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Original Research Article

An Expression of Protein 53 (P53) did not Correlate with Staging of Ovarian Cancer

I Gde Sastra Winata*, I Ketut Suwiyoga, I Wayan Megadhana

Obstetrics and Gynecology Department, Faculty of Medicine Udayana University, RSUP Sanglah Bali

***Corresponding Author's email: dr.igsw@yahoo.com**

Abstract

Analyze the correlation protein 53 (p53) expressions and staging of ovarian cancer. A cross-sectional study of Obstetrics and Gynecologic, Pathology Anatomy and Medical Record in Sanglah General Hospital, Denpasar, conducted from July 2011 to December 2013 with a total of 44 paraffin blocks sample. Paraffin block samples are grouped based on the stage of ovarian cancer: ovarian cancer stage I, II, III, and IV. Then each group did p53 expression examination by immunohistochemical techniques. Then we do further assessment of the correlation between p53 and stage of ovarian cancer by using Spearman Test. Average age, body mass Index (IMT), parity, history of hormonal contraceptives in four group stage of ovarian cancer is homogeneous. Based on the test of correlation obtained a value of r =-0,099 (p = 0,522) indicated that there was no relationship between the ovarian cancer stages with p53 expression. p53 Expression is not associated with the staging of ovarian cancer.

Keywords: p53 expression, stages of ovarian cancer, (Add 3 more)

INTRODUCTION

Ovarian cancer is a malignant tumor on ovaries with a histogenicity variability because it can be derived from these three kind of dermoblast; ectoderm, mesoderm and endoderm. Recently the exact causes of ovarian cancer are still unknown. In the United States, the number of new cases and the death rate of ovarian cancer is increased every year, which in 2002 incidence as much as 23.300 case with the mortality rate of 56.29%. In 2003 increased to 25.400 cases with a mortality rate of 59.66% and in 2007 were 22.430 with increased death rate reached 68.12%. Even in 2010 is estimated to be as much as a 21.880 new case will be diagnosed with the mortality rate to 63.30% (American Cancer Society, 2010). High mortality rates and low life expectancy over the past five years on ovarian cancer, greatly determined by how early we recognized the stage of ovarian cancer. When stage of cancer found earlier, life expectancy of patients with ovarian cancer will be longer (Ari, 2008). Lately, various studies have been developed to improve early detection of ovarian cancer, with purpose to lower morbidity and mortality rates as well as increase life expectancy of the patient. But so far we haven't found an ideal early detection tool for patients with ovarian cancer. This phenomenon, make experts started to think of different methods in conducting early detection of ovarian cancer through genetic approaches. Some genes and protein expression of genes suspected of having abnormalities and are involved in the carcinogenesis of ovarian cancer have been known. One of the genes that is expected to take a leading role in etiopatogenesis were P53 gene, a gene that encodes or expressing protein 53 (p53). Research conducted by adiyanti (2007) obtain the result that there is a significant relation exists between p53 with stage of ovarium (Adiyanti, 2007). Research conducted by Rauf and Masadah (2009) with outcomes of 58.5% samples had positive p53 expression in which a positive outcome is mostly found in the stage iv ovarian cancer then followed by stadium iii, ii, and I (Rauf and Masadah, 2009). Other research conducted by Lobna Ayadi (2010) obtains the result that a positive result of

Table 1. Distribution Of Age, BMI, Parity, And Hormonal Contraceptive History In Ovarian Cancer Staging Group

Variable	Ovarian Cancer Stage				*p*
	I (n=7) mean±2SD	II (n=9) mean±2SD	III (n=21) mean±2SD	IV (n=7) mean±2SD	
Age(years)	40.86±5.24	43.56±12.70	45.57± 9.77	57.86±8.78	0.814
BMI (kg/m^2)	19.9±1.51	25.15±4.04	21.76±4.95	21.38±3.75	0.304
Parity	1.57±0.78	1.33 ±0.70	2.00±1.30	2.43±0.97	0.057
Hormonal contraception	1.71±0.48	1.78±0.44	1.90±0.30	1.71±0.48	0.562

Table 2. Correlation Between P53 Expression With Ovarian Câncer Stage

Variable		Ovarian Cancer Stage				r	*p*
		I (n=7)	II (n=9)	III (n=21)	IV (n=7)		
p53 expression	(+)	0	2	5	1	-0.099	0.522
	(-)	7	7	16	6		

p53 expression correlates with stage of ovarian cancer especially at an advanced stage. Research conducted by Marks (2006) concluded that the p53 expression is not associated with staging and histopatologis degrees of ovarian cancer, moreover it's closely related to gen p53, but is associated with the incidence of P53 gene mutation itself (Marks et al., 2006). Research by Psyarii et al., (2007) also concluded that p53 expression is not associated with the stage and the degree of differentiation of ovarian cancer (Psyrri et al., 2007). Research conducted by Marcus (2010) concluded that the mutation of the P53 gene is found in the early stages of ovarian cancer compared with advanced stages and p53 expression was not related to the degree of ovarian cancer stage (Marcus et al., 2010). Having related with all above , this thesis will be made through the efforts of the utilization of the genetic protein p53, in particular, as a means of detection to the extent of the severity or stage of ovarian cancer which has been experienced by patients. The assessment is done by exploiting the correlation or relationship between p53 and stage of ovarian cancer.

METHOD

This research using analytic observational designs (cross-sectional) at the Obstetrics and Gynaecology departement, Pathology Anatomy and Medical record in Sanglah General Hospital, Denpasar, conducted from July 2011 to December 2013 with a total of 44 research sample fruit paraffin blocks. Paraffin block samples are grouped based on the stage of ovarian cancer: stage I, II, III, and IV. Then each group did examination of p53 expression by immunohistochemical techniques. Then we do further assessment of the correlation between p53 and stage of ovarian cancer by using Spearman Test.

RESULTS

In this research has done normality test for data with of kolmogorov-smirnov test and its homogenicity data test with Levene's test to variables of age, body mass Index (BMI), parity and hormonal contraceptive history. Analysis show that variable data on the age, BMI, parity, and hormonal contraceptive history have normal distribution ($p > 0.05$) and homogeneous ($p > 0.05$), while to compare mean value of each variable we used One Way Anova test. (Table 1)

Assessment of the correlation between the expressions of p53 with ovarian cancer stage analyzed using the Spearman correlation test. The results of these analyses are presented in Table 2

Table 2 showed that no positive p53 expression in stage I, stage II positives for 2 sample, stage III 5 sample, and stage IV 1 sample. Assessment to correlation between p53 and stage of ovarian cancer done by Spearman correlation test, whereas found that there were no corelation of p53 expression and ovarian cancer stage ($p>0.05$).

DISCUSSION

In this study the average age in the group of ovarian cancer stage I is 40.86 ± 5.24 years, stadium II is 43.56 ± 12.70 years, stage III is 45.57±9.77 year and stage IV is 57.86 ± 8.78. The mean BMI on each group of ovarian cancer stage I is 19.9 ± 1.51 kg/m2, stadium II was 25.15 ± 4.04 kg/m2, stage III is 21.76 ± 4.95 kg/m2, and stage IV was 21.38 ± 3.75 kg/m2. The mean parity on the group of ovarian cancer stage I is 0.78±1.57, stage II is 1.33±0.70, stage III is 2.00±1.30, and stage IV is 2.43±0.97. As many as 8 out of 44 (18.18%) paraffin block samples obtained a positive expression of p53,

where each of the two pieces on stage II, 5 pieces on stage III, and stage IV in 1 piece. At the stage we didn't found one positive sample undergoes p53 expression. After a statistical analysis we can't prove the correlation between the expression of p53 with staging of ovarian cancer or histopathologic degree. The research results similar to research that conducted by Marks (2006) where it concluded that the expression is not associated with p53 positive cancer ovarian staging and the degree of histopatologis (Marks et al., 2006). Research conducted by Psyarii et al., (2007) also concluded that p53 expression is not associated with the stage and the degree of differentiation of ovarian cancer (Psyrri et al., 2007). The same Research also conducted by Marcus (2010) which concluded that the mutation of the P53 gene is found on early-stage ovarian cancer compared with advanced stages and p53 expression is not associated with ovarian cancer stage (Marcus et al., 2010). In this research we not found any relationship between the expression of p53 with staging of ovarian cancer, possibly because carcinogenesis of ovarian cancer are multistep, where various lines of carcinogenesis played an important role in determining the occurrence of ovarian cancer, beside the p53 gene inactivation of a tumor suppressor as a subject that is analyzed in this study (Kumar et al., 2010). In addition, cells that have changed into cancer has lost the function of the P53 gene, so that it can be ascertained that p53 expression for activating the transcription process on target gene that resulted in DNA repair is not happening (Kumar et al., 2010; Syaifudin, 2007). The p53 protein expressed by P53 gen is a protein antigen that has quite unstable properties. The result of unstable nature of these proteins is it difficult to arrest or bound by antibody immunohistochemical examination, so immunohisto-chemical examination of p53 tend to give negative results. On this research we use, paraffin block sample from ovarian cancer tissue of patients who have undergone surgery at the Sanglah from 2008 until 2013. After a study in retrospective at the Pathology Anatomy was obtained information that at Sanglah hospital, for paraffin blocks sample made under the year 2012, the tissue fixation method is not done by using formalin buffer but rather by using alcohol fixation. The use of alcohol will certainly damage the protein gene expression in tissues. The number of samples of research should be determined based on the amount of samples obtained from the prevalence of each group of ovarian cancer staging, not based on the prevalence of ovarian cancer in the population. This research uses the prevalence of ovarian cancer in a population as a benchmark in determining the number of samples for research due to the prevalence each group in population still unavailable

CONCLUSIONS and RECOMMENDATIONS

Based on the research results above it can be concluded that p53 expression is not correlated with the staging of ovarian cancer. Because of the carcinogenesis of ovarian cancer are multistep, continuing research is needed to assess the other, such as on the track of oncogenes, apoptosis, gene and changes of genes involved in DNA repair. Due to the unstable nature of the p53 expression, then we needed a standard protocol for immunohisto-chemical examination of p53 from the tissue until it becomes ready for interpretation.

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