

Epstein-Barr virus: a cause of human invasive breast cancer.

Ilija Barukčić*,¹

¹ DE-26441 Jever, Germany. <http://www.barukcic-causality.com/>

Abstract

Background. Breast cancer is a progressive and many times a deadly ending disease of the human breast. A or the cause of breast cancer is still unknown.

Methods. In this publication, we will reanalyse the study of Bonnet et al. (Bonnet 1999) using the conditio per quam relationship and the mathematical formula of the causal relationship c . All P values are one-sided; significance is indicated by a P value of less than 0.05.

Results. Using the conditio per quam relationship, it could be proofed that when infection of human breast with Epstein-Barr virus then development of human breast cancer. On the other hand, using the mathematical formula of the causal relationship c , it could be found that Epstein-Barr virus is at the same time a cause of human breast cancer.

Conclusions. When infection of the human breast with Epstein-Barr virus then development of human breast cancer. Epstein-Barr virus is a cause of breast cancer. A successful vaccine against Epstein-Barr virus will prevent from breast cancer.

Key words: Causal relationship, Epstein-Barr virus, Breast Cancer, Cause, Effect, Barukčić

1. Introduction

Breast cancer is a progressive disease that forms in tissues of the human breast usually in the glands that make milk and in the tubes that carry milk to the nipple. Male breast cancer is rare but breast cancer occurs in both men and women. Human breast cancer is the most common type of cancer among women in the United States. Based on estimates of The National Cancer Institute (Ries et al. 2006), about 12.7 percent of women born today in USA will be diagnosed with breast cancer at some time in their lives.

Scientists studying breast cancer found many different risk factors that may increase the chance of developing breast cancer. Age, family history, personal history of breast cancer, *BRCA1*, *BRCA2* and other gene changes, reproductive and menstrual history, drinking alcohol and many other too. Only, it is also important to keep in mind that a risk faktor is not identical with a cause. Most of the women who have some known risk factors do not get breast cancer.

Surgery, radiation therapy, chemotherapy, hormone therapy and others too are used to treat breast cancer. According to estimates of The American Cancer Society 40,970 women will die of cancer of the breast in 2006. Much is known about breast cancer but many unanswered questions remain.

An exact exact cause or some exact causes of breast cancer still remain unknown.

* Corresponding author: e-mail: Barukcic@t-online.de. Phone: +00 49 44 61 99 11 11, Fax: +00 49 44 61 91 21 46. GMT +1h.

2. Methods

2.1 Patients

Mathilde Bonnet et al. (Bonnet 1999) investigated the presence of the *Epstein-Barr virus (EBV)* genome, a ubiquitous human herpesvirus, in human tissues from 100 consecutive primary invasive human breast carcinomas, one of the most prevalent malignancies in Western countries, as well as 30 healthy tissues. Bonnet et al. detected the EBV genome by the polymerase chain reaction (PCR) in 51% of the tumours, whereas in 90% of the cases studied, the EBV genome was not detected in healthy tissue. The diagnosis of invasive breast carcinoma were made by use of the criteria described by Contesso. Let us show this data in the following 2-2-table.

Epstein-Barr virus and breast cancer.				
		Human breast cancer		
		Yes	No	
Epstein-Barr virus infection of human breast	Yes	51	3	54
	No	49	27	76
		100	30	130

2.1 Statistical Analysis

All statistical analyses were performed by self-programmed software. The new statistical techniques developed by Barukčić (Barukčić 1989, 2006a, 2006b; Thompson 2006) were used. The formula of the *conditio per quam* was used to detect a **conditio per quam relationship** like **when A then B** between investigated random variables.

The mathematical formula of the **causal relationship c** (Barukčić 1989, 2006a, 2006b; Thompson 2006) discovers causal relationships between experimental/non-experimental data. This formula was used to proof whether there is a significant causal relationship between Epstein-Barr virus and human breast carcinoma. All P values are one-sided; significance was indicated by a P value of less than 0.05.

3. Results

3.1. **When** infection of human breast with Epstein-Barr virus **then** development of human invasive breast carcinoma.

According to the study above, 3 out of 54 EBV-infected patients did not develop breast cancer, could there be still a relationship? Let us reanalyse the data Bonnet et al. (Bonnet 1999) . Our hypothesis are:

Ho: Null-Hypothesis: $p(\text{ Epstein-Barr virus infection human breast } \rightarrow \text{ Human breast cancer }) = 1.$

HA: Alternative-Hypothesis: $p(\text{ Epstein-Barr virus infection human breast } \rightarrow \text{ Human breast cancer}) < 1.$

3.1.1 The probability of the conditio per quam relationship

The probability of the when infection of human breast with Epstein-Barr virus then development of human invasive breast cancer can be calculated from the data above (Barukčić 2006a, pp. 282-284) as

$$p(\text{ Epstein-Barr virus infection human breast } \rightarrow \text{ Human breast cancer}) = 0,9769230.$$

