

SECTION 2

Family History and Mortality in the Japan Collaborative Cohort Study for Evaluation of Cancer (JACC)

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Abstract

To determine the influence of family medical history on mortality from cancer and other chronic diseases, participants in the JACC study were questioned about tuberculosis, apoplexy, hypertension, heart disease, diabetes mellitus and malignant diseases and followed up. Consistent across the sexes, a family history of tuberculosis was apparently linked to reduced risk of lung cancer, and also lowered ischemic heart disease. No consistent findings were obtained for hypertension, diabetes mellitus or cancer.

Keywords: Family medical history - risk - cancer - circulatory disease

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Introduction

Associations between the family histories and the deaths of the malignant and circulatory diseases were analyzed. Because of the prospective nature of the study design, no recall bias was expected.

Materials and Methods

Subjects were asked their family (parents and siblings) histories of tuberculosis, apoplexy, hypertension, heart disease, diabetes mellitus and malignant diseases (cancer).

Results

The observed person-years are shown in Table 1 and the associations are shown in Table 2.

A family history of tuberculosis was positively associated with deaths of multiple myeloma in men (HR=2.69) and stomach, rectal, and uterine cancers in women, with HRs of 1.64, 2.24, and 3.60, respectively. With deaths of lung cancer, it showed a negative association in women (HR=0.36) and a weak negative one in men. It also showed weak negative associations with deaths of ischemic heart diseases and apoplexy.

A family history of apoplexy increased deaths of apoplexy in men (HR=1.18), and was negatively associated

with deaths of stomach (HR=0.75) and all cancers in women. A family history of hypertension was positively associated with deaths of myeloid leukemia in men (HR=2.60), and of uterine cancer (HR=2.37). It was negatively associated with deaths of stomach (HR=0.70), all cancers, and all causes in women. In men, it showed weak positive associations with deaths of gallbladder and prostate cancers, and a weak negative one with liver cancer.

In women, a family history of heart disease was positively associated with deaths of urinary tract cancer (HR=2.27) and negatively with all causes. It showed weak negative associations with deaths of breast cancer and myeloid leukemia in women. A family history of diabetes mellitus showed weak negative associations with deaths of ischemic heart diseases and apoplexy in men, and a weak one with liver cancer in women.

A family history of cancer at any site was positively associated with stomach, gallbladder, and pancreatic cancers in men, with HRs of 1.45, 1.72, and 1.46, respectively, and negatively with apoplexy (HR=0.84) and all causes in males, and with lung cancer and ischemic heart disease in women, the HRs being 0.60 and 0.65, respectively. It further showed weak positive links with deaths of prostate cancer and multiple myeloma in men, and breast cancer, as well as weak negative ones with ischemic heart disease in men and all causes in women.

Table 1. Observed Person-years for Family Histories

Family history	Males		Females	
	No	Yes	No	Yes
Apoplexy	459,620	115,856	655,147	162,522
Tuberculosis	547,635	27,841	780,148	37,522
Hypertension	435,064	140,413	623,185	194,484
Heart disease	494,258	81,218	693,252	124,417
Diabetes mellitus	539,744	35,733	772,497	45,172
Cancer	467,493	107,984	656,715	160,954

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Table 2. Associations between Family Histories and Risks of Mortality from Cancer and Circulatory Disease

