

Prospective cohort study of comprehensive prevention to gastric cancer

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Abstract

AIM: To evaluate the preliminary effects of comprehensive prevention of gastric cancer in Zhuanghe County epidemiologically.

METHODS: Stratified sampling and cluster sampling were applied to define the intervention group and the control group. The prospective cohort study was used for evaluating the effect of preventing gastric cancer. The relative risk (RR) and attributable risk percent (AR %) of intervention on gastric cancer death were calculated. Potential years of life lost (PLYL) of the disease was analyzed, and the RR and AR % of PLYL were calculated. Survival analysis was applied among the screened patients.

RESULTS: In the first 4 years after intervening, the relative risk (RR) of intervention on death was 0.5059 (95 % CI: 0.3462~0.7392, $P<0.05$) with significance statistically. AR % of the intervention on death was 49.41 %. The RR of intervention on cumulative PLYL was 0.6778 (95 % CI: 0.5604~0.8198, $P<0.05$) with statistic significance. AR % of the intervention on cumulative PLYL was 30.32 %. The four-year survival rate of the screened patients was 0.6751 (95 % CI: 0.5298~0.9047).

CONCLUSION: The initiative intervention results showed that the intervention approach used in the trial was effective, it reduced mortality and increased survival rate, and alleviated the adverse effect of gastric cancer on the health and life of screened population.

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INTRODUCTION

Gastric cancer is one of the most common malignant tumor, its prevalence in 1999 was 138.60×10^{-5} according to the report of WHO^[1], however, its prevalence (300.87×10^{-5}) and mortality

(29.31×10^{-5}) are even higher in China^[1]. The incidence of gastric cancer has been declining globally during the recent decades, but not in China^[2]. It was believed that the main reasons of the declining were prevention and diagnosis, but not therapy^[3]. Most studies show that the incidence of gastric cancer is related to dietary factors, infection of helicobacter pylori(Hp), etc.^[4-9]. If these relative factors were eliminated or decreased, the incidence and mortality of gastric cancer would be lowered., thus gastric cancer could be prevented^[10-13]. So it is very important to find an effective comprehensive preventive method for gastric cancer.

Zhuanghe is a county in Liaoning Province with total population of approximate 900 000, locates along the seaside of the Huanghai Sea. The previous survey showed that the incidence of gastric cancer in this county was higher than the average level of other areas. In 1994, the mortality rate was 49.55×10^{-5} in male, and 22.23×10^{-5} in female The population in Zhuanghe County has been surveyed in census and studied for 18 years by the Stomach Investigation Group of China Medical University because of higher incidence and mortality of gastric cancer. A series of comprehensive preventive approaches have been applied since 1997, including primary and secondary prevention. The goal was to explore a series of comprehensive preventive approaches to reduce the incidence and the mortality of gastric cancer. The initiative effect of intervention approaches by epidemiological study was evaluated in this paper.

MATERIALS AND METHODS

Definition of sample

Stratified sampling and cluster sampling were applied to define the intervention group and the control group. Each village in this county was stratified into two groups according to location geographically close seaside or not, then the sampled villages were defined by cluster sampling in the two groups, and the number of the sampled villages in each group was proportional to its location stratification. All individuals of the sampled villages were used as the samples.

Sixteen villages were sampled as the intervention group, other 14 villages were used as the control based on location, economic level, and proportion of population in each intervention village. 63 133 persons from 30 villages, 16 870 in the intervention group, and 14 900 in the control group were observed, respectively. The age and sex were proportional in each group.

Intervention approaches

The design of the intervention was as the following (Figure 1). **Common approaches in intervention and control group** Knowledge of prevention and treatment of gastric cancer, especially dietary habits was provided for all residents through broadcasting, video, brochures and face-to-face conversation. **Approaches in intervention groups** Initially 3 033 persons were selected as suspected high risk population from intervention villages according to the epidemiological survey and clinical symptoms. Persons who had the family history of

gastric cancer, and/or were over 35 years old and had history of gastric illness, or had obvious symptoms of gastric illness were grouped as suspected high risk population, from which 1781 persons were further detected and grouped as high risk population of gastric cancer^[16-18], and were treated with antibiotics, Chinese herb medicine, and nutritional therapy, based on X-ray, HP detected, and gastroscopic and pathological examination^[19-21]. Patients with gastric cancer screened from the high risk population were treated promptly.