3.1.2 The lower confidence bound of the conditio per quam relationship

The lower confidence bound of the conditio per quam relationship above was calculated from the data above (Barukčić 2006a, pp. 283-284) as

$$p_{\text{ lower}} = 0,9278684.$$

The probability of the conditio per quam relationship

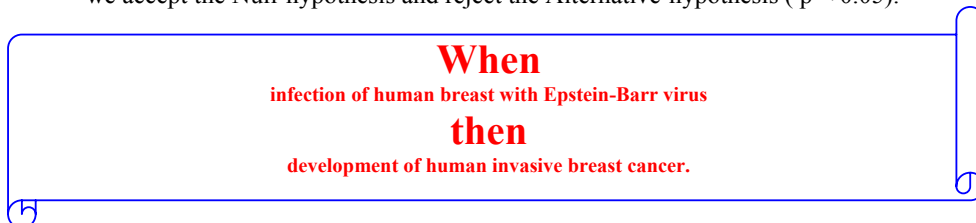
$$p(\text{ Epstein-Barr virus infection human breast } \rightarrow \text{ Human breast cancer}) = 0,9769230$$

is higher then

$$p_{\text{ lower}} = 0,9278684.$$

In so far, the data above do support our Null-hypothesis:
when infection of human breast with Epstein-Barr virus
then development of human invasive breast cancer,

we accept the Null-hypothesis and reject the Alternative-hypothesis ($p < 0.05$).



3.2 Epstein-Barr virus: a cause of human invasive breast cancer

The infection of human breast with Epstein-Barr virus could be a cause of human breast cancer too. Let us reanalyse the data Bonnet et al. (Bonnet 1999) with the help of the mathematical formula of the **causal relationship c** (Barukčić 2006a) under this point of view. Our hypothesis are:

Ho: Null-Hypothesis: **c (Epstein-Barr virus \Rightarrow Breast cancer) ≤ 0 .**
or there is no causal relationship between Epstein-Barr virus and breast cancer.

HA: Alternative-Hypothesis: **c (Epstein-Barr virus \Rightarrow Breast cancer) > 0 .**
or there is a causal relationship between Epstein-Barr virus and breast cancer.

3.2.1 The calculated causal relationship **c** calculated

The **causal relationship c** between an infection of human breast with Epstein-Barr virus and the development of breast cancer was calculated according to Barukčić (Barukčić 2006a, p. 331) as

$$\mathbf{c = + 0,350542603629094.}$$

3.2.2 The critical value of the causal relationship **c** critical

The critical value of the **causal relationship c** critical was calculated according to Barukčić (Barukčić 2006a, p. 331) as

$$\mathbf{c = + 0,144263206677778.}$$

3.2.3 The P value of the causal relationship **c**

The P value of the causal relationship **c** above was calculated according to Barukčić (Barukčić 2006a , pp. 331) as

$$\mathbf{P\ value = 0,0000321021661870979.}$$

3.2.3 The Power of the causal relationship **c**

The power of the causal relationship **c** above was calculated according to Barukčić (Barukčić 2006a, p. 332-335) as

$$Z_{\beta} = - 2,351946991081612393756275217239.$$

$$\mathbf{power = 1 - p (Z_{\beta} = -2,351946991081612393756275217239) = + 0,990662281953314,}$$

a very strong and highly significant result. Thus, we reject our Null-Hypothesis and accept the alternative hypothesis.

There is a highly significant causal relationship between an infection of human breast with Epstein-Barr virus and the development of human invasive breast cancer
(P value = 0,0000321021661870979, Power = 0,990662281953314).

Epstein-Barr virus is a cause of human breast cancer.

4. Discussion

The result above is highly significant and thus very important. **When infection of human breast with Epstein-Barr virus then development of human invasive breast cancer.** An infection with Epstein-Barr virus is thus a *conditio per quam* of human breast cancer. But at the same time, Epstein-Barr virus is a cause of human invasive breast cancer (p value = 0,0000321021661870979, power = 0,990662281953314). Not all, but just about $100 \cdot (51/100) = 51$ percent of human breast cancer are caused by Epstein-Barr virus. Finally, **a main cause of human invasive breast cancer is identified.** A vaccine against Epstein-Barr virus will prevent from breast cancer.

Acknowledgement

In particular, I am extremely grateful to the Scientific Program Committee of the XXIIIrd International Biometric Conference scheduled from July 16-21, 2006 in Montréal, Canada and especially to Alain Vandal for the trust and support provided by reviewing and accepting my paper entitled: "New Method for Calculating Causal Relationships" for presentation at the XXIIIrd International Biometric Conference in Montréal, Canada. The results of this publication were presented at the XXIIIrd International Biometric Conference in Montréal, Canada, too. I wish to thank Bonnet et al. for the data they have delivered.

References

- Barukčić, Ilija. (1989). Kausalität. First Edition. Wissenschaftsverlag, Hamburg.
- Barukčić, Ilija. (2006a). Causality. New Statistical Methods. Second Edition. Books on Demand, Hamburg.
- Barukčić, Ilija. (2006b). New Method For Calculating Causal Relationships, Montréal: XXIII International Biometric Conference, July 16 - 21 2006.
- Bonnet M, Guinebretiere JM, Kremmer E, Grunewald V, Benhamou E, Contesso G, Joab I. (1999). "Detection of Epstein-Barr Virus in Invasive Breast Cancers, " *Journal of the National Cancer Institute*, Vol. 91, No. 16, 1376-1381.
- Ries LAG, Harkins D, Krapcho M, et al. "SEER Cancer Statistics Review, 1975-2003." Bethesda, MD: National Cancer Institute, 2006.
- Thompson, M. E. (2006). "Reviews. Causality. New Statistical Methods. I. Barukčić," Editor Dr. A. M. Herzberg, International Statistical Institute. *Short Book Reviews*, Volume 26, No. 1, p. 6.