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Helicobacter pylori: the cause of human gastric cancer.

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Abstract

Background. Many studies found an association between an infection of human stomach with Helicobacter pylori and the development of human gastric cancer, but none of the studies identified Helicobacter pylori as the cause of human gastric cancer. The basic relation between gastric cancer and Helicobacter pylori still remains uncertain.

Methods. Naomi Uemura et al. conducted a long-term, prospective study of 1526 Japanese patients, 1246 had H. pylori infection and 280 did not (mean follow up 7.8 years, endoscopy at enrollment and then between one and three years after enrollment). None of the uninfected patients developed gastric cancer. Uemura et al. could not use Cox proportional-hazards models to calculate the difference in the incidence of gastric cancer, other insufficient statistical methods (Kaplan-Meyer analysis, chi-square test or Fisher's exact test) were used. In so far, Uemura et al. failed to detect the basic relationship between Helicobacter pylori and human gastric cancer. The study of Uemura et al. was reanalysed using the conditio sine qua non relationship and the mathematical formula of the causal relationship c. This methods are already known since 1989. All P values are one-sided; significance was indicated by a P value of less than 0.05.

Results. Using the conditio sine qua non relationship, it could be proofed that without an infection of human stomach with Helicobacter pylori no development of human gastric cancer. On the other hand, using the mathematical formula of the causal relationship c, it was able to proof that Helicobacter pylori is at the same time the cause of human gastric cancer.

Conclusions. Without an infection of human stomach with Helicobacter pylori no development of human gastric cancer. Helicobacter pylori is the cause of human gastric cancer. The successful treatment of a Helicobacter pylori infection of human stomach will prevent from human gastric cancer.

Key words: Causal relationship, Human gastric cancer, Helicobacter pylori, Cause, Effect, Barukčić

1. Introduction

Gastric cancer, essentially a disease of older age, is a relatively common and serious malignancy. The prognosis of patients with gastric cancer is more or less related to tumour extent. The 5-year survival rate of patients with proximal gastric cancer is about 10% to 15%. The precise aetiology is still unknown. The development of this malignancy has been associated with Helicobacter pylori since the discovery (No authors, 1983) of this bacterium. The World Health Organisation and the International Agency for Research on Cancer consensus group (WHO, 1994) declared Helicobacter pylori as a definite carcinogen. Many recent studies found H. pylori to be associated with gastric cancer. None of the studies (Uemura, 2001) identified H. pylori as the cause of human gastric cancer. The role of *Helicobacter pylori* infection in gastric cancer still remains uncertain.

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2. Methods

2.1 Patients

Naomi Uemura et al. (Uemura, 2001) at the Department of Gastroenterology, Kure Kyosai Hospital, 2-3-28 Nishi-chuo, Kure City, Japan, prospectively studied 1526 Japanese patients, 1246 had *H. pylori* infection and 280 did not (mean follow-up 7.8 years, endoscopy with biopsy at enrollment and then between one and three years after enrollment). Gastric cancers developed in 36 of the infected patient. None of the uninfected patients developed gastric cancer. Let us show this data in the following 2-2-table.

Helicobacter pylori and gastric cancer.

Uemura et al, N Engl J Med., Vol. 345, No 11 (2001), 784-789.		Human gastric cancer		
		Yes	No	
Helicobacter pylori infection of human stomach	Yes	36	1210	1246
	No	0	280	280
		36	1490	1526

2.1 Statistical Analysis

All statistical analyses were performed by self-programmed software. The new statistical techniques developed by Barukčić (Barukčić 1989, 2006; Thompson 2006) were used. The formula of the conditio sine qua non was used to detect a **conditio sine qua non relationship** like **without** A **no** B between investigated random variables.
The mathematical formula of the **causal relationship c** (Barukčić 1989, 2006; Thompson 2006) discovers causal relationships between experimental/non-experimental data. This formula was used to proof whether there is a significant causal relationship between Helicobacter pylori and human gastric cancer. All P values are one-sided; significance was indicated by a P value of less than 0.05.

3. Results

3. 1. Without an infection of human stomach with Helicobacter pylori no gastric cancer

During the follow-up of the study above none of the 280 uninfected patients developed gastric cancer. Let us reanalyse the data of Naomi Uemura et al. (Uemura, 2001). Our hypothesis are:

Ho: Null-Hypothesis: p (Helicobacter pylori ← Gastric cancer) = 1.
HA: Alternative-Hypothesis: p(Helicobacter pylori ← Gastric cancer) < 1.

