

**Table 2.20. Case-control studies of consumption of alcoholic beverages and cholangiocarcinoma**

Reference, study location and period	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	Exposed cases/controls	Relative risk (95% CI)	Adjustment for potential confounders	Comments
<i>Cholangiocarcinoma and Intrahepatic cholangiocarcinoma (IHCCA)</i>								
Parkin <i>et al.</i> (1991) Thailand 1987–88	101 cases (less than 75 years, male: 68.9%) Either diagnosed by histology, or with findings on ultrasound examination or by percutaneous cholangiography with or without an elevated titre ( $\geq 40$ units/ml) of CA19–9) from three hospitals, Maharat Nakornratchasima Hospital (Korat) and Sappasithppasong Hospital, Ubonratchathani (Ubon) both in north-eastern Thailand, and the National Cancer Institute, Bangkok,	101 matched controls by sex and age ( $\pm 5$ years) from inpatients (non-malignant diseases-unrelated tobacco or alcohol consumption) of the same hospital or clinic	Interviewed with a structured questionnaire	Occasional, ex-, non drinker Regular drinker (2 or more glasses of spirits per week)	11 numerator Versus 4 denominator Among 102 pairs	1.0 2.8 (0.9–8.2)	Univariate analysis of matched-pair analysis	Regular drinker (2 or more glasses of spirits per week) is equivalent to approximately 20 g of ethanol per day)

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Shin <i>et al.</i> (1996) Korea (Republic of) 1990–93	41 newly diagnosed cases (30 males, 11 females) (51.2%: histologically confirmed, 49.8%: non-histologically using a combination of ultrasonogram, angiography, liver scanning, CT and MRI) Pusan Paik Hospital, Busan 36 cases were included in the analysis (total cases were 41 CCA and 203 HCC)	406 controls which were age- and sex- matched for HCC cases (Control I; from inpatients in the department of ophthalmology or ENT) Control II: healthy control from the screenees for health check-up	Interviewed with a structured questionnaire	Drinking history No Moderate Heavy (80 g ethanol per day during last three years and drank for ≥ 10 years)	18/167 14/194 9/45	1.0 1.5 (0.6–3.8) 4.6 (1.4–15.2)	Age group, sex and socioeconomic status, HBsAg, anti-HCV, liver fluke (CS eggs in stool) transfusion history, liver fluke history, smoking history	Including Klaskin tumour (hilar cholangiocarcinoma)
Donato <i>et al.</i> (2001) Italy 1995–2000	26 intrahepatic cholangiocarcinoma – histology-based diagnosed (among 370 primary liver cancer) From 2 main hospitals in Brescia	824 controls From the inpatients in other department of hospital (frequency matched with PLC cases by sex, age, date, and hospital of admission)	Interview using a standardized questionnaire	Alcohol intake (g/day) 0–40 41–80 > 80	15/321 5/232 6/271	1.0 0.3 0.4	Adjusted for sex, age, residence, HCV, HBV, history of hepatolithiasis	

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Yamamoto <i>et al.</i> (2004) Osaka, Japan 1991–2002	50 IHCCA cases with pathologically diagnosed Osaka City University Hospital and Osaka City General Hospital	205 other surgical patients without primary liver cancer (2–5 controls matched by sex, age group, operation date (within 1 year))	Information from the medical record-converted into Sake (Japanese wine) equivalent	Alcohol consumption Mild ( $\leq 3$ go) or moderate Heavy (at least 5 go per day for more than 10 years))	49/94  1/11	1.0  0.97 (0.49–4.37)	Univariate analysis (not include in the multivariate analysis due to insignificant result))	One “go” (180 ml) of sake contains about 27 ml of ethanol (equal in alcohol content to 60 ml of whisky, 240 ml of wine, 633 ml of beer 5 go per day (heavy drinker) is equivalent 135 ml of ethanol