Family history Cancer site/ disease	Male			Female		
	N for No	N for Yes	Hazard ratio [#] (95%CI)	N for No	N for Yes	Hazard ratio [#] (95%CI)
Tuberculosis						
All causes	9,811	419	0.97 (0.88, 1.07)	6,930	244	0.92 (0.81, 1.05)
All cancers	3,735	159	0.95 (0.81, 1.11)	2,223	102	1.11 (0.91, 1.36)
Esophagus	150	3	0.43 (0.14, 1.34)	27	0	NA
Stomach	738	39	1.23 (0.89, 1.71)	363	23	1.64 (1.07, 2.51)*
Colon	209	10	1.02 (0.54, 1.93)	215	5	0.54 (0.22, 1.31)
Rectum	161	3	0.41 (0.13, 1.29)	82	7	2.24 (1.03, 4.91)*
Liver	448	15	0.80 (0.48, 1.35)	217	10	1.18 (0.62, 2.24)
Gallbladder	71	1	0.34 (0.05, 2.47)	90	5	1.32 (0.53, 3.26)
Pancreas	211	13	1.31 (0.75, 2.31)	203	14	1.57 (0.91, 2.72)
Lung	875	29	0.71 (0.49, 1.03) ⁺	264	4	0.36 (0.13, 0.97)*
Breast				99	4	0.88 (0.32, 2.40)
Cervix uteri				31	5	3.60 (1.37, 9.46)**
Prostate	163	6	0.92 (0.40, 2.08)			
Kidney	45	1	0.44 (0.06, 3.17)	19	0	NA
Urinary tract	89	5	1.35 (0.54, 3.35)	39	2	1.56 (0.37, 6.55)
Non-Hodgkin's lymphoma	89	4	0.97 (0.36, 2.67)	62	3	1.03 (0.32, 3.31)
Multiple myeloma	44	5	2.69 (1.05, 6.89)*	47	2	1.03 (0.25, 4.27)
Myeloid leukemia	41	3	1.47 (0.45, 4.78)	31	2	1.59 (0.37, 6.74)
Ischaemic heart diseases	643	23	0.81 (0.53, 1.23)	449	9	0.56 (0.29, 1.08) ⁺
Cerebrovascular diseases	1,266	56	1.01 (0.77, 1.32)	1,121	30	0.71 (0.49, 1.02) ⁺
Apoplexy						
All causes	8,025	2205	1.02 (0.97, 1.07)	5,739	1,435	0.96 (0.90, 1.02)
All cancers	3,075	819	1.00 (0.93, 1.09)	1,896	429	0.87 (0.78, 0.97)**
Esophagus	121	32	0.93 (0.62, 1.39)	20	7	1.19 (0.50, 2.86)
Stomach	617	160	0.96 (0.80, 1.15)	322	64	0.75 (0.57, 0.99)*
Colon	179	40	0.81 (0.57, 1.15)	162	58	1.27 (0.94, 1.73)
Rectum	133	31	0.89 (0.59, 1.33)	75	14	0.69 (0.38, 1.23)
Liver	389	74	0.87 (0.67, 1.12)	189	38	0.84 (0.59, 1.21)
Gallbladder	57	15	0.97 (0.54, 1.74)	75	20	1.01 (0.61, 1.67)
Pancreas	172	52	1.11 (0.81, 1.53)	179	38	0.76 (0.53, 1.09)
Lung	702	202	1.04 (0.89, 1.22)	219	49	0.88 (0.64, 1.22)
Breast				86	17	0.84 (0.49, 1.44)
Cervix uteri				33	3	0.38 (0.12, 1.26)
Prostate	129	40	1.18 (0.82, 1.70)			
Kidney	39	7	0.76 (0.34, 1.74)	12	7	1.95 (0.76, 5.00)
Urinary tract	70	24	1.33 (0.82, 2.15)	34	7	0.98 (0.42, 2.29)
Non-Hodgkin's lymphoma	72	21	1.13 (0.69, 1.87)	50	15	1.19 (0.66, 2.16)
Multiple myeloma	41	8	0.80 (0.37, 1.75)	43	6	0.53 (0.22, 1.26)
Myeloid leukemia	34	10	1.13 (0.55, 2.33)	26	7	1.03 (0.44, 2.42)
Ischaemic heart diseases	517	149	1.06 (0.88, 1.28)	360	98	1.09 (0.86, 1.37)
Cerebrovascular diseases	991	331	1.18 (1.04, 1.34)*	881	270	1.11 (0.97, 1.28)
Hypertension						
All causes	8,269	1,961	0.97 (0.92, 1.02)	5,957	1,217	0.94 (0.88, 1.00)*
All cancers	3,098	796	1.00 (0.92, 1.09)	1,909	416	0.89 (0.80, 0.99)*
Esophagus	113	40	1.20 (0.82, 1.74)	21	6	1.13 (0.44, 2.85)
Stomach	620	157	0.98 (0.82, 1.17)	331	55	0.70 (0.53, 0.94)*
Colon	177	42	0.91 (0.64, 1.28)	170	50	1.19 (0.86, 1.64)
Rectum	127	37	1.12 (0.76, 1.63)	73	16	0.84 (0.48, 1.47)
Liver	389	74	0.79 (0.61, 1.03) ⁺	187	40	0.89 (0.63, 1.27)
Gallbladder	52	20	1.72 (1.00, 2.96) ⁺	76	19	1.02 (0.61, 1.71)
Pancreas	172	52	1.16 (0.84, 1.60)	178	39	0.87 (0.61, 1.24)
Lung	723	181	0.95 (0.80, 1.12)	216	52	1.01 (0.74, 1.38)
Breast				85	18	0.68 (0.41, 1.16)
Cervix uteri				23	13	2.37 (1.15, 4.90)*
Prostate	132	37	1.38 (0.94, 2.02) ⁺			
Kidney	39	7	0.77 (0.34, 1.75)	17	2	0.46 (0.11, 2.02)
Urinary tract	79	15	0.81 (0.46, 1.44)	37	4	0.61 (0.21, 1.75)
Non-Hodgkin's lymphoma	73	20	1.08 (0.65, 1.81)	53	12	0.84 (0.44, 1.60)
Multiple myeloma	42	7	0.74 (0.32, 1.68)	43	6	0.56 (0.23, 1.33)
Myeloid leukemia	26	18	2.60 (1.38, 4.90)**	25	8	1.27 (0.56, 2.91)
Ischaemic heart diseases	524	142	1.12 (0.92, 1.35)	378	80	1.11 (0.86, 1.42)
Cerebrovascular diseases	1,076	246	0.93 (0.81, 1.08)	939	212	1.05 (0.91, 1.23)

