

RISING INCIDENCE OF BILIARY TRACT CANCERS IN SHANGHAI, CHINA

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Cancers of the biliary tract, including cancers of the gallbladder, extra-hepatic bile ducts, and ampulla of Vater, are relatively uncommon malignancies. From 1972 to 1994, biliary tract cancer was the most rapidly rising malignancy in Shanghai, China, with a 119% increase in men and 124% in women. The increase in incidence was seen for all 3 subsites, both sexes, and all age groups. Future studies are needed to identify reasons for the large increases in these rates. Int. J. Cancer 75:368–370, 1998.

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Cancers of the biliary tract encompass tumors arising from the gallbladder, extra-hepatic bile ducts and ampulla of Vater. These malignancies are relatively uncommon in most parts of the world, though elevated rates have been reported in Japan, Eastern Europe and Central and South America and among Native Americans and Hispanic Americans (Parkin *et al.*, 1992; Nectoux and Coleman, 1993; Tominaga and Kuroishi, 1994; Carriaga and Henson, 1995; Fraumeni *et al.*, 1996). Geographic variation is most pronounced for gallbladder cancer, which is characterized also by a female predominance (Fraumeni *et al.*, 1996). Patients with biliary tract cancers have a generally poor prognosis (5-year relative survival rates of 10–20%), with most cases having advanced disease at the time of presentation (Carriaga and Henson, 1995). Little is known about the origins of biliary tract cancers, apart from a close association with gallstones (Fraumeni *et al.*, 1996).

Data from the population-based tumor registry in Shanghai, China, indicate that biliary tract cancer has increased more rapidly than any other malignancy in this area (Jin *et al.*, 1993). To provide leads for etiologic studies, we evaluated further the age-specific incidence trends for biliary tract tumors according to subsite.

Details of the Shanghai Cancer Registry (SCR) have been described elsewhere (Jin *et al.*, 1993). Briefly, the SCR collects information on all newly diagnosed cancer cases among Shanghai residents. The population of the 10 districts within the urban area for which incidence data are available for the entire time period was 7.3 million people in 1992. Cases were coded according to 4-digit rubrics of the 9th revision of the *International Classification of Diseases* (World Health Organization, 1977), and all cases classified as biliary tract cancers (first 3 digits = 156) were selected for analysis. Population estimates were based on periodic censuses, with age- and sex-specific annual estimates derived by linear interpolation and extrapolation for the remaining years. Incidence rates per 100,000 person-years for the 7 3-year periods (1972–1974 to 1990–1992) and 1 2-year period (1993–1994) were calculated for 10-year age groups and age-adjusted to the world population using the direct method (Parkin *et al.*, 1992). Annual percent changes in incidence were estimated by means of a linear regression of the logarithm of the respective rates on calendar year, weighted by the number of cases.

During 1993–1994, biliary tract cancers accounted for 1.2% of cancers in men and 2.8% of cancers in women in Shanghai. From 1972 through 1994, there were 1,665 men and 2,949 women diagnosed with biliary tract cancers. During this 23-year interval, age-adjusted incidence rates rose 119% or 4.5% per year (from 1.18 to 2.59 per 100,000) in men and 124% or 4.4% per year (from 1.74 to 3.90 per 100,000) in women (Table I).

When examined by subsite, the respective increases among men and women were 140% and 126% for gallbladder cancer, 108% and 134% for extra-hepatic bile duct cancer and 39% and 15% for ampullary cancer. The rate of increase for gallbladder cancer was greater in men than in women (6.0% vs. 4.7% per year), while the rate of increase for bile duct cancer was somewhat higher in women (4.8% vs. 4.2% per year) (Fig. 1). Because of small numbers, the trends for ampullary cancer were unclear.

For all 3 subsites and both sexes, incidence rates increased over time in all age groups, doubling between the ages of 65 and 84 (Table II). Not shown are cases over the age of 85, which were too few to yield reliable rate estimates. For gallbladder cancer, the rates rose faster in men than in women from 55 to 74 years of age, but at all ages and calendar periods the rates were at least 50% higher in women than in men. The excess in women was most pronounced at younger ages and decreased with increasing age. For cancer of the extra-hepatic bile ducts, the rates increased faster in men than in women at all ages except 75–84 years, when the upward trend was much greater in women. The overall sex ratios showed a male predominance at 45–54 and 75–84 years of age and an excess in women at 55–74 years of age. The numbers with ampullary cancer were small and the rates unstable, though the sex ratios by age were similar to those for bile duct cancer.

Reasons for the rising incidence of biliary tract cancers in Shanghai are unclear, though improvements in diagnosis and classification may contribute to the trend. Most of the increase, however, is likely to be real since the proportion of cases histologically confirmed did not change over time, the survival patterns remained the same and the rising incidence at all subsites began before new diagnostic methods were introduced in the early 1980s.