The whole process of screening and treatment was performed under strict quality control. Twenty five percent of intervened individuals were randomly selected and checked for the compliance to medication by interviewing with individuals and their family and measuring the metabolites of medicine in urine, results showed that the compliance rate was 96.6 %. The screening and surveying were initiated in 1997 and had been processed successfully since then.

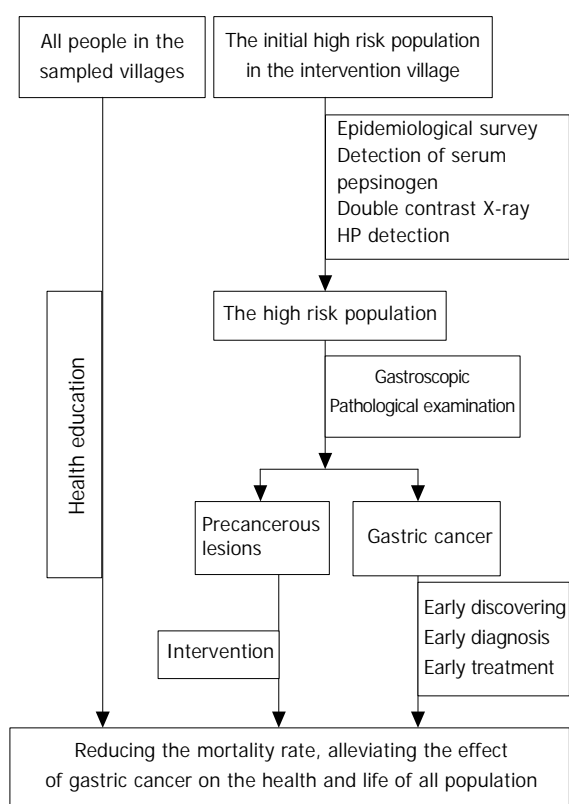


Figure 1 The intervention trial sketch.

Analysis of data

The prospective cohort study was applied to observe the samples. The cause of all death including gastric cancer from 1996 to 2000 were documented in both intervention group and control groups. The screened patients with gastric cancer were observed and reported annually.

The relative risk (RR) and attributable risk percent (AR %) of intervention on death of gastric cancer, potential years of life lost (PLYL) of the disease, and the RR and AR % of PYLL were calculated. The survival rate of all the screened patients with gastric cancer was evaluated.

The maximum expectancy method was adopted to calculate PYLL^[22].

$$PYLL = \sum a_i d_i, a_i = L - x - 0.5$$

L: the upper limit age, evaluated at 70.

x: the middle value of age interval.

a_i: the residual years from age interval (i~i+1) to the maximum expect age (L).

d: the death number of age interval (i~i+1) from the disease. PYLL= (PYLL/N)*1000‰.

N: the number of total observed population or person-years.

Life-table method and product-limit method^[23] were applied to analyze the survival rate of all the screened patients with gastric cancer.

$$S(t) = \prod (1 - d_i/n_i)$$

n_i: the adjusted population at the beginning of the period i.

d_i: the death number of the period i.

RESULT AND ANALYSIS

General

The composition of the sample is shown in Table 1.

Table 1 Composition of the samples

	Male	Female	Total
Intervention group	26 922	26 256	53 178
Control group	23 840	23 924	47 788
Total	50 762	50 204	100 966

During the first screening in 1997, 32 patients with gastric cancer were diagnosed, in which 18 patients were early gastric cancer, and 14 were advanced gastric cancer. The incidence of cancer in the screened group was 1.80 % (32/1781). In addition, 1 306 persons were detected having other gastric diseases. The screening rate of all gastric diseases was 75.13 % (1 338/1 781), therefore the screening method was very effective. From 1998 to 1999, 12 patients with gastric cancer were detected, in which 7 patients were early gastric cancer, and 5 were advanced gastric cancer.