3.1.1 The probability of the conditio sine qua non relationship

The probability of the without an infection of human stomach with Helicobacter infection no gastric cancer conditio sine qua non relationship was calculated from the data above (Barukčić 2006, pp. 236-267) as

$$p(\text{Helicobacter infection} \leftarrow \text{Gastric cancer}) = 1.0.$$

3.1.2 The lower confidence bound of the conditio sine qua non relationship

The lower confidence bound of the conditio sine qua non relationship above was calculated from the data above (Barukčić 2006, pp. 253-254) as

$$p_{lower} = 0{,}9789467.$$

The probability of the conditio sine qua non relationship

$$p(\text{Helicobacter infection} \leftarrow \text{Gastric cancer})$$

is higher then

$$p_{lower}.$$

In so far, the data above do support our Null-hypothesis:
without an infection of human stomach with Helicobacter pylori
no development of human gastric cancer,

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

Without
an infection of human stomach with Helicobacter pylori
no
development of human gastric cancer.

3.2 Helicobacter pylori: the cause of human gastric cancer

The infection of human stomach with Helicobacter pylori could be the cause of human gastric cancer. Let us reanalyse the data of Naomi Uemura et al. (Uemura, 2001) using the mathematical formula of the **causal relationship c** (Barukčić 2006) under this point of view. Our hypothesis are:

Ho: Null-Hypothesis: **c (Helicobacter pylori $\Rightarrow$ Gastric cancer) $\leq$ 0**.
or there is no causal relationship between Helicobacter pylori and gastric cancer.

HA: Alternative-Hypothesis: **c (Helicobacter pylori $\Rightarrow$ Gastric cancer) > 0**.
or there is a causal relationship between Helicobacter pylori and gastric cancer.

3.2.1 The calculated causal relationship $c_{calculated}$

The **causal relationship c** between an infection of the human stomach with Helicobacter pylori and the development of human gastric cancer was calculated according (Barukčić 2006, p. 254, p. 317, p. 349) as

c = + 0,07368483420791516649783459080949 1.

3.2.2 The P value of the causal relationship c

The P value of the causal relationship c above was calculated (Barukčić 2006 , p. 325-327) as

P value = 0,00199831220992897.

3.2.3 The Power of the causal relationship c

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

Z_{β} = -1,23357441547384

power = 1 - p (Z_{β} = -1,23357441547384) = + **0,89131923420017,**

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 stomach with Helicobacter pylori and the development of human gastric cancer (P value = 0,00199831220992897, Power = 0,89131923420017).

Helicobacter pylori is the cause of human gastric cancer.

4. Discussion

The result above is highly significant. **Without** an infection of human stomach with Helicobacter pylori **no** development of human gastric cancer. An infection of human stomach with Helicobacter pylori is not only a conditio sine qua non of human gastric cancer. Helicobacter pylori is at the same time the cause of human gastric cancer (p value = 0,00199831220992897, power = 0,89131923420017). The power suffered a little bit because of study design. **Finally, the cause of human gastric cancer is identified.** The eradication of Helicobacter pylori will prevent from gastric cancer.

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References

No authors, (1983). Unidentified curved bacilli on gastric epithelium in active chronic gastritis. *Lancet* **1**, 1273-1275.

Barukčić. I. (1989). Kausalität. First Edition. Wissenschaftsverlag, Hamburg.

Barukčić. I. (2006). Causality. New Statistical Methods. Second Edition. Books on Demand, Hamburg. pp. 488.

Naomi Uemura, M.D., Shiro Okamoto, M.D., Soichiro Yamamoto, M.D., Nobutoshi Matsumura, M.D., Shuji Yamaguchi, M.D., Michio Yamakido, M.D., Kiyomi Taniyama, M.D., Naomi Sasaki, M.D., and Ronald J. Schlemper, M.D. (2001). "Helicobacter pylori Infection and the Development of Gastric Cancer," *The New England Journal of Medicine* 345: 784-789.

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.

WHO : International Agency for Research on Cancer. (1994). IARC monographs on the evaluation of the carcinogenetic risks to humans. Schistosomes, liver flukes and Helicobacter pylori. F-69372 Lyon, France. Vol. 61, 177-241.