A large portion of cancers of the gallbladder and, to a lesser extent, the bile duct is related to the presence of gallstones, particularly of the cholesterol type (Fraumeni *et al.*, 1996). Cholesterol stones tend to be common in Western populations (Diehl, 1980; Lowenfels *et al.*, 1985), while pigment stones often prevail in Asian countries (Johnston and Kaplan, 1993); but the prevalence of cholesterol stones has increased in China, especially in urban areas (National Collaborative Group, 1987). Further studies are needed to clarify the relation between gallstones and biliary tract cancers in China and to identify risk factors for both conditions, particularly the effects of increases in body weight and other aspects of a more westernized diet (Popkin *et al.*, 1995). Also deserving of study are bacterial infections of the biliary tract that often accompany stones in China (National Collaborative Group, 1987) and hormonal factors, including the increasing use of menopausal estrogens and oral contraceptives in this area (Shu *et al.*, 1991). Infection with liver flukes, in particular *Clonorchis sinensis*, has been linked mainly to intra-hepatic bile duct cancer (cholangiocarcinoma) in China (IARC, 1994); its role in cancers of

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TABLE 1 – AGE-ADJUSTED INCIDENCE RATES¹ FOR CANCERS OF THE BILIARY TRACT IN URBAN SHANGHAI (1972–1974 to 1993–1994)

Period	Males				Females			
	Total	Gallbladder	Extra-hepatic bile ducts	Ampulla of Vater	Total	Gallbladder	Extra-hepatic bile ducts	Ampulla of Vater
1972–1974	1.18 (90) ²	0.53 (36)	0.43 (37)	0.22 (16)	1.74 (159)	1.05 (96)	0.35 (32)	0.25 (23)
1975–1977	1.12 (87)	0.46 (31)	0.37 (32)	0.25 (22)	1.76 (195)	1.06 (105)	0.36 (36)	0.22 (22)
1978–1980	1.31 (129)	0.53 (50)	0.42 (44)	0.29 (29)	2.15 (237)	1.30 (143)	0.46 (51)	0.28 (31)
1981–1983	1.81 (189)	0.58 (60)	0.64 (65)	0.42 (46)	2.40 (292)	1.24 (154)	0.62 (74)	0.26 (31)
1984–1986	2.03 (247)	0.79 (95)	0.69 (83)	0.46 (58)	3.17 (437)	1.85 (259)	0.73 (101)	0.40 (52)
1987–1989	2.49 (322)	1.05 (133)	0.83 (111)	0.48 (63)	3.38 (570)	2.08 (310)	0.81 (124)	0.39 (59)
1990–1992	2.44 (348)	1.27 (180)	0.76 (107)	0.37 (55)	3.70 (630)	2.23 (381)	0.90 (152)	0.44 (73)
1993–1994	2.59 (253)	1.27 (125)	0.89 (85)	0.31 (29)	3.90 (429)	2.37 (263)	0.83 (92)	0.29 (32)
% Change	119.2	140.3	108.5	38.9	124.2	126.0	133.7	14.6
Annual % change	4.5 ³	6.0 ³	4.2 ³	2.0	4.4 ³	4.7 ³	4.8 ³	2.7 ³

¹Per 100,000 person-years, age-adjusted using world standard.– ²Number of cases in parentheses. Total biliary tract includes gallbladder, extra-hepatic bile duct, ampulla of Vater and biliary tract NOS.– ³*p* < 0.01.

