衞生防護中心
Centre for Health Protection

Cancer Expert Working Group on Cancer Prevention and Screening

Recommendations on Prevention and Screening for Liver Cancer For Health Professionals

Local epidemiology

1. In 2015, liver cancer was the fourth commonest cancer in men and the tenth commonest cancer in women. A total of 1,791 liver cancer cases were recorded, accounting for 5.9% of all newly diagnosed cancer cases. The age-standardised incidence rate (ASIR) was 22.7 for male and 6.2 for female per 100,000 standard population. The median age at diagnosis was 65 for males and 73 for females.[1]

2. There were 1,540 deaths due to liver cancer in 2016, ranking third as leading cause and constituting 10.8% of all cancer deaths. The age-standardised mortality rates (ASMR) of liver cancer were 18.0 for male and 4.9 for female per 100,000 standard population. After adjusting for population ageing, both the ASIR and ASMR in males and females showed a consistently downward trend in the past two decades. 62% of its deaths were registered under hepatocellular carcinoma (HCC) in 2016.[2,3] More information on liver cancer statistics can be found at the Centre for Health Protection (CHP) website: http://www.chp.gov.hk/en/content/9/25/52.html.

Risk factors

3. HCC is a complex disease entity with multiple possible etiologies, and associated with many risk factors and cofactors. The major risk factors for HCC include:

(a) chronic infection with hepatitis B virus (HBV) or hepatitis C virus (HCV)[4,5]
(b) cirrhosis from all causes[6]
(c) consumption of alcoholic drinks [5,7,8]
(d) ingestion of foods contaminