RESEARCH ARTICLE

Risk of Malignancy Associated with a Maternal Family History of Cancer

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Abstract

This study was conducted in order to obtain a screening and early detection reference for children whose mothers had been diagnosed with cancer. Data for 276 mother-child pairs with malignant tumors were analyzed. The distribution of cancers in affected families was generally similar to that of the general Chinese population, and correspondingly breast cancer was the most common malignancy amongst daughters whose mother had cancer (32.7%). The most prevalent cancer amongst sons with affected mothers was gastric cancer, rather than lung cancer. Daughters were more likely to have the same kind of malignant tumor as their mother (P<0.05), and were more likely to develop breast cancer than any other malignant disease if their mother had a breast tumor (P<0.0001). Likewise, if the mother was diagnosed with breast or gynecological cancer, the daughter was more likely to be diagnosed with breast or gynecological cancer than any other cancer (P<0.01). Daughters and sons developed malignant diseases 11 and 6.5 years earlier than their mothers, respectively (P<0.0001).Women with a mother who suffered cancer should be screened for malignancy from 40 years of age especially for breast, lung, and gynecological cancers. For men with affected mothers, screening should start when they are 45 years old focusing particularly on lung and digestive system cancers.

Keywords: Cancer - family history - mother - son - daughter - malignant tumor - early detection

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Introduction

As the incidence of cancer increases worldwide, the proportion of individuals with a parent who has cancer will also increase. A study that surveyed 27,000 people reported that about 25% of the general population had first-degree relatives with malignancies (Ramsey et al., 2006). Thus, a growing number of individuals will require screening or other approaches to allow early tumor detection when they have an affected family member. Cancer diagnosis in a first-degree relative is associated with significant psychological effects: for example, the sons of prostate cancer sufferers were concerned about their risks of inheriting the disease and were therefore inclined to undergo screening (Bratt et al., 1997). Research based on Swedish Cancer Registry records from 1958-1996 showed the risk of developing 21 out of 23 types of cancer increased if an individual's mother or father had the same malignancy (Hemminki et al., 2001). Furthermore, a mother who had breast cancer is an important risk factor for her daughters (Colditz et al., 1993).

Identifying risk factors for cancer could be useful for its prevention and early detection. Hereditary and environmental factors both contribute to the development of malignant tumors, and a familial cancer study does not separate shared lifestyle factors and hereditary factors. We designed this study of 276 mother-child pairs to identify possible risk factors for cancer, especially the risk associated with having a mother with cancer, and to establish whether the type of malignancy suffered by the mother is more prevalent amongst her children.

Materials and Methods

Study population

The 276 mother-son or mother-daughter pairs were identified from the family history of 15,000 people who had undergone physical examination from various places of China in the Department of Cancer Prevention, Cancer Hospital/Institute, Chinese Academy of Medical Sciences between January 2009 and May 2013. The inclusion criteria were that both the mother and at least 1 child were diagnosed with primary malignant tumors pathologically and the ages at diagnosis were available. Either of the mothers or the children with an unknown primary site was excluded from the research population. The mother was the biological mother of the diagnosed child and they lived together for at least 18 years. At the same time, the child's father had not been diagnosed with malignant disease until the time of interview. This study was approved by the ethical committee board of the Cancer Hospital/Institute of the Chinese Academy of Medical Sciences.

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Data analysis

Chi-square tests were used to evaluate the similarity of malignant diseases between mothers and children. The age differences between mothers and their children were analyzed using a nonparametric test. Data analysis was carried out using the SPSS software package, version 11.0 (SPSS Inc., Chicago, IL, USA).

Results

General information

Among the 276 pairs of mothers and children from 214 families, 167 pairs (78.0%) were a mother with just 1 child with a malignant disease, whilst 47 mothers (22.0%) had multiple children with a malignant disease. Among these 47 mothers, 3 had 4 children diagnosed with malignant diseases, 9 had 3 children diagnosed with malignant diseases, and 35 had 2 children diagnosed with malignant diseases.

Of the 3 mothers with 4 children diagnosed with malignant diseases, one of them had 4 sons, and the other 2 had 3 daughters and 1 son. For the 9 mothers with 3 children diagnosed with malignant diseases, 2 had 3 sons, 2 had 3 daughters, 3 had 2 sons and 1 daughter and 2 had 2 daughters and 1 son. Among the 35 mothers with 2 children diagnosed with malignant disease, 13 had 2 daughters, 19 had 1 son and 1 daughter, and only 3 had 2 sons. Therefore, there were 214 mothers with a total of 276 children, of whom 168 (60.9%) were daughters and 108 were sons (39.1%) in the research population.

