Research Article ISSN 2639-9342

Gynecology & Reproductive Health

Prognosis After Treatment of Cervical Cancer IB1: Comparison Between Radical Histerectomy Piver II and Piver III

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Received: 30 March 2020; **Accepted:** 26 April 2020

Citation: Ketheryn Adna Souza de Almeida, Fernando Lopes Cordeiro, Fabio Bustos Russomano, et al. Prognosis After Treatment of Circus Cancer IB1: Comparison Between Radical Histerectomy Piver II and Piver III. Gynecol Reprod Health. 2020; 4(2): 1-4.

ABSTRACT

Objective: *The article compares prognosis post - surgery in patients with cervical cancer Ib1 (FIGO 1988) with more than 2.0 cm, operated by technical type Piver II and Piver III in a hospital sample in Rio de Janeiro.*

Material and Method: *The method used consists of a historical analysis of a group of women with cervical cancer in the aforementioned stage submitted to the two surgical techniques analyzed. The work seeks to compare them to find an outcome of interests, considering data related to the disease, treatment and post-treatment follow-up obtained from medical records.*

Results: *Patients undergoing both surgical techniques did not have a significant difference in overall and disease-free survival. The prognostic factors such as lymph node and parametrial commitment , surgical margins, deep invasion of miocervix and lymphovascular space shown to be related to worse overall and disease - free survival.*

Conclusion: *Although there was no difference in global and disease-free survival, the group undergoing the Piver III technique had more severe tumors, so it would not be possible through the study to suggest a change in technique.*

Keywords

Cervical cancer, Hysterectomy, Postoperative, Malignant neoplasm, Intraoperative complications, Surgical techniques, Survival analysis.

Introduction

Radical hysterectomies of the type Piver II and Piver III have been considered the two main sources and treatment for cervical cancer confined to the cervix, stages Ib1 (FIGO 1988) [1-3]. The radicality in the parametrium and height of the uterine artery ligation is the big difference between the two techniques. Studies indicate that, because it is a less invasive approach, hysterectomy type Piver II can bring less morbidity compared to Piver III [4,5].

At the National Cancer Institute José Alencar Gomes da Silva (INCA) patients with stages Ia2, Ib1 and IIa1 are surgically treated with radical hysterectomies Piver II or Piver III, which enabled a comparative analysis of the two techniques. The intention of the study is to understand if, in fact, we can reduce the risks of tumoral regional recurrence and less complications, thus contributing to the decision for less radical techniques and reducing complications and postoperative morbidities.

Surgical treatment of cervical cancer

In INCA, as well as other centers of gynecologic oncology, the surgical treatment of staging Ia2, Ib1 and IIa1 consist in initially with pelvic lymphadenectomy, to define radiotherapy associated with chemotherapy in case of commitment lymph node positive in freezing perioperative. If the freezing is negative, follow the Piver II or III hysterectomy.

Despite the excellent rates of locoregional control with global

survival in five years of around 90% [6], the treatment continues to be known for its complications, which are mainly the lower urinary tract, sexual dysfunction and colorectal dysmotility, such complications are associated with partial denervation of the pelvic organs due to injury to the autonomic nervous plexus during parametrectomy [7,8]. Although surgical techniques with nerve preservation decrease these complication rates, no study guarantees such a result [9].

Although postoperative survival rates are high, surgical treatment has significant morbidity, the main complication being intraoperative blood loss causing, in up to 80% of cases, the need for blood transfusion [10,11]. In the postoperative period, complications are usually: febrile syndrome, deep vein thrombosis, pulmonary embolism and dehiscence of surgical wound [12,13]. As late complications, patients can often present urinary tract fistula, hypotonic or atonic bladder, when is necessary to undergo the catheterization, urethral stenosis and a lower limb chronic linfadema [13-15].

Prognosis of cervical cancer

The cancer stage is crucial to calculate your average survival and some reports show the survival of each cancer stage. In the work published by Quinn and collaborators in 2006, he estimated that cancer in stages Ib1 (FIGO 1988) has a survival rate of 89.1% in five years.

