

The Age Like Decisive Risk of the Cervical Cancer: A Vision from the Secondary Prevention

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Abstract

Introduction: At the present, many countries show a global tendency to the increment of the specific mortality with the increment of the age, being reported 70% of the deaths in women older than 50 years.

Objectives: To design a performance proposal based on a model of risk in patient older than 50 years with diagnosis of cervical cancer.

Design Methodological: The case-control study was carried out with the 102 patients with cervical cancer during the period 2014-2018 in the Youth's Island, to determine those clinical-epidemiological variables related with the biggest probability in the illness in women older than 50 years of age and that it allowed to design a proposal that it will allow to optimize the focus diagnosis of this pathology.

Results: At 43% of the patients had more than 50 years and this group represented 74% of the patients in stage II-IV. At 65% of the patients was concentrated on the area of La Fé and the northwest of the urban area of Gerona, being significant the rate of incidence of the rural area of La Fé. Only one-half of the cases they had an abnormal cytology, prevailing the inadequate cytological screening in women older than 50 years, with risk of death smaller to two years.

Conclusions: The presence of the habit of tobacco, with their first childbirth before the 20 years, more than a non-useful cytology in last 10 years and without having Pap screening in the last 5 years it meant 86% of probability of developing an invasive cervical cancer in patient older than 50 years of age.

Keywords: Cervical Cancer; Age; Risk Prediction

Introduction

The cervical cancer constitutes the fourth more common malignancy in the woman at world level and it represents a great global challenge of health. Approximately 90% of the 270 thousand deaths happened in 2015 by this cause took place in countries in development, where the mortality is 18 times adult to of the women which they live in countries of the first world" [1].

In 2018, 569 847 new cases of cervical cancer were diagnosed and occurred 311 365 deaths at world level, evidencing an incidence and very variable mortality in relation to the geographical region [1]. It's possible that the number of new cases increases in approximately 70% in next 20 years [2].

Among the available different strategies of prevention of the cervical cancer at the present time continues occupying an outstanding place the screening with the technique of Papanicolaou. From their development, in the years 40 of last century, it has extended all over the world, having contributed from an outstanding way to the decrease of the mortality for this cause.

In South Africa, 25% of the cases diagnosed among 2004 - 2012 was in the group 40-49 year-old [3]. However, many countries show a global tendency at the present time to the increment of the specific mortality with the increment of the age, being reported 70% of the deaths in women older than 50 years. A population study during seven years that it studied 70 thousand cases of cervical cancer showed that in bigger women the diagnosis spreads to be in more advanced stages (16,5% in women 21 - 34 years-old vs 42,4% in older than 70 years) [4].

In United States of America, the incidence and mortality for this cancer is also high in women bigger than 70 years (6,5 for 100 thousand women vs 3,2 in 40 - 44 year-old women). Evidences also suggest that the women older than 65 years that they received the benefits of an appropriate screening have a significantly smaller incidence to those that were not sieved [5].

A published study in Holguín (Cuba) for Cordero Díaz., *et al.* [6] found that 65% of the malignancies of its series was presented in women older than 65 years and the cervical cancer, it represented 28% of the total of malignancies in this age group.

The problem of the precocious diagnosis of the illness (that includes the programs of screening) it has particular and interesting characteristics [7]. Among the most important, we can pointout:

- The aging per it doesn't look like each other to be the fundamental cause of the illness; it is generally accepted that as it is prolonged the individual's life, it increases proportionally the period of exhibition to numerous cancerigenic agents, that which increases the risk for the cancer.
- The presence of symptoms of several chronic illnesses can mask the early manifestations of the wicked neoplasm.
- In many cases, the old women don't receive all the benefits of the programs of precocious detection for the cancer. She owes it to diverse reasons (inadequacy of the medical insurance to cover the diagnostic actions of the screening, the individual's self-isolation, inadequate sanitary education and the existence of a health politics that, in general lines, it is more directed to the therapy that to the prevention of the illness).

In the Youth's Island, the period 2014-2017 concentrate 62% of the new cases of the period 2003- 2017 [8]; however, after the highest incidence in the last 25 years in 2004 with 93 cases (including carcinoma *in situ*) a progressive decrease of the number of cases is observed up to 28 cases in 2018 (author's data), with more than 80% of them in precocious stages (stages 0-I).

Then the following idea and query that it motivates this investigation arises: If these women take as minimum 25 years in the screening, carrying out cytologies every three years (at least eight cytologies) with a sensibility among 60 - 70%, with a sexual life of less risk for the characteristic of this stage of the life, why so many cases they are diagnosed in late stage, with the rising negative repercussion in the individual, family health and the society, in general.