In the 167 pairs with 1 mother and 1 child diagnosed with cancer, there were 104 daughters (62.3%) and 63 sons (37.7%). As a group, mothers who had multiple children diagnosed with malignant disease group had more daughters (64, 58.7%) than sons (45, 41.3%).

Incidence of malignant diseases

According to the NCCR 2007 data, the 10 most prevalent cancers amongst women were breast cancer (17.5%), lung cancer (13.9%), colorectal cancer (10.8%), gastric cancer (8.8%), hepatic cancer (5.7%), esophageal cancer (5.2%), cervical cancer (4.7%), uterine cancer (3.5%), ovary cancer (3.5%) and thyroid cancer (3.4%) (Chen et al., 2012). In this study, the most common cancer developed by the mother was also breast cancer (39 cases, 18.2%), followed by lung cancer (38 cases, 17.8%), esophageal cancer (24 cases, 11.2%), colorectal cancer (20 cases, 9.3%), gastric cancer (19 cases, 8.9%), uterine cancer (16 cases, 7.5%), ovarian cancer (11 cases, 5.1%), hepatic cancer (10 cases, 4.7%), pancreatic cancer (10 cases, 4.7%), and cervical cancer (6 cases, 2.8%). Thus, the most common cancer and the second most common cancer of the mothers was the same as that in the NCCR 2007 data, but there was a higher proportion of esophageal cancer (Chen et al., 2012).

Breast cancer was also the most common cancer amongst daughters. The proportion of breast cancer was 32.7%, much higher than that based on the NCCR 2007 data (17.5%). The second most common was lung cancer, the prevalence of which was similar to the general population. Uterine cancer (8.3%) and ovarian cancer (7.1%) ranked 5th and 6th for the daughters, respectively, making them more prevalent than suggested by the NCCR 2007 data set, in which was the 8th most common cancer was uterine cancer (3.5%) and the 9th most common was ovarian cancer (3.5%). However, the prevalence of esophageal cancer amongst daughters (2.4%) was much lower than that mentioned in the NCCR 2007 data (5.2%). Lung, breast and gynecological (ovary, uterine, cervical) cancer accounted for 65.5% (110) of cases in which a daughter developed cancer.

The 2007 NCCR data shows that the 10 most prevalent malignant tumors in men and their proportion in the general population were lung cancer (22.3%), gastric cancer (14.9%), hepatic cancer (13.1%), colorectal cancer (10.7%), esophageal cancer (8.8%), bladder cancer (3.5%), prostate cancer (3.2%), pancreatic cancer (2.6%), renal and other tumors of urinary system (2.4%), and lymphoma (2.3%) (Chen et al., 2012). The most common cancer of the sons in this study was gastric cancer, rather than lung cancer. The proportion of gastric cancer cases was 21.3%, higher than indicated by the NCCR 2007 data (14.9%). Correspondingly, the proportion of sons with lung cancer (18.5%) was lower than that suggested by the NCCR data (22.3%). The 3rd, 4th, and 5th most common cancers amongst sons were the same as that indicated by the NCCR 2007 data.

Compared with the NCCR 2007 data, a greater proportion of sons in this study (57.4%) had digestive system malignancies (gastric, colorectal, esophageal, and hepatic cancer) than the general population (47.4%). Furthermore, if lung cancer was added to these digestive system malignancies, they together accounted for 82 cases (75.9%), also higher than that of the general population (69.7%).

Disease category

Daughters were more likely to suffer the same cancer as their mother than were sons: 81 (48.2%) of the 168 daughters had a cancer from the same system as their mothers, and 56 cases (one third) of the daughters had exactly the same cancer as their mother. Amongst these 56 cases, there were 23 (41.1%) breast cancers, 10 (17.9%) lung cancers, 7 (12.5%) uterine cancers, 6 (10.7%) colorectal cancers, 3 (5.4%) esophageal cancers, 3 (5.4%) gastric cancers, and a single case each (1.8%) of ovarian, cervical, thyroid cancer, and malignant lymphoma.