Mortality of gastric cancer

The mortality rate of gastric cancer in Zhuanghe from 1996 to 2000 was between 45.21×10⁻⁵~63.29×10⁻⁵, the annual rate was 53.24×10⁻⁵ (person· year)⁻¹, whose 95 % CI is 44.57×10⁻⁵-61.91×10⁻⁵, which is higher than the average rate in China (29.31×10⁻⁵). The rate in male was 75.11×10⁻⁵ (95 % CI: 60.60×10⁻⁵-89.61×10⁻⁵), and in female was 30.08×10⁻⁵ (95 % CI: 20.98×10⁻⁵-39.18×10⁻⁵). The death from gastric cancer was 8.25 % of all death from any reasons, and 38.94 % of all carcinoma deaths, which were higher than that of the national average level (P<0.05)^[24-26].

The annual mortality rate of gastric cancer in Zhuanghe was shown in Figure 2. The alterations of mortality from 1996 to 2000 were not statistically significant.

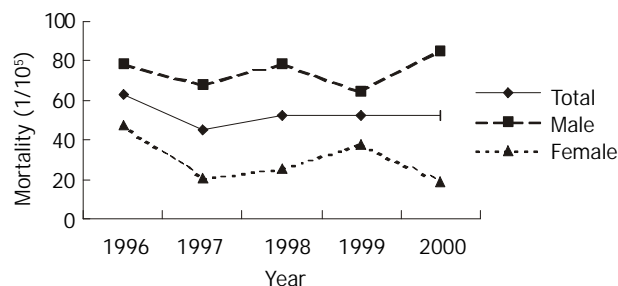


Figure 2 Mortality of gastric cancer in Zhuanghe County from 1996 to 2000.

The annual mortality rates of gastric cancer in intervention groups were shown in Figure 3. The rates in the period from 1997 to 2000 were lower than that in 1996 with no significance by Poison test^[27] (P>0.05 except that in male in 2000. In

contrast, the average mortality rate (34.97×10^{-5}) in intervention groups during post-intervention period (1997-2000) was lower significantly than that (59.31×10^{-5}) in pre-intervention period (1996) (one-sided test, $\chi^2=2.930, P<0.05$). However, no statistical decrease of mortality was found in control groups (Figure 4).

The tendency of descending in mortality of gastric cancer was observed (Figure 3). The linear correlation analysis is shown in Table 2. No obvious alteration in the mortality of gastric cancer in control group from 1996 to 2000 was observed.

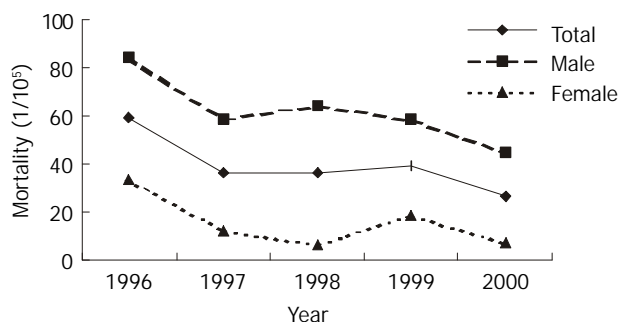


Figure 3 Mortality of gastric cancer in intervention groups from 1996 to 2000.

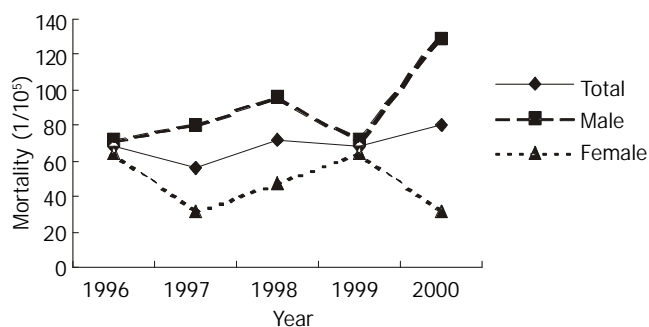


Figure 4 Mortality of gastric cancer in control groups from 1996 to 2000.