Table 2. Continued. Associations between Family Histories and Risks of Mortality

Heart disease								
All causes	8,891	1339	0.99	(0.93, 1.05)	6,286	888	0.92	(0.86, 0.99)*
All cancers	3,372	522	1.00	(0.91, 1.10)	2,021	304	0.93	(0.82, 1.05)
Esophagus	132	21	0.95	(0.59, 1.51)	23	4	1.01	(0.35, 2.93)
Stomach	673	104	1.02	(0.82, 1.25)	340	46	0.86	(0.63, 1.18)
Colon	193	26	0.85	(0.56, 1.28)	191	29	0.88	(0.60, 1.31)
Rectum	140	24	1.10	(0.71, 1.71)	77	12	0.95	(0.51, 1.77)
Liver	408	55	0.99	(0.74, 1.32)	199	28	0.90	(0.60, 1.35)
Gallbladder	62	10	1.06	(0.54, 2.09)	87	8	0.55	(0.27, 1.15)
Pancreas	195	29	0.92	(0.62, 1.37)	186	31	0.97	(0.66, 1.43)
Lung	782	122	0.98	(0.80, 1.18)	228	40	1.11	(0.79, 1.56)
Breast					94	9	0.54	(0.27, 1.07) ⁺
Cervix uteri					29	7	1.47	(0.63, 3.42)
Prostate	153	16	0.74	(0.44, 1.25)				
Kidney	39	7	1.20	(0.53, 2.72)	16	3	1.05	(0.31, 3.61)
Uninary tract	78	16	1.41	(0.82, 2.45)	32	9	2.27	(1.04, 4.95)*
Non-Hodgkin's lymphoma	79	14	1.17	(0.66, 2.08)	60	5	0.47	(0.19, 1.17)
Multiple myeloma	42	7	1.16	(0.51, 2.62)	42	7	1.02	(0.45, 2.30)
Myeloid leukemia	37	7	1.16	(0.51, 2.64)	32	1	0.18	(0.03, 1.36) ⁺
Ischaemic heart diseases	574	92	1.06	(0.85, 1.33)	400	58	1.02	(0.77, 1.34)
Cerebrovascular diseases	1,147	175	0.98	(0.84, 1.15)	999	152	0.97	(0.82, 1.15)
Diabetes mellitus								
All causes	9,820	410	0.94	(0.85, 1.04)	6,938	236	1.00	(0.88, 1.14)
All cancers	3,729	165	0.93	(0.79, 1.09)	2,235	90	1.00	(0.81, 1.23)
Esophagus	149	4	0.47	(0.17, 1.27)	27	0	NA	
Stomach	747	30	0.85	(0.59, 1.23)	370	16	1.16	(0.70, 1.93)
Colon	207	12	1.19	(0.66, 2.13)	211	9	1.08	(0.55, 2.11)
Rectum	158	6	0.76	(0.34, 1.73)	85	4	1.16	(0.42, 3.20)
Liver	440	23	1.10	(0.72, 1.69)	214	13	1.62	(0.92, 2.86) ⁺
Gallbladder	72	0	N.A		90	5	1.31	(0.53, 3.24)
Pancreas	215	9	0.86	(0.44, 1.69)	206	11	1.29	(0.70, 2.38)
Lung	865	39	0.94	(0.68, 1.30)	262	6	0.56	(0.25, 1.25)
Breast					99	4	0.70	(0.26, 1.91)
Cervix uteri					36	0	NA	
Prostate	162	7	1.18	(0.55, 2.52)				
Kidney	45	1	0.45	(0.06, 3.30)	18	1	1.42	(0.19, 10.8)
Uninary tract	90	4	1.08	(0.39, 2.96)	40	1	0.85	(0.12, 6.25)
Non-Hodgkin's lymphoma	87	6	1.43	(0.62, 3.29)	62	3	1.02	(0.32, 3.29)
Multiple myeloma	47	2	1.01	(0.24, 4.21)	47	2	1.06	(0.26, 4.44)
Myeloid leukemia	41	3	1.23	(0.38, 4.02)	33	0	NA	
Ischaemic heart diseases	647	19	0.66	(0.42, 1.05) ⁺	445	13	0.99	(0.57, 1.72)
Cerebrovascular diseases	1,281	41	0.75	(0.55, 1.02) ⁺	1,113	38	1.08	(0.78, 1.49)