Among the 108 sons whose mother had developed cancer, 43 (39.8%) pairs had diseases originating from the same system and 24 (22.2%) had the same kind of malignant tumor as their mother. Among these 24 cases, there were 6 (25.0%) lung cancers, 6 (25.0%) gastric cancers, 4 (16.7%) esophageal cancers, 3 (12.5%) colorectal cancers, 2 (8.3%) hepatic cancers, 2 (8.3%) bladder cancers and a single case (4.2%) of bile duct cancer. The likelihood that a daughter would develop the same disease as their mother was significantly higher than that of a son ($P<0.05$).

The sons and daughters of the 110 mothers who were diagnosed with a digestive system malignancy showed different disease profiles. Thirty-three of the 46 (71.7%) sons whose mother developed this malignancy were diagnosed with the same cancer, whilst in the case of daughters with similarly affected mothers, only 23 (35.9%) were digestive cancer patients, and more of them (28 cases, 43.8%) had breast or gynecological cancers.

Among 50 mothers who were diagnosed with lung cancer, 60.9% of them had sons who were diagnosed with a digestive system cancer and only 6 out of 23 (26.1%) of them had sons who were also diagnosed with lung cancer. Ten out of 27 (37.0%) mothers had a daughter who was diagnosed with lung cancer, and there were more cases (11/27, 40.7%) of breast and gynecological malignancy.

In the 48 cases in which the mothers were diagnosed with breast cancer, 5 out of 12 (41.6%) of the sons had digestive system malignant diseases, while 23 out of 36 (63.9%) of the daughters were also diagnosed with breast cancer. When the mothers were diagnosed with cancers other than breast cancer, only 31 (23.5%) daughters of a total of 132 developed breast cancer. When the mother developed a breast cancer, their daughters were more likely to have breast cancer than to be diagnosed with another malignancy (P<0.0001). When the mothers were diagnosed with a reproductive system cancer, the proportions of daughters with breast and reproductive cancer were 10/31 (32.3%) and 11/31 (35.5%), respectively.

Among the 67 mother/daughter pairs in which the mother was diagnosed with breast or gynecological cancer, 46 of 67 (68.6%) daughters also had breast or gynecological cancer. However, when mothers were diagnosed with a malignancy other than breast or gynecological cancer, only 43/101 (42.6%) of the daughters were diagnosed with breast or gynecological cancer. Those daughters with a mother who had breast or gynecological cancer had a significantly increased risk of developing the same cancer type (P<0.001) (Table 2).

For the sons, when the mothers were diagnosed with digestive system cancer, lung cancer or other malignancies, 54 out of 81 (66.7%) were diagnosed with a digestive system cancer, while if their mother had been diagnosed with breast or gynecological cancer, only 12 of 27 (44.4%) were diagnosed with a digestive system cancer. Compared with other cancers, a sons' probability of being diagnosed with digestive system cancer was relatively lower if their mother was diagnosed with breast or gynecological cancer (P<0.05) (Table 2).

Age at diagnosis

A total of 117 (69.6%) of the daughters were diagnosed with cancer at a younger age than their mothers, whilst 10 (6.0%) daughters were diagnosed at the same age as their mother and 41 (24.4%) daughters were diagnosed at an older age than their mothers. For the sons, 68 (63.0%) were diagnosed at a younger age than their mothers, 5 (4.6%) were diagnosed at the same age as their mothers, and 35 (32.4%) were diagnosed at an older age than their mothers.

The mean age at diagnosis of cancer for the mothers, sons, and daughters was 64.9±12.5 (SD) years, 56.5±12.5 (SD) years, and 53.0±13.4 (SD) years, respectively. The median age at diagnosis of the mothers, sons, and daughters was 65 years, 58.5 years, and 54 years, respectively. Based on the median age at diagnosis, sons were diagnosed cancer 6.5 years earlier than their mothers (P<0.0001), and the daughters were diagnosed cancer 11 years earlier than their mothers (P<0.0001). As a group, the daughters were diagnosed with cancer 4.5 years earlier than the sons (P<0.05).