General Objective

To design a performance proposal on the indications of the National Program of Precocious Diagnosis of the Cervical Cancer in Cuba, based on a model of stratification of risk in patient older than 50 years with diagnosis of cervical cancer.

Methodological Design

A case-control study was developed to determine those clinical-epidemiological variables that were related with the biggest probability in appearance of the cervical cancer in women older than 50 years in the Youth’s Island during the years 2014 - 2018, selected as case (n = 44) the patients older than 50 years and like controls (n = 58) the patients with less than 50 years of age, what embraced as universe the entirety of 102 cases of cervical cancer of the period. Variables were studied as age, origin, risk factors, sign and symptoms, cytological screening and clinical stage. Significance statisticians were determined with 95% (odds ratio) and the variables that showed statistical significance in analysis univariado, were included in model of multiple regression with SPSS version 22. The obtained result was validated with test of adjustment of Hosmer and Lemeshow.

Results

During the period of study, 43% of the patients with cervical cancer had more than 50 years, being the 51 - 60 year-old group the more represented with almost the third part of the cases (29%), followed by the 21 - 30 year-old group with 24% and the 41 - 50 year-old group with 22%; being the rate x 1000 women smaller than 50 years of 3,41 with the 21 - 30 year-old group like the stratum of more rate (4,50 x 1000 women) while the rate average in women older than 50 years was of 2,29, with the biggest value among 51 - 60 years with 4,33.

However, if they decrease the sample to the patients in later stage (II-IV) according to FIGO classification it is obtained 30% of the initial sample and a rate of 22,5 cases by 10,000 women. In such a sense, the 51 - 60 years-old group represented more than fifth two parts of the cases (42%), followed by the 41 - 50 years-old group with 23% and the 61 - 70 years-old group with 19%. That is to say, the group of patient older than 50 years represented 74% (three of each four) of all the patients diagnosed belatedly, with a rate average for 10,000 women of 16,2 versus a rate average of 6,3 in women younger than 50 years old.

As for the distribution, both study groups according to consultation reason, it is observed that the control group the number of patients with abnormal cytology duplicated to the group of patients that went for a cervical lesion, while the visible lesion was the main cause of attendance in the group of cases. Between both groups, it was only a significant difference in those that went for the abnormal cytology (chi. C: 4,84, p = 0,03).

Regarding the cytological diagnosis, it is appreciated that in the group of cases the patients prevailed with positive cytology to neoplasm cells, negative or not carried out in the last 5 years, while in the control group the patients prevailed with cytology of high degree, of low degree and negative, in that order. Between both groups were significant the difference in the patients with cytology of low degree, negative or of high degree (p < 0,05).

So, the sixth part of the patients of the group of cases only had an appropriate one sieved cervical, with three cytologies in the last 10 years, prevailing in this group the patients without cytology in the last 5 years, the patients with two cytologies in the last 10 years, the patients with previous abnormal cytologies and the patients with more than a non-useful cytology in the last 10 years. In the control group, the patients prevailed with having sieved normal (40%), with two cytologies in the last 10 years, the patients with previous abnormal cytologies and the patients without cytology in the last 5 years. Only in the patients with more than a non-useful cytology in the last 10 years, without cytology in the last 5 years and with having sieved normal, in that order, it was a significant difference between both study groups (Table 1).

Pap smear	Cases	Controls	Chi-Square	p (< 0,05)
More than a non-useful cytology in the last 10 years	11	2	8,60	0,003
Without cytology in the last 5 years	24	16	6,54	0,011
Three cytology in the last 10 years	7	23	5,69	0,017
Non-useful last cytology	9	5	2,04	0,153
Previous abnormal cytology	7	5	0,68	0,041
Previous cytology with CIN/cancer	12	17	0,05	0,821
Two cytology in the last 10 years	13	19	0,02	0,896

Table 1: Patients with cervical cancer by pap smear previous. Youth Island, 2014 - 2018.

As for the risk factors, four epidemiological variables showed statistical significance in the single analysis: the previous diagnosis of CIN2+ (OR = 6,88), the first childbirth before the 20 years old (OR = 5,54), the tobacco habit (OR = 5,04) and the biggest parity at two (OR = 4,38). In the rest of the studied variables it was not significance (Table 2).