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Honjo <i>et al.</i> (2005) Thailand 1999–2001	129 cases diagnosed on abdominal ultrasonography with CA 19–9 (> 40 units/ml) and normal level of $\alpha$ fetoprotein (AFP: < 20 ng/ml) 85 male and 44 female case-control pairs Nakhon Phanom provincial hospital, Nakhon Phanom,	129 community controls Matched sex, age ( $\pm$ 5 years) and place of residence No ultrasonographic findings	Interviewed using a structured questionnaire	Never Occasional Ex-regular Regular ( $\geq$ 1 per week)	30/46 41/54 15/7 41/21	1.0 2.2 (0.65–7.5) 6.2 (1.2–31.6) 4.3 (1.1–16.6)	Adjusted for anti-OV Ab, smoking and alcohol drinking	3 cases and 5 controls: no information on alcohol consumption  Results stratified by GSTM1 and GSTT1 polymorphism were similar for wild type and polymorphic genotypes, and showed statistically non-significant increase in risk associated with alcohol consumption.
Shaib <i>et al.</i> (2007) Texas, USA 1992–2002	83 IHCCA (37 females, 46 males) Histologically confirmed M.D. Anderson Cancer Center, Also 163 extrahepatic cholangiocarcinoma cases (see below)	236 healthy controls (102 females, 134 males)	Review medical record (data were collected using structured data collection sheet)	No Yes Mild/moderate (< 80 g/day) Heavy (80 g of ethanol per day or more)	37/113 46/123 28/114 18/9	1.0 1.1 (0.6–1.9)* 1.6 (0.9–2.8)* 5.9 (2.1–17.4)	Race, age, gender, HCV, HBV markers, heavy drinking	* results from univariate analysis

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Lee <i>et al.</i> (2008) Seoul, Korea (Republic of) 2000–04	622 IHCCA cases – histologically confirmed Asan Medical Center, Seoul	2488 controls from health examinees in the same hospital (4 controls per each case matched age, sex, date of visit or admission)	Medical record review for cases Self-administered questionnaire for controls	Ethanol gram per day Less than 80 g/day Heavy (at least 80 g /day)	510/2410 112/78	1.0 6.6 (4.8–9.2)	HBV, <i>C.sinensis</i> in stool, hepatolithiasis, cholesterol cyst, liver cirrhosis, Diabetes	
Zhou <i>et al.</i> (2008) China 2004–2006	312 intrahepatic cholangiocarcinoma underwent surgical resection (diagnosed by pathological examination) 207 males and 105 females (mean age = 53.2 ± 10.4) Eastern Hepatobiliary Surgery Hospital, Shanghai, Second Military Medical University	312 controls matched by age (± 5 years), sex and date of admission from patients –unaffected by liver disease from the Changhai hospital of the second Military Medical University 276 males and 162 females (mean age = 54.8 ± 11.8)	Review clinical records	No Ever drinker Alcoholic beverages ≥ 1 day week for ≥ 6 months	273/397 39/41	1.0 0.8 (0.5–1.3)	HBV, HCV, Diabetes mellitus, hypertension, hepatolithiasis, cigarette smoking,	

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<i>Extra hepatic cholangiocarcinoma (EHCCA)</i>								
Shaib <i>et al.</i> (2007)	163 EHCCA (67 females, 96 males) Histologically confirmed (including Klaskin tumour) M.D. Anderson Cancer Center,	236 healthy controls (102 females, 134 males)	Review medical record (data were collected using structured data collection sheet)	No Yes Mild/moderate (< 80 g/day) Heavy (80 g of ethanol per day or more)	90/113 73/123 44/114 29/9	1.0 0.7 (0.5–1.1)* 0.5 (0.3–0.8) 3.6 (1.5–9.4)	Race, age, gender, HCV, HBV markers, mild/moderate and heavy drinking	* results from univariate analysis
Hsing <i>et al.</i> (2008) China 1997–2001	134 extrahepatic bile duct cancer from Shanghai Cancer Institute (SCI) and 42 collaborating hospitals in 10 urban districts of Shanghai,  Response rate: 95%	762 population –based controls Response rate: 82%	Interview using a structured questionnaire	Alcohol use (%) of current drinker (drinking alcohol regularly at the time of interview)	32.1% in cases / 20.9% in controls	Not shown in the paper	None	1.8 (1.2–2.8) Odds ratio (univariate) was calculated using information in the paper