The cases diagnosed during 5 years period were summarized in table 3. The cases diagnosed over 5 years of the daughters was more than 10% from the age of 40 years, but only reached 10% from 45 years for the sons (Table 3). Based on the NCCR data, the incidence

Table 1. The 10 Most Frequently Occuring Cancers in the 276 Mother-Child Pairs

No.	Mothers		Sons		Daughters	
	Disease	Cases (%)	Disease	Cases (%)	Disease	Cases (%)
1	Breast cancer	39(18.2)	Gastric cancer	23(21.3)	Breast cancer	55(32.7)
2	Lung cancer	38(17.8)	Lung cancer	20(18.5)	Lung cancer	22(13.1)
3	Esophageal cancer	24(11.2)	Hepatic cancer	17(15.7)	Gastric cancer	15(8.9)
4	Colorectal cancer	20(9.3)	Colorectal cancer	14(13.0)	Colorectal cancer	14(8.3)
5	Gastric cancer	19(8.9)	Esophageal cancer	8(7.4)	Uterine cancer	14(8.3)
6	Uterine cancer	16(7.5)	Malignant lymphoma	6(5.6)	Ovarian cancer	12(7.1)
7	Ovarian cancer	11(5.1)	Pancreatic cancer	3(2.8)	Hepatic cancer	7(4.2)
8	Hepatic cancer	10(4.7)	Bladder cancer	3(2.8)	Cervical cancer	7(4.2)
9	Pancreatic cancer	10(4.7)	Leukemia	3(2.8)	Malignant lymphoma	5(3.0)
10	Cervical cancer	6(2.8)	Prostate cancer	2(1.9)	Esophageal cancer	4(2.4)
	Sum	193(90.2)		99(91.7)		155(92.3)

Table 2. System and Disease Distribution of 276 Mother-child Pairs with Malignant Diseases

Diagnosis of mother	Digestive system (110)		Lung cancer (50)		Breast cancer (48)		Reproductive system (46)		Others (22)	
	sons	daughters	sons	daughters	sons	daughters	sons	daughters	sons	daughters
Digestive System	33 (71.7)	23 (35.9)	14 (60.9)	4 (14.8)	5 (41.7)	5 (13.9)	7 (46.7)	8 (25.8)	7 (58.3)	2 (18.2)
Lung cancer	6 (13.0)	5 (7.8)	6 (26.1)	10 (37.0)	0	4 (11.1)	6 (40.0)	1 (3.2)	2 (16.7)	2 (18.2)
Breast cancer	0	14 (21.9)	0	6 (22.2)	0	23 (63.9)	1 (6.7)	10 (32.3)	0	1 (9.1)
Reproductive system	0	14 (21.9)	0	5 (18.5)	1 (8.3)	2 (5.6)	1 (6.7)	11 (35.5)	0	1 (9.1)
Others	7 (15.2)	8 (12.5)	3 (13.0)	2 (7.4)	6 (50.0)	2 (5.6)	0	1 (3.2)	3 (25.0)	4 (36.4)
Total	46	64	23	27	12	36	15	31	12	10

Table 3. Distribution of the Age at Diagnosis of 276 Mother-child Pairs with Malignant Disease

Age	Mothers(%)	Sons(%)	Daughters(%)
<30	0(0)	3(2.8)	6(3.6)
30-34	1(0.5)	2(1.9)	9(5.4)
35-39	5(2.3)	5(4.6)	12(7.1)
40-44	4(1.9)	7(6.5)	18(10.7)
45-49	11(5.1)	12(11.1)	22(13.1)
50-54	20(9.3)	10(9.3)	18(10.7)
55-59	28(13.1)	19(17.6)	27(16.1)
60-64	27(12.6)	18(16.7)	16(9.5)
65-69	32(15.0)	18(16.7)	16(9.5)
70-74	36(16.8)	8(7.4)	16(9.5)
75-79	23(10.7)	5(4.6)	6(3.6)
80-84	15(7.0)	1(0.9)	2(1.2)
85-89	10(4.7)	0	0
>90	2(0.9)	0	0
Sum	214	108	168

of female population during a 5-year period began to increase and it was nearly 200 per 10^5 women from 40 years of age, while for the male population, the incidence remained below 200 per 10^5 men until 45 years of age. In this respect, daughters and sons showed the same trend as women and man in the general population (Chen et al., 2012).

Discussion

Our findings differ from those of previous studies on family clusters of cancer. We found that the broad disease profile in our group of patients was similar to that of the general population, and we suggest that this could act as a reference for the screening and early detection of cancer for individuals with a maternal history of this disease, rather than one that is disease-specific.