Table 2 Linear correlation in gender of gastric cancer mortality in intervention groups

Group	r	F	P
Male	0.8688	9.2369	0.0559
Female	0.6690	2.4308	0.2169
Total	0.8148	5.9256	0.0930

The difference of the mortality rate of gastric cancer between the intervention group and the control group in 1996 was not significant ($\chi^2=0.0283, P>0.05$). The annual average rates between the intervention group and the control group from 1997 to 2000 differed significantly ($\chi^2=5.873, P<0.05$) (Figure 5).

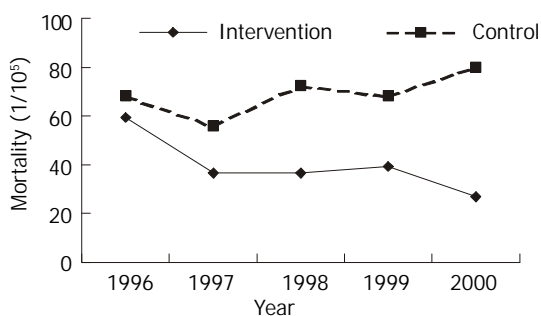


Figure 5 Mortality rate in intervention and control groups from 1996 to 2000.

Relative risk analysis

One hundred and ten patients in both groups had died from gastric cancer since the beginning the trial in 1997. The cumulative mortality rate (CMR) was 34.97×10^{-5} in intervention villages, and 69.13×10^{-5} in control villages. The relative risk (RR) of intervention was 0.5059 (95 % CI: 0.3462~0.7392, $P<0.05$) with statistic significance. The attributable risk percent of the intervention was 49.41 %, which indicated that intervention reduced gastric cancer death by 49.41 % of all population. All these data showed that the intervention approaches can reduce the death of gastric cancer.

Table 3 Cumulative mortality rate and relative risk

	Total person-year	Death No.	CMR (10 ⁻⁵)	RR	RR 95%CI	AR%
Control	99 816	69	69.13			
Intervention	117 234	41	34.97	0.5059	0.3462~0.7392	49.41

Potential years of life lost in gastric cancer

From 1996 to 2000, the potential years of life lost (PYLL) of gastric cancer were 731 person-years, and the PYLL was 3.07 ‰ which meant the lost years of 1 000 people from gastric cancer were 3.07 every year. In the intervention group, the PYLL was 300 person-years, and the PYLL was 2.89 ‰. The PYLL of the control group was 431 person-years, and the PYLL was 3.94 ‰ (Figure 6). The PYLL in intervention group in 1996 and 1998 was not significantly different from that in control group ($\chi^2=1.3948, 0.2074, P>0.05$), and the differences in 1997, 1999 and 2000 were statistically significant ($\chi^2=5.0603, 73.2124, 11.4119, P<0.05$). Difference of the total PYLL from 1997 to 1999 between the intervention group and the control group was significant ($\chi^2=16.1527, P<0.01$).

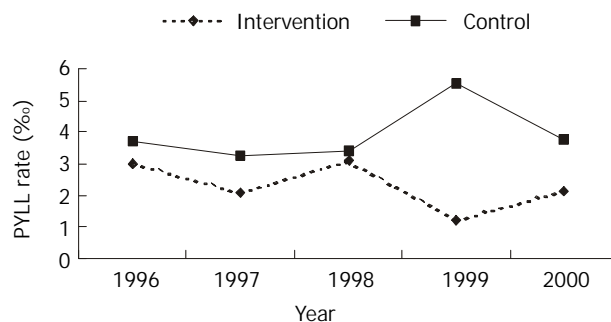


Figure 6 PYLL in intervention group and control group from 1996 to 2000.