But when we talk about risk factors for recurrence in the same stage, Van der Putte and employees, in 2005, reviewed the criteria developed by Delgado and accepted by the Gynecologic Oncology Group (GOG), creating for the stage Ib three risk criteria locoregional or distance recurrence, dividing them into high, low or intermediate risk, which are: tumor size greater than 2.0 cm, invasion of the lymphovascular space and deep invasion of the myocervix.

In the case of the presence of these factors, the intermediate risk has a disease-free survival in five years of 80 to 90%. In the event of two or three of these risk factors, recurrence-free survival is 57% in five years, requiring adjuvance to better locoregional control. If these factors of risk of recurrence are absent, the three years disease free survival is 100%.

Considering the risks presented and the surgical procedures indicated for cervical cancer, authors observed the results of two types of surgical procedure for radical hysterectomy, type Piver II and type Piver III compared in stage Ib1 and IIa 1 tumors. Evaluating post-surgical morbidity and mortality, the authors found 24% fewer complications, mainly urinary in the groups in which the procedure performed was Piver II, therefore, recurrence or survival is not considered [16].

Subsequently, authors evaluate morbidity and survival after the procedures and no significant differences were found between the groups, however the group also presented 13% less urological complications in those submitted to the Piver II procedure against 27% of the Piver III procedure [5].

We can conclude that the complications of long-term radical hysterectomies are important, especially in the urinary tract. The risk of compromising the parametrium in early stages is usually low and is directly related to lymphovascular invasion, tumor size, deep invasion of the myocervix and the presence of compromised lymph nodes. Such criteria presented are used by the GOG, which, associated with the compromised parametric limits, are indication factors for adjuvant treatment [2,11,15,17-19].

Material and Method

A historical cohort study was conducted in patients with cervical cancer stage Ib1 stage tumors (FIGO 1988) with tumors 2.0 cm larger that undergone radicals hysterectomies, at least five years in surgical techniques Piver II and Piver III at the oncology surgery service at the Hospital do Câncer II, in Rio de Janeiro from January 2005 to December 2009.

The follow-up was based on weekly consultations with symptom assessment, physical exams, vaginal cytology collection and total transvaginal and abdominal ultrasound exams. In case of suspicion of locoregional recurrence, Computed Tomography (CT) or MRI was performed and directed biopsy.

Deaths, locoregional recurrence and distant metastasis were defined as therapeutic failures. After post five years with no evidence of recurrence, the patients were discharged.

Patients with immunodeficiency, other neoplasms or any pathologies that would affect the results were excluded. The project was evaluated by the Inca Research Ethics Committee with Human Beings and there was no risk in patient participation.

Result

The inclusion and analysis criteria, exclusion losses can be assessed by Figure 1.

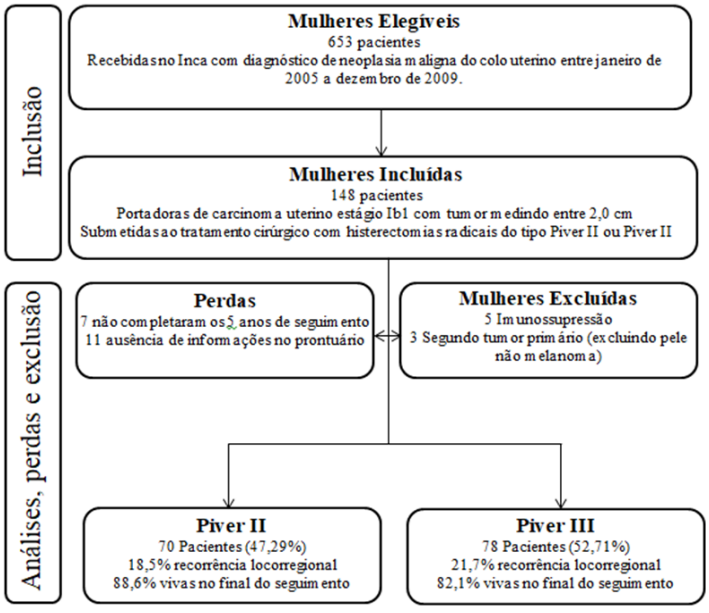

Figure 1: Study flowchart.

Among those evaluated, we considered demographic criteria those presented in Table 1. Demonstrating a very equal sample regarding the two techniques.