The Jerusalem Perinatal Study (JPS) based on 39,724 mothers and their 88,829 children showed that if both the mother and at least 1 child were diagnosed with a malignant disease, the interval between diagnosis of the mother and child was on average only 5.9 years, and in 33% of cases, this interval was shorter than 3 years. Given that the average age of the mother at the birth of their child was 27 years, children developed malignant disease much earlier than their mothers. This was concordant with our findings, in that children on average had an earlier diagnosis age than their mothers. In the JPS research, 15 out of 105 pairs had the same malignancy, which was breast cancer in 7 cases, malignant lymphoma in 3 cases, malignant melanomas and colorectal cancer both in 2 cases, and thyroid cancer in a single case. Our research also showed that breast cancer was the most common malignancy when mothers and children had exactly the same cancer type. In the JPS study, the difference in age at diagnosis between mothers and their children was not analyzed (Paltiel et al., 2007). However, other studies have shown that familial aggregation of prostate cancer was associated with earlier disease onset (before 65 years) (Kiciński et al., 2011) whilst the median age of a diagnosis of invasive melanoma fell by 11 to 16 years in successive generations (Goldstein et al., 1994). Our data corroborates these findings and we also show that children were diagnosed with cancer at a younger age than their mothers, even when the mother and child had completely different disease profiles. With similar genetic background, the tendency of the younger generation to be diagnosed of cancer earlier might be attributed to environmental factors such as air pollution, the same high risk life style factor exposure as their mothers, psychological factors. It is less likely caused by medical advances, more positive attitude to undergo medical examination with a family history of their mothers , etc. First, there has been not a national project of cancer screening. Second in China, medical resources is quite limited, few hospitals in China can provide physical examination for cancer early detection purpose and no medical insurance would pay for it until now. Third, most of the cases were diagnosed decades ago.

In this study we found that the incidence of esophageal cancer amongst mothers with cancer was 11.2%, making it the third most prevalent malignancy and more frequent than was apparent from the NCCR 2007 data (5.16%, 6th most common), whilst amongst the daughters it was the 10th most common malignancy (2.4%), and less frequent than suggested by the NCCR data. Amongst the sons of women with cancer, it was the 5th most common malignancy (7.4%). This difference in incidence between mothers and their children reflects the reduction in the prevalence of esophageal cancer in China (Ke, 2002)

The incidence of breast cancer amongst the daughters was much higher than suggested by the NCCR data, together with the findings that when both the father and the daughter were diagnosed with cancers, incidence of breast cancer was also higher than national data (Ju et al., 2013) reflects the increasing incidence of female breast cancer nationwide (Yang et al., 2006). On the other hand, hereditary factors also contributed to these findings. Among 55 daughters with breast cancer, 23 (41.8%) of their mothers were also breast cancer patients, and 23 (41.1%) out of the 56 mother-daughter pairs who had exactly the same type of malignancy had breast cancer. This finding also concurs with previous studies showing that a daughter's breast cancer risk increased significantly when her mother was diagnosed with breast cancer (Gail et al., 1989; Colditz et al., 1993), and with familial research in Sweden which found that the breast cancer risk of daughters increased if their mother also suffered from cancers such as breast or ovarian cancer (Hemminki et al., 1997).

When mothers were diagnosed with breast or a gynecological cancer, the probability of the daughter being diagnosed with one of these malignancies was greater than that of being diagnosed with any other cancer (P<0.001). Furthermore, both the mothers and the daughters had a higher incidence of uterine cancer (7.5% and 8.3%) and ovarian cancer (5.1% and 7.1%) than the national average, which was 3.5% and 3.5% (Chen et al., 2012). Breast, uterine, and ovarian cancer all have some degree of hormone dependence (Colditz et al., 1993; Crosbie et al., 2010; Gong et al., 2013). When mothers were diagnosed with breast cancer, their daughters had an increased risk of both breast and ovarian cancer (Kazerouni et al., 2006) whilst for cervical cancer, for which the main risk factor is HPV infection (Walboomers et al., 1999) both the mother and daughters (2.8% and 4.2%) had a low incidence (4.7%) close to that of the national average based on the NCCR data. In the 56 pairs of mothers and daughters with exactly the same cancer type, 53.6% of them (30 pairs) had breast or uterine cancer. Therefore, hormone related factors may be involved in the inherited mother-daughter risk of these cancers.