The RR of intervention to cumulative PYLL was 0.6778 (95 % CI: 0.5604~0.8198, $P<0.05$), which was statistically significant. The AR % of the intervention to cumulative PYLL was 30.32 %, which showed that the intervention decreased PYLL of gastric cancer by 30.32 % of all population.

Table 4 PYLL and its RR

	Total person-year	PYLL	PYLL (%)	RR	RR 95%CI	AR%
Control	87 757	272	3.10			
Intervention	103 191	223	2.16	0.6778	0.5604~0.8198	30.32

Survival analysis

During the 4-year observation after intervening, 32 patients with gastric cancer were detected by screening, of which 9 patients died. The annual survival rates were shown in Table 5.

Table 5 Annual survival rate and its 95 % CI

Year	Survival rate	Standard error	95 % CI of survival rate
1-	0.8305	0.0691	0.6951, 0.9659
2-	0.7173	0.0852	0.5503, 0.8842
3-	0.7173	0.0852	0.5503, 0.8842
4-	0.6751	0.0956	0.5298, 0.9047

The one-year and three-year survival rate of the screened patients with cancer was 0.8305 (95 % CI: 0.6951~0.9659), and 0.7173 (95 % CI: 0.5503~0.8842), respectively, which are higher than those in Changde County of Fujian Province^[28]. In this study, all screened patients were not operated due to some reasons; otherwise, the survival rate would be higher.

DISCUSSION

All intervention approaches were based on the following studies: (1) Many epidemiological and histological studies showed gastric cancer is related with infection of *Helicobacter pylori*, which cause excessive hyperplasia and reduction of apoptosis of gastric epithelium. These cellular dynamic changes lead to injury of DNA and the generation of gastric cancer cell clone^[29-33]. (2) Garlic oil can inhibit malignant proliferation of cancer cells, and induce their differentiation. The mechanism is likely to adjust the expression of oncogene. Garlic oil can restrain and reverse experimental gastric cancer and precancerous lesions^[34,35]. (3) Surveys showed that cancer is correlated with precancerous lesions. Not all precancerous lesions will develop to cancers, but the generation of cancers may be prevented if the precancerous lesions are cared and cured early^[36,37].

It was reported that gastric cancer was related with high-salt diet and preserved-food diet^[14,15,38,39]. These dietary habits are extremely common in Zhuanghe County, and may be the main cause of gastric cancer^[40]. Accordingly, health education for applying and maintaining right dietary habits was stressed in intervention and control groups.

The analysis of the mortality and PYLLs was focused on all the population instead of a single patient in evaluating the initiative effects of comprehensive preventive approaches. The intervention can reduce the mortality rate of patients with gastric cancer and alleviate the effect of gastric cancer on the health and life of all population. The analysis of PYLL endues the death with weight according to the age of the death, and age standardized mortality rate is applied, so this method reflects the "early death" and the "deferred death". At the initial period of prevention, the decrease of the mortality may not be obvious, but the time on the mortality may be deferred, that is, the survival time of the patients may be prolonged due to early discovering, early diagnosis, and early treatment. It is more suitable to analyze and evaluate the initial effect of comprehensive prevention and treatment of gastric cancer than mortality analysis. Analysis of survival is based on patients with gastric cancer rather than the whole population, and thus it reflects whether the approaches have prolonged the life of patients with gastric cancer.

The results of the survey show that although local mortality rate of gastric cancer in Zhuanghe County is still higher than that of national level in China, the initial outcome of the intervention indicates that the intervention approaches used in the trial are effective, as these approaches have prolonged the screened patients' life, reduced the mortality rate, and alleviated the adverse effect of gastric cancer on the health and life of all population screened. Because effect of chemical intervention effect is behind of the approaches, the initial outcome showed

in this article is mostly due to secondary prevention, that is early discovering, early diagnosis and early treatment.

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