# ABSENCE OF EXCESS BODY FATNESS

**VOLUME 16** 

This publication represents the views and expert opinions of an IARC Working Group on the Evaluation of Cancer-Preventive Interventions, which met in Lyon, 5–12 April 2016

LYON, FRANCE - 2018

IARC HANDBOOKS OF CANCER PREVENTION

# 2.2.6 Cancers of the biliary tract

Intrahepatic bile duct cancers occur in the smaller bile duct branches within the liver and comprise about 10% of bile duct cancers. Extrahepatic bile duct cancers occur outside of the liver. Perihilar (also called hilar) extrahepatic bile duct cancers occur where the left and right hepatic ducts join and are the most common type of bile duct cancer, accounting for about two thirds of all bile duct cancers. Nearly all bile duct cancers are cholangiocarcinomas, of which most are adenocarcinomas. This section reviews studies of all subtypes of cancer of the biliary tract.

### (a) Cohort studies

See Table 2.2.6a (web only; available at: <a href="http://publications.iarc.fr/570">http://publications.iarc.fr/570</a>).

Only one prospective study (i.e. the EPIC cohort) assessed the association between body weight and intrahepatic bile duct cancer specifically; relative risk estimates for all measurements (BMI, weight, waist or hip circumference, waist-to-hip ratio, or weight change) as continuous measures were greater than 1, but none of the associations were statistically significant (Schlesinger et al., 2013).

The association between BMI and extrahepatic bile duct cancer specifically (excluding the gall bladder) was examined in the Japan Public Health Center Study. In that study, BMI was positively associated with risk in men and women combined, with a relative risk of 1.78 for BMI  $\geq$  27 kg/m² compared with < 23 kg/m² ( $P_{\rm trend} = 0.03$ ) (Ishiguro et al., 2008).

The association between BMI and intra- or extrahepatic bile duct cancer was examined in the Korea National Health Insurance Corporation Study, which included only men and found a statistically significant positive dose–response relationship ( $P_{\rm trend} = 0.005$ ) (Oh et al., 2005).

The association between BMI and cancer of the bile ducts and gall bladder combined was examined in two prospective studies. In the Japan Public Health Center Study, the relative risk estimates for the highest versus lowest categories of BMI in men and in women were greater than 1 but were not statistically significant (Ishiguro et al., 2008). In the EPIC study, in which cancers of the extrahepatic bile ducts included cancers of the gall bladder, associations of BMI and weight in men and women combined were not statistically significant. [The median BMI in the highest tertile was 29.9 kg/m<sup>2</sup> for men and 29.6 kg/m<sup>2</sup> for women, which includes people with a BMI in the overweight and obese category.] Similarly, no association was found with average annual weight change from age 20 years, or with waist circumference (Schlesinger et al., 2013).

In a meta-analysis of gall bladder or biliary tract cancer incidence or mortality that included seven studies, BMI was statistically significantly positively associated with risk in men and women combined (RR for highest vs lowest category of BMI, 1.40; 95% CI, 1.15–1.65) (Park et al., 2014).

### (b) Case-control studies

See Table 2.2.6b (web only; available at: <a href="http://publications.iarc.fr/570">http://publications.iarc.fr/570</a>).

The associations of BMI with cancers of the biliary tract system (including gall bladder or not) were examined in six population- or hospital-based case–control studies.

For extrahepatic bile duct cancer, two population-based case–control studies, one in Europe (Ahrens et al., 2007) and one in China (Hsing et al., 2008), showed a statistically significant higher risk for BMI > 25 kg/m² versus 18.5–25 kg/m², whereas a lower risk with high BMI was observed in one study in China (Kato et al., 1989). No association was observed in a study of cholangiocarcinoma (Grainge et al., 2009). No association was observed with waist circumference in the only study that examined such association (Shebl et al., 2011).

For overall biliary tract cancer, a 2.5-fold increase in risk was observed with BMI  $\geq$  30 kg/m<sup>2</sup> at age 35 years, but not with BMI 1–5 years before study entry (Ahrens et al., 2007).

Shebl FM, Andreotti G, Meyer TE, Gao YT, Rashid A, Yu K, et al. (2011). Metabolic syndrome and insulin resistance in relation to biliary tract cancer and stone risks: a population-based study in Shanghai, China. *Br J Cancer*, 105(9):1424–9. doi:10.1038/bjc.2011.363 PMID:21915122

## References

- Ahrens W, Timmer A, Vyberg M, Fletcher T, Guénel P, Merler E, et al. (2007). Risk factors for extrahepatic biliary tract carcinoma in men: medical conditions and lifestyle: results from a European multicentre case-control study. *Eur J Gastroenterol Hepatol*, 19(8):623–30. doi:10.1097/01.meg.0000243876.79325. al PMID:17625430
- Grainge MJ, West J, Solaymani-Dodaran M, Aithal GP, Card TR (2009). The antecedents of biliary cancer: a primary care case-control study in the United Kingdom. *Br J Cancer*, 100(1):178–80. doi:10.1038/sj.bjc.6604765 PMID:19018260
- Hsing AW, Sakoda LC, Rashid A, Chen J, Shen MC, Han TQ, et al. (2008). Body size and the risk of biliary tract cancer: a population-based study in China. *Br J Cancer*, 99(5):811–5. doi:10.1038/sj.bjc.6604616 PMID:18728671
- Ishiguro S, Inoue M, Kurahashi N, Iwasaki M, Sasazuki S, Tsugane S (2008). Risk factors of biliary tract cancer in a large-scale population-based cohort study in Japan (JPHC study); with special focus on cholelithiasis, body mass index, and their effect modification. *Cancer Causes Control*, 19(1):33–41. doi:10.1007/s10552-007-9067-8 PMID:17906958
- Kato K, Akai S, Tominaga S, Kato I (1989). A case-control study of biliary tract cancer in Niigata Prefecture, Japan. *Jpn J Cancer Res*, 80(10):932–8. doi:10.1111/j.1349-7006.1989.tb01629.x PMID:2515177
- Oh SW, Yoon YS, Shin SA (2005). Effects of excess weight on cancer incidences depending on cancer sites and histologic findings among men: Korea National Health Insurance Corporation Study. *J Clin Oncol*, 23(21):4742–54. doi:10.1200/JCO.2005.11.726 PMID:16034050
- Park M, Song Y, Je Y, Lee JE (2014). Body mass index and biliary tract disease: a systematic review and meta-analysis of prospective studies. *Prev Med*, 65:13–22. doi:10.1016/j.ypmed.2014.03.027 PMID:24721739
- Schlesinger S, Aleksandrova K, Pischon T, Fedirko V, Jenab M, Trepo E, et al. (2013). Abdominal obesity, weight gain during adulthood and risk of liver and biliary tract cancer in a European cohort. *Int J Cancer*, 132(3):645–57. doi:10.1002/ijc.27645 PMID:22618881