	Piver II	Piver III	Total	p-valor
Número de pacientes (%)	70 (47,3)	78 (52,7)	148 (100)	-
Idade média em anos (DP)	45,99 (12,2)	46,40 (12,11)	46,2 (12,07)	0,7424*
Número médio de parceiros (DP)	2,47 (0,847)	2,9 (1,392)	2,69 (1,17)	0,003*
Tabagismo a época do diagnóstico (%)	28 (47,5)	31 (52,5)	59 (39,8)	0,975†

*Teste t de Student

† Teste do Exato de Fisher

Table 1: Demographic characteristics of the patients included (INCA 2005-2009).

In Table 2 we can see that the tumors submitted to the Piver II technique were smaller than the ones normally approached by Piver III. The histological types being common among the samples are the epidermoid and adenocarcinoma. Table 3 shows treatment, early complications and their characteristics, while Table 4 shows the characteristics of complications that occurred during follow-up.

	Piver II	Piver III	Total	p-valor
Número de pacientes (%)	70 (47,3)	78 (52,7)	148 (100)	-
Tamanho médio do tumor ao exame físico em cm (DP)	1,88 (0,512)	3,1 (0,616)	2,53 (0,83)	0,020*
Grau Tumoral				0,081†
Grau 1	10 (76,9)	3 (23,1)	13 (8,7)	
Grau 2	45 (44,6)	56 (55,4)	101 (68,2)	
Grau 3	15 (44,1)	19 (55,9)	24 (23,1)	
Tamanho médio do tumor na avaliação histopatológica em cm (DP)	2,32 (0,406)	3,12 (0,548)	2,74 (0,62)	<0,0001*
Presença de invasão linfovascular (%)	14 (20)	31 (39,7)	45 (30,4)	0,009†
Presença linfovascular profunda (%)	26 (37,1)	39 (50)	65 (43,9)	0,196†
Margens cirúrgicas comprometidas (%)	2 (2,8)	6 (7,6)	8 (5,4)	0,194†
Presença de linfonodo comprometido (%)	2 (2,8)	9 (11,5)	11 (7,4)	0,044†
Presença de paramétrio comprometido (%)	3 (4,2)	8 (10,2)	11 (7,4)	0,167†
Tipo Histopatológico				0,459**
Carcinoma epidemóide	42 (60)	41 (52,5)	83 (56)	
Adenocarcinoma	21 (30)	26 (33,3)	47 (31,7)	
Carcinoma adenoescamoso	6 (8,5)	11 (14,2)	17 (11,4)	
Carcinoma adenoide basal	1 (1,5)	0 (0)	1 (0,9)	

*Teste t de Student

† Teste do Exato de Fisher

** Teste do Qui-quadrado

Table 2: Characteristics of the tumor and the surgical specimen resulting from the treatment (INCA, 2005-2009).

The Table 5 focuses show recurrence risks locoregional and deaths in each group analyzed using the incidence density ratio and the ratio of charges, in order to observe association between the results and techniques used.

Among patients undergoing adjuvant treatment with radiotherapy associated or not with chemotherapy, 11.4% were approached by the Piver II surgical technique, against 21.7% approached by the Piver III technique.

	Piver II	Piver III	Total	Risco relativo (IC95%)	p-valor
Número de pacientes (%)	70 (47,3)	78 (52,7)	148 (100)	-	-
Tempo médio de cirurgia em min (DP)	216 (37,071)	249 (44,710)	233,91 (44,2)	-	0,345*
Sangramento per-operatório com necessidade de hemotranfusão (%)	4 (5,7%)	3 (3,8)	7 (4,7)	1,48 (0,34-6,40)	0,593†
Complicações pós-operatórias (%)	14 (20)	39 (50)	53 (35,81)	0,41 (0,21-0,69)	0,003†
Fístula vésico-vaginal	1 (1,4)	7 (8,9)	8 (5,4)	0,12 (0,02-1,26)	0,043†
Discinesia vesical (%)	5 (7,14)	17 (21,9)	22 (14,86)	0,32 (0,12-0.84)	0,012†
Outras complicações (%)	8 (12,8)	15 (17,9)	23 (15,54)	0,59 (0,26-1,31)	0,20†
Abcesso pélvico	1	4	5	0,27 (0,03-2,43)	0,43†
Estomose uretal	0	1	1	-	-
Evisceração	1	0	1	-	-
Íleo prolongado	0	1	1	-	-
Infecção de ferida operatória	1	0	1	-	-
Linfonocele	3	4	7	0,83 (0,19-3,60)	-
Perfuração Intestinal	0	1	1	-	-
Sepse urinária	1	0	1	-	-
Suboclusão intestinal	1	5	6	0,22 (0,02-1,86)	0,26†
Realização de tratamento adjuvante (%)	8 (11,4)	17 (21,7)	25 (16,9)	052 (0,24-1,13)	0,093*
Recorrência locorregional durante o seguimento (%)	13 (18,5)	17 (21,7)	30 (20,2)	0,85 (-44-1,62)	0,6†
Óbito durante o segmento	8 (11,4)	14 (17,9)	22 (14,8)	0,63 (0,28-1,42)	0,37†