Risk factors	Cases	Controls	Chi-C	p	OR
Previous diagnosis of CIN2+	12	3	8,06	0,005	6,88 (1,92 - 9,31)
The first childbirth before the 20 years old	19	7	11,17	0,001	5,54 (2,09 - 8,57)
Smoker	25	12	12,61	0,000	5,04 (2,13 - 9,96)
Parity > 2	21	10	9,59	0,002	4,38 (1,79 - 9,67)
Abnormal previous cytology	7	5	0,68	0,041	2,01 (0,62 - 6,47)
Previous cytology CIN2+	19	30	0,43	0,512	0,71 (0,32 - 1,55)
Family history of cancer	5	11	0,59	0,441	0,55 (0,18 - 1,65)
Miscarriages > 3	3	10	1,59	0,206	0,35 (0,09 - 1,28)
First sex < 16 years old	8	30	10,65	0,001	0,21 (0,08 - 0,52)

Table 2: Patients with cervical cancer by risk factors. Youth Island, 2014 - 2018.

Source: Individual clinical history.

In table 3, the analysis of multiple regression of the variables finding that four of the included variables reflected a causal analysis, reflecting the presence of more than a non-useful cytology in the last 10 years a risk 8,5 times, followed by the first childbirth before the 20 years with a risk 6,8 times, the smoking with a risk 5,6 times and the not cytology realization in the last five years, with a risk 5,2 times. That is to say, according to the proposed pattern a patient older than 50 years, smoker, with their first childbirth before the 20 years old, with more than a non-useful cytology in the last 10 years and without cytologies in the last 5 years has 86% of probability of developing an invasive cervical cancer.

Risk factor's	EE	Sig	OR (IC 95%)	Coef
More than a non-useful cytology in the last 10 Years	1,008	0,020	8,46 (4,45 - 9,38)	2,347
The first childbirth before the 20 years old	0,677	0,001	6,77 (2,59 - 9,87)	2,228
Smoker	0,581	0,003	5,56 (1,78 - 7,38)	1,716
Without cytology in the last 5 years	0,585	0,005	5,21 (1,65 - 6,38)	1,650
Diagnosis CIN2+	0,887	0,165	3,42 (0,60 - 6,49)	1,231
Parity > 2	0,642	0,155	2,49 (0,71 - 5,77)	0,913

Table 3: Multiple Regression. Cervical Cancer, Youth Island, 2014 - 2017.

Constant: 1,703

Coef-beta-0: -2.56

Likelihood ratio: 86.01 p = 0.001.

According to the classification of the International Federation of Gynecology and Obstetrics (FIGO), finding that only in the most precocious stage (stage I) the young patients and the groups of cases prevailed (> 50 years) it only meant 24% of the total of diagnoses. In the rest of the stages (later stages) the patients older than 50 years meant 73% in the stage II, 63% in the stage III and the fifth three parts for the stage IV. That is to say that had more than 50 years of the total of patients diagnosed in the stage II-IV 68%.

As for the survival of the patient's deceased in the period, one can observe that around 90% of the cases with survival smaller than 24 months had more than 50 years of age, while 60% of the patients younger than 50 years had a survival bigger than two years.

Discussion of the Results

According to the data presented by the International Agency for Research on Cancer (IARC) [9], the incidence of cervical cancer in Spain during 2012 was of 7,8 new cases and 2,1 deaths for each 100.000 women, with an age of presentation it is located around the 50 years and alone 10% of the cases happens in older than 75 years. Presently study the age stocking belonged to $45,6 \pm 4,5$ years and the patients older than 75 years they only represented 4,6% of the sample.

As National recognizes Health Interview Survey (NHIS) [10] in a series studied between 2013 and 2015, although it is calculated that for that period the group of patient > 65 years represented the fifth part of the new cases and the third part the deaths for this cause in the United States, these values are undervalued when not reflecting the true proportion of patient in risk. If among the 40 - 44 years, 12% is calculated they are hysterectomized for varied causes, this value is increased until more than 40% to the 70 years, influencing notably in the real rates of morbidity and mortality; to that which should be added that in the female population non hysterectomized the cytological sieved can be as different as 12% without investigation in the fifth decade of the life and 24 - 28% among the 60 - 64 years of age. Based on this series of the NHIS in the 2015, near 845,000 North American women among 61 - 65 years were not sieved recently.

In the article "Trends in cervical cancer mortality rates in Lithuania, 1987 - 2016", Everatt and Intait [11] point out that the mortality in patient older than 50 years (22,6%) it duplicated the deaths below that age (11,7%). Gopalani, *et al.* [12] point out that, in United States, between 1999 and 2013 the tendency of the illness was toward the decrease with the increment of the age, except starting from the 60 years, when a second pick of incidence was reached, while the biggest rates of adjusted mortality to the age were reached above the 70 years.

In 2016, around the third part of the cases of cervical cancer in Denmark was found in women older than 60 years, in which it was a rate of mortality four times adult to the rate in women up to 59 years of age [13]. To revert this tendency are important to understand that this behavior obeys an insufficient one sieved (or not sieved), a bad pursuit of the detected cases or a faulty quality of the realization of the Pap smear.

The basic explanation to this behavior is related with the own natural evolution of the infection for the VPH considered necessary cause for the development of an intraepithelial lesion or a cervical cancer. In young population, although the prevalence of the infection is very high, it is also it the clearing capacity for the immune system. However, after the 30 - 35 years, this clearing capacity diminishes and the infection for the VPH persists in the cervical epithelium developing its oncogenic capacity and the prevalence of CIN2+ that requires surgical treatment increasing.

In a study in Spain [14] (Marta Castillo, 2018) the included population's half age was of 56,5 years (range 33 - 83 years). The reason of more frequent consultation was the presence of some symptom (78,7%). 47,9% of the women was diagnosed in stage I, 36,2% in stage II, 11% in stage III and 5,1% in stage IV. These results you consistent to the opposing ones in the present investigation where 51% of the patients only went for an abnormal cytological result and less than half of the patients they were diagnosed in precocious stage, what denotes the late clinical appearance of symptoms that they motivate the attention of women with negative cytologies.

Diver, *et al.* [15] found in their series of 1.119 patients that in the patients younger than 65 years 42% of them was diagnosed in stage II-IV and in the patients older than 75 years this group represented 70% of the cases; being also bigger the percentage of smokers (39% vs 47%).

Another distinctive element of the pap smear in the post-menopausal women, like they meditate Wang, *et al.* [16] are the frequency of had not been conclusive that they are presented as a consequence of physiologic changes characteristic of the ceasing of the estrogenic

action, many of those which they are interpreted erroneously as negative and they don't receive a specific evaluation. This element was opposing significantly in the study series.

In the study of Vasconcelos [17] of the 374 included women, 288 were in an age range understood between the 25 and the 70 years. In 189 women (65,6%) it didn't consist at least in their clinical history any cytology in the 5 and a half years previous to the diagnosis. This percentage was related with the oldest age to the diagnosis, meeting an inverse relationship among the stage to the diagnosis and the percentage of women with cytological history in the last years.

In the analysis of the history of having sieved in the diagnosed women of invasive cervical cancer with an age older than 70 years reflected that in 83,3% it didn't consist the realization of any cytology previously to the moment of the diagnosis and in this group of women they presented symptoms in 95,3% of the cases, and in 87,7% of those diagnosed in a stage II or superior didn't consist any previous cytology. This study concluded that the superior age to 50 years and a sieved inadequate they were risk factors associated to the advanced stage of illness. Besides that, the frequency of later diagnoses can until being duplicated in this group of patient in the rural areas. To the authors' opinion, in this means it is not the accessibility to the services of health a decisive element to the practice of the one sieved cervical after the 50 years, like some authors refer, but rather it obeys a phenomenon multicausal in which influences the scarce perception of risk sustained in a deficit primary prevention a lot and to ingrained sociocultural elements and that in the present investigation it is not only illustrated in the percentage of patient with having sieved cervical inadequate, but also in the precocity or not of the diagnosis and the present symptomatology in them.

Numerous researcher has tried to show the effect of the age on the survival. According to Rossana Ruiz [18], in a series presented by Meanwell with 10 022 patients treaties between 1957 and 1981 of which 1605 were smaller than 40 years, it was a difference statistically significant in the survival stage, favoring the youngest patients. It also mentions Kosary, *et al.* to the who they demonstrated that the survival and for stage to five years was bigger in the women younger than 30 years and this it constantly declined as the age increased; as well as other more modern comparative studies where they have not found differences in the survival among young and older patients.

It is coincident the opinion of the authors with other researcher that the global survival in patient older than 50 years can differ significantly, in terms of the biggest prevalence of co-morbidity that influence negatively in this indicator as they are the values hemoglobin average, the natural deterioration of the hepatic and renal function or motivated by affections like arterial hypertension and diabetes mellitus, as well as the tendency to the late diagnosis - like one argued previously in this study - where they are tributary of treatments adjuvant radiotherapy-chemotherapy.

Conclusions

The women older than 50 years had a statistical significance in the morbidity and mortality for cervical cancer in the Youth's Island.

The patient older than 50 years associated significantly to the advanced diagnoses and the mortality for this illness.

It was a significant difference between both study groups in the patients with more than a non-useful cytology in the last 10 years, without cytology in the last 5 years and with having sieved normal, prevailing both first in the group of patient bigger than 50 years.

The presence of the habit of smoking, with their first childbirth before the 20 years, more than a non- useful cytology in last 10 years and without having cytological sieved in the last 5 years it meant 86% of probability of developing an invasive cervical cancer in patient older than 50 years of age.

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