The median age at diagnosis of the daughters was 54 years, which was 11 years younger than their mothers were at diagnosis. The proportion of cases in which a daughter developed cancer within 5 years exceeded 10% from 40 years of age which was similar to NCCR data, the incidence of malignant disease among women began to increase significantly from 40 years of age and that the female age-specific incidence was nearly 200 per 10^5 women from 40 years of age. Studies of cervical cancer have suggested that there is a preclinical phase before a malignant disease is diagnosed (Hemminki et al., 1999), so we suggest that women with a maternal family history of cancer should begin screening for early detection by the age of 40 years just as the general population.

Among the 168 daughters, there were 81 cases (48.2%) of ovarian, uterine and breast cancer whilst their combined incidence based on the NCCR data is only 24.5%. The combined incidence of lung, breast, and gynecological cancer was 65.5% (110 cases). The incidence of lung cancer is increasing due to air pollution and passive smoking (Zhao et al., 2006) and it was the second most common cancer amongst women in the NCCR data. We therefore suggest that the screening of women with a maternal family history of cancer should emphasize breast, lung, and gynecological cancers.

When mothers were diagnosed with breast cancer, their daughters' probability of developing breast cancer was significantly higher than for other cancers; when mothers were diagnosed with breast or gynecological cancer, their daughters also had a higher rate of breast and gynecological cancer than other kind of cancers. Thus, if the mother is diagnosed with breast or gynecological cancer, daughters should be intensely screened for both malignancies and doctors should talk to them about cancer prevention, screening, and early detection.

Helicobacter pylori (HP) infection and insufficient nutritional intake are established risk factors for gastric cancer (Li et al., 2012; Conteduca et al., 2013), whilst, for example, the consumption of fruit and vegetables has been shown to have a protective effect for esophageal cancer (Beretta et al., 2012) and colon cancer is thought to be related to diet and nutritional factors (Vargas et al., 2012). Considering most of the risk factors of digestive system cancer are related to diet and infection, lifestyle factors, especially diet related factors, might be major risk factors for the development of cancer in mother-son pairs. Thirteen of the 24 mother-son pairs (54.2%) in which both had exactly the same cancer were alimentary tract cancer (esophageal, gastric and colorectal cancer), which also supports this possibility. Preventative measures, such as maintaining a healthy diet and taking precautions against hepatitis virus and HP infection, can thus be important strategies in limiting the risk of cancer in sons who have a family history of cancer on the maternal side.

The median age at diagnosis of sons was 58.5 years, which was 6.5 years earlier than their mothers' diagnosis. and the cases diagnosed within 5 years period exceeded 10% of the sons from the age of 45 years. This was accordant with the NCCR data, the incidence of cancer during 5 years period exceeded 200 per 10^5 from 45 years of age for the men. There is a preclinical phase before a malignant disease is clinically diagnosed (Hemminki et al., 1999) and we therefore suggest that men with a maternal family history of cancer should be screened to improve early detection from 45 years of age just as the general population. The most common cancer of the sons in this study was gastric cancer, rather than lung cancer that is the most prevalent male cancer nationally based on NCCR data. Likewise, the sons in this study suffered digestive system cancer more frequently than the general population. There were a total of 45 gastric, esophageal, and colorectal cancers (41.7% of all the sons in this study), also higher than in the general population (34.3%) (Chen et al., 2012). In total there were 82 cases of lung, gastric, esophageal, colorectal and hepatic cancer, accounting for three-quarters of all the sons included in this study.

The mothers,sons and daughters shared only part of both hereditary and environmental factors, and that might be the reason when mothers were dignosed with digestive system diseases, only a small part of daughters also had digestive system diseases while a larger part of sons also had digestive system cancers.

For screening and early detection, we suggest that men with a maternal family history of cancer should be checked particularly carefully for alimentary tract malignancies (esophageal, gastric and colorectal cancer), which would make endoscopy a particularly useful approach. The high incidence of alimentary tract cancers may not be cauced by the high heritability of these diseases. The reasons rest on the fact that the incidence and orders of the esophageal, gastric and colorectal cancer for the sons was similar to that of the NCCR data. Though gastric cancer ranks the first for the sons, the mothers had a relatively lower incidence of gastric cancer and relatively higher incidence of esophageal cancer.

Because we selected mother-children pairs as study population, cancers with high heritability such as breast cancer tends to be included in the sample, and this may be the reason why there were more daughters than sons in the research population. There might be other reasons for this which deserves further study.