*Teste t de Student

† Teste do Exato de Fisher

** Teste do Qui-quadrado

Table 3: Treatment characteristics and complications (INCA, 2005-2009).

	Piver II	Piver III	Total
Número de pacientes (%)	70 (47,3)	78 (52,7)	148 (100)
Cistite actínica	0	1	1
Estenose uretal	1	4	5
Exclusão renal	2	2	4
Insuficiência renal	0	2	2
Fistula retovaginal	1	0	1
Trombose venosa profunda	2	2	4
Edema de membros inferiores	3	1	4
Necrose pododátictlo	0	1	1
Total (%)	9 (12,85)	13 (16,6)	23 (15,54)*

*P-valor = 0,557 (Teste do Qui-quadrado).

Table 4: Characteristics of complications that occurred during the follow-up (INCA, 2005-2009).

	Densidade de Incidência (por 1.000 pacientes-mês)		Razão das taxas de densidade de incidência (IC 95%)	
Fator prognóstico	**Piver II**	**Piver III**	**Recorrência locorregional**	**Óbito**
Presença de linfonodo comprometido	0,43	1,65	-	-
Margens cirúrgicas comprometidas	0,43	1,10	1,88 (0,72-4,91)	-
Presença de paramétrio comprometido	0,65	1,47	3,04 (1,58-5,99)	5,37 (2,55-11,3)
Presença de invasão profunda	5,67	7,17	2,19 (1,11-4,34)	5,05 (1,75-14,47)
Presença de invasão linfovascular	3,05	5,70	2,18 (1,20-3,96)	3,77 (1,70-8,35)

*Não foi possível calcular.

Table 5: Incidence density rates for locoregional recurrence and death according to the presence of the studied prognostic factors (INCA, 2005-2009).

Conclusion

The study sought to compare post-surgical prognosis of patients with cervical cancer, stage Ib1, greater than 2.0 cm, approached by the Piver II and Piver I II surgical techniques.

The hypothesis presented was intended to prove that the Piver II surgical technique could be used as a less radical approach to treatment and less morbidity.

The discussion regarding the extent of the resection of the parametrium is present in the world literature, mainly due to the low risk of parametrial involvement in the pieces of radical hysterectomies [2,8,12,17,20]. Considering that the tumors approached by the Piver II and Piver III techniques had, on average, 2.32 cm and 3.12 cm, respectively, it leads us to conclude that the oncological gynecology service has opted for more radical surgeries in larger tumors.

As expected, Piver III hysterectomy had higher morbidity compared to Piver II. The CIs analyzed using the Kaplan-meier method proved that radical hysterectomy type Piver II is no less effective than type Piver III, in oncological terms. However, we noticed that Inca surgeons have a tendency to be more radical in larger tumors of the same stage.

When it comes to adjuvance, we point out that 11.4% of patients covered by the technical Piver II, underwent adjuvant treatment with radiotherapy and / or chemotherapy, compared to 21.7% of the patients submitted to the technical Piver III.

However, the hypothesis presented that patients approached by the Piver II technique present risks of locoregional recurrence less than 10% in relation to those submitted to the Piver III technique for the treatment of cervical cancer, in Ib1 staging, greater than 2.0 cm, is not supported only on the basis of the study presented. The conclusion is mainly due to the sample showing bias in conduction by Inca surgeons.

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