Cancer								
All causes	8,532	1698	0.93	(0.88, 0.99)*	6,051	1123	0.94	(0.88, 1.00) ⁺
All cancers	3,205	689	1.02	(0.93, 1.11)	1,900	425	1.08	(0.97, 1.21)
Esophagus	129	24	0.92	(0.59, 1.44)	22	5	0.98	(0.36, 2.63)
Stomach	655	122	0.91	(0.74, 1.12)	302	84	1.45	(1.12, 1.87)**
Colon	179	40	1.06	(0.74, 1.53)	190	30	0.75	(0.50, 1.11)
Rectum	132	32	1.14	(0.75, 1.72)	70	19	1.42	(0.83, 2.43)
Liver	394	69	0.93	(0.71, 1.22)	188	39	1.17	(0.82, 1.69)
Gallbladder	65	7	0.61	(0.27, 1.37)	69	26	1.72	(1.05, 2.81)*
Pancreas	184	40	1.03	(0.72, 1.47)	163	54	1.46	(1.06, 2.03)*
Lung	720	184	1.13	(0.96, 1.35)	237	31	0.60	(0.40, 0.88)**
Breast					78	25	1.59	(0.99, 2.56) ⁺
Cervix uteri					32	4	0.50	(0.17, 1.46)
Prostate	134	35	1.43	(0.96, 2.13) ⁺				
Kidney	38	8	0.83	(0.38, 1.84)	16	3	0.82	(0.23, 2.99)
Uninary tract	83	11	0.58	(0.30, 1.12)	38	3	0.45	(0.13, 1.56)
Non-Hodgkin's lymphoma	71	22	1.51	(0.91, 2.52)	51	14	1.17	(0.62, 2.21)
Multiple myeloma	36	13	1.96	(0.97, 3.96) ⁺	38	11	1.39	(0.68, 2.81)
Myeloid leukemia	32	12	1.60	(0.79, 3.27)	27	6	1.33	(0.52, 3.37)
Ischaemic heart diseases	563	103	0.82	(0.66, 1.02) ⁺	405	53	0.65	(0.49, 0.88)**
Cerebrovascular diseases	1,117	205	0.84	(0.72, 0.99)*	967	184	0.97	(0.82, 1.14)

⁺Adjusted for age, area of study. ** p<0.01, * p<0.05, + p<0.10 NA: HR not calculated because of the SAS stratifying option

Discussion

A family history of tuberculosis showed several associations with malignant and circulatory diseases, but few associations have been referred to by studies so far. Family history of apoplexy increased deaths of apoplexy in men, which has been reported (Kondo et al., 2005), but did not show marked associations with any diseases. Family histories of hypertension and heart diseases were not related with risks of circulatory diseases.

A family history of diabetes mellitus showed weak negative associations with risks of ischemic heart diseases and apoplexy, and did not increase risks of any diseases markedly. Family history of cancer showed significant associations with several cancers in women, while with no cancers in men. Among the relationships, one between risk of gastric cancer and its family history was remarkable in those under 40 years of age (Kikuchi et al., 1996), and was also observed in the elderly population of the current study (Kondo et al, 2003; Yatsuya et al., 2002; 2004).

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