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References

Berretta M, Lleshi A, Fisichella R, et al (2012). The role of nutrition in the development of esophageal cancer: what do we know? *Front Biosci*, **4**, 351-7.

Bratt O, Kristoffersson U, Lundgren R, et al (1997). Sons of men with prostate cancer: their attitudes regarding possible inheritance of prostate cancer, screening, and genetic testing. *Urology*, **50**, 360-5.

Colditz GA, Willett WC, Hunter DJ, et al (1993). Family history, age, and risk of breast cancer. prospective data from the nurses health study. *JAMA*, **270**, 338-43.

Conteduca V, Sansonno D, Lauletta G, et al (2013). H. pylori infection and gastric cancer: state of the art (review). *Int J Oncol*, **42**, 5-18.

Crosbie EJ, Zwahlen M, Kitchener HC, et al (2010). Body mass index, hormone replacement therapy, and endometrial cancer risk: a meta-analysis. *Cancer Epidemiol Biomarkers Prev*, **19**, 3119-30.

Gail MH, Brinton LA, Byar DP, et al (1989). Projecting individualized probabilities of developing breast cancer for white females who are being examined annually. *J Natl Cancer Inst*, **8**, 1879-86.

Goldstein AM, Fraser MC, Clark WH, et al (1994). Age at diagnosis and transmission of invasive melanoma in 23 families with cutaneous malignat melanoma/dysplastic nevi. *J Natl Cancer Inst*, **86**, 1385-90.

Gong TT, Wu QJ, Vogtmann E, et al (2013). Age at menarche and risk of ovarian cancer: a meta-analysis of epidemiological studies. *Int J Cancer*, **132**, 2894-900.

Hemminki K, Vaittinen P (1997). Effect of paternal and maternal cancer on cancer in the offspring: a population-based study. *Cancer Epidemiol Biomarkers Prev*, **6**, 993-7.

Hemminki K, Dong C, Vaittinen P (1999). Familial risks in cervical cancer: is there a hereditary component? *Int J Cancer*, **82**, 775-81.

Hemminki K, Dong C, Vaittinen P (2001). Cancer risks to spouses and offspring in the family-cancer database. *Genet Epidemiol*, **20**, 247-57.

Ju Liu, Ni Li, Sheng Chang, et al (2013). Characteristics of 240 father-child pairs with malignant disease. *Asia Pacific Journal of Cancer Prevetnion*, **14**, 6501-5

Kazerouni N, Greene MH, Lacey JV Jr, et al (2006) .Family history of breast cancer as a risk factor for ovarian cancer in a prospective study. *Cancer*, **107**, 1075-83.

Ke L (2002). Mortality and incidence trends from esophagus cancer in selected geographic areas of China circa 1970-90. *Int J Cancer*, **102**, 271-74.

Kicinski M, Vangronsveld J, Nawrot TS (2011). An epidemiological reappraisal of the familial aggregation of prostate cancer: a meta-analysis. *PLoS One*, **6**, 1-7.

Li L, Ying XJ, Sun TT, et al (2012). Overview of methodological quality of systematic reviews about gastric cancer risk and protective factors. *Asian Pac J Cancer Prev*, **13**, 2069-79.

Paltiel O, Friedlander Y, Deutsch L, et al (2007). The interval between cancer diagnosis among mothers and offspring in a population-based cohort. *Fam Cancer*, **6**, 121-9.

Ramsey SD, Yoon P, Moonesinghe R, et al (2006). Population-based study of the prevalence of family history of cancer: implications for cancer screening and prevention. *Genet Med*, **8**, 571-5.

Vargas AJ, Thompson PA (2012). Diet and nutrient factors in colorectal cancer risk. *Nutr Clin Pract*, **27**, 613-23.

Walboomers JM, Jacobs MV, Manos MM, et al (1999). Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. *J Pathol*, **189**, 12-9.

Wan-qing Chen, Hong-mei Zeng, Si-wei Zhang et al (2012). Cancer incidence and mortality in China. *Chin J Cancer Re*, **24**, 1-8.

Yang L, Li LD, Chen YD, et al (2006). Time trends, estimates and projects for breast cancer incidence and mortality in China. *Zhonghua Zhong Liu Za Zhi*, **28**, 438-40.

Zhao Y, Wang S, Aunan K, et al (2006). Air pollution and lung cancer risks in China-a meta-analysis. *Sci Total Environ*, **366**, 500-13.