radiol 2009;19:1529. https://doi.org/10.1007/s00330-008-1271-8
17. Haldorsen IS, Salvesen HB. Staging of endometrial carcinomas with MRI using traditional and novel MRI techniques. Clin Radiol Jan. 2012;67(1):2-12. https://doi.org/10.1016/j.crad.2011.02.018
18. Olawaiye AB, Rauh-Hain JA, Withiam-Leitch M, Rueda B, Goodman A, Del Carme MG. Utility of pre-operative serum CA-125 in the management of uterine papillary serous carcinoma. Gynecol Oncol. 2008;110:293-8. https://doi.org/10.1016/j.ygyno.2008.05.027
19. Convery PA, Cantrell LA, Di Santo N, Broadwater G, Modesitt SC, Secord AA, et al. Retrospective review of an intraoperative algorithm to predict lymph node metastasis in low-grade endometrial adenocarcinoma. Gynecol Oncol. 2011;123(1):65-70. https://doi.org/10.1016/j.ygyno.2011.06.025
20. Berek JS, Hacker NF. Cancer uterino. En: Berek JS, Hacker NF, editors. Oncología Ginecológica de Berek & Hacker. 5 ed. Philadelphia: Lippincott Williams & Wilkins; 2010. p. 396-442.
21. Kazuaki I, Hisamori K, Kayoko K, Kazuho N, Aiko K, Ayaka I, et. al. A preoperative risk-scoring system to predict lymph node metastasis endometrial cancer and stratify patients for lymphadenectomy. Gynecol Oncol. 2016;142(2):273-7. https://doi.org/10.1016/j.ygyno.2016.06.004
22. Jorge S, Hou JY, Tergas AI, Burke WM, Huang Y, Hu JC, et al. Magnitude of risk for nodal metastasis associated with lymphvascular space invasion for endometrial cancer. Gynecol Oncol. 2016;140(3):387-93. https://doi.org/10.1016/j.ygyno.2016.01.002
23. Kumar S, Mariani A, Bakkum-Gamez JN, Weaver AL, McGree ME, Keeney GL, et al. Risk factors that mitigate the role of paraaortic lymphadenectomy in uterine endometrioid cancer. Gynecol Oncol. 2013;130(3):441-5. https://doi.org/10.1016/j.ygyno.2013.05.035
24. Vargas R, Rauh-Hain JA, Clemmer J, Clark RM, Goodman A, Growdon WB, et al. Tumor size, depth of invasion, and histologic grade as prognostic factors of lymph node involvement in endometrial cancer: A SEER analysis. Gynecol Oncol. 2014;133(2):216-20. https://doi.org/10.1016/j.ygyno.2014.02.011
25. Schiaffino A, Rodriguez M, Pasarin MI, Regidor E , Borrell C, Fernández E. Odds ratio o razón de proporciones? Su utilización en estudios transversales. Gac Sani. 2003;17(1):70-4. https://doi.org/10.1016/S0213-9111(03)71694-X
26. Chi DS, Barakat RR, Palayekar MJ, et al. The incidence of pelvic lymph node metástasis by FIGO standing for patients with adecuquately surgically staged endometrial adenocarcinoma of endometrioid hystology. Int J Gynecol Cancer. 2008;18:269-73. https://doi.org/10.1111/j.1525-1438.2007.00996.x
27. Mariani A, Dowdy SC, Cliby WA, Gostout BS, Jones MB, Wilson TO, et al. Prospective assessment of lymphatic dissemination in endometrial cancer: A paradigm shift in surgical staging. Gynecol Oncol. 2008;109(1):11-8. https://doi.org/10.1016/j.ygyno.2008.01.023

28. Ortoft G, Hogdall C, Juhl C, et al. The effect of introducing pelvic lymphadenectomy on survival and recurrence rates in Danish endometrial cancer patients at high risk: A Danish Gynecological Cancer group study. Int J Cancer Gynecol. 2019;29:68-76. https://doi.org/10.1136/ijgc-2018-000023
29. Wakayama A, Kudaka W, Matsumoto H, Aoyama H, Ooyama T, Taira Y, et al. Lymphatic vessel involvement is predictive for lymph node metastasis and an important prognostic factor in endometrial cancer. Int J Clin Oncol. 2018;23(3):532-8. https://doi.org/10.1007/s10147-017-1227-6

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