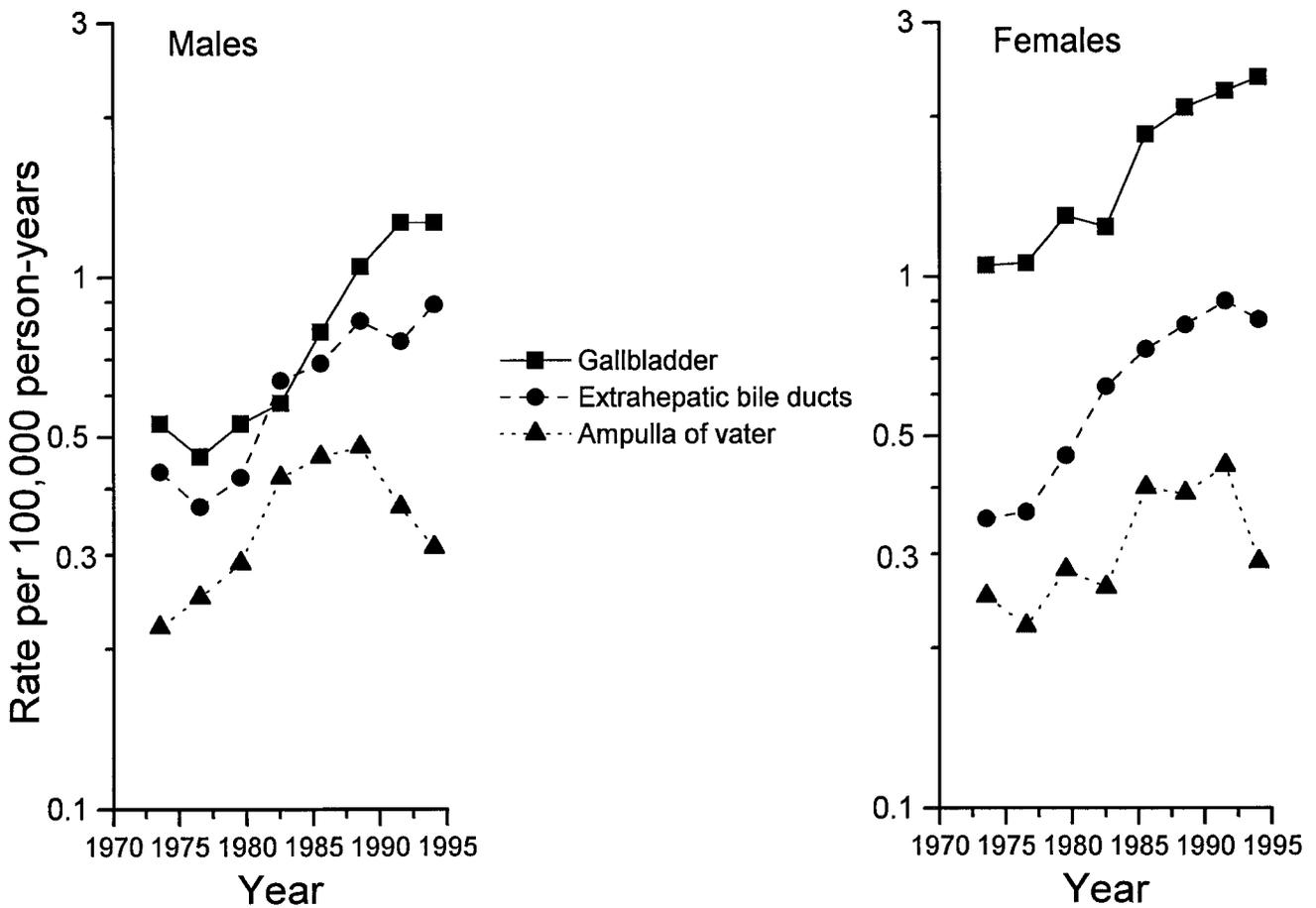


FIGURE 1 – Age-adjusted incidence trends for biliary tract cancers in urban Shanghai by subsite, sex and year of diagnosis, 1972–1974 to 1993–1994.

TABLE II – AGE-SPECIFIC INCIDENCE RATES¹ FOR CANCERS OF THE BILIARY TRACT IN URBAN SHANGHAI BY SEX AND SUBSITE (1972–1983 TO 1984–1994)

Subsite/age (years)	Males			Females			Sex ratio (M/F)	
	1972–1983	1984–1994	% Change	1972–1983	1984–1994	% Change	1972–1983	1984–1994
Gallbladder								
45–54	0.51 (26) ²	0.83 (34)	63	1.39 (70)	2.32 (93)	67	0.37	0.36
55–64	1.76 (55)	3.12 (130)	77	5.51 (189)	7.89 (352)	43	0.32	0.40
65–74	3.83 (65)	9.26 (231)	140	7.63 (150)	16.12 (467)	111	0.50	0.57
75–84	4.78 (22)	12.32 (102)	158	8.11 (62)	20.68 (240)	155	0.59	0.60
Extra-hepatic bile ducts								
45–54	0.68 (34)	1.07 (45)	57	0.63 (32)	0.80 (33)	27	1.08	1.34
55–64	2.11 (71)	2.46 (102)	47	2.21 (76)	3.04 (136)	37	0.95	0.81
65–74	2.12 (36)	5.66 (141)	167	2.86 (56)	6.14 (178)	115	0.74	0.92
75–84	4.78 (22)	8.37 (70)	75	1.57 (12)	7.20 (84)	358	3.04	1.16
Ampulla of Vater								
45–54	0.48 (24)	0.49 (21)	2	0.56 (28)	0.38 (15)	–32	0.86	1.29
55–64	0.98 (31)	1.26 (53)	28	1.18 (41)	1.56 (70)	32	0.83	0.81
65–74	2.46 (42)	2.89 (72)	17	1.07 (21)	2.94 (85)	175	2.29	0.98
75–84	1.81 (9)	5.77 (48)	219	1.05 (8)	2.72 (32)	159	1.72	2.12

¹Per 100,000 person-years, age-adjusted using world standard.– ²Number of cases in parentheses.

the extra-hepatic biliary tract is less clear, and its low prevalence (2%) in Shanghai has not changed over time. The role of smoking deserves further investigation, especially since a relation to extra-hepatic bile duct cancer has been suggested (Chow *et al.*, 1994).

Although causal mechanisms may vary by subsite, the remarkable increase in the incidence of biliary tract cancers in Shanghai provides a special opportunity for epidemiologic studies into the origins of these tumors and the means of prevention.

ACKNOWLEDGEMENTS

We thank Ms. Shu-Zen Zhou, Ms. Rong-Fang Tao, Ms. Ai-Qing Chen, Ms. Ru-Rong Fang and Mr. Yi-Ling Jiang of the Shanghai Cancer Registry for assistance in data collection and management. Dr. Yong-Bing Xiang and Ms. Lu Sun of the Shanghai Cancer Institute and Ms. Joan Hertel of IMS, Inc., provided skilled assistance in data preparation, computing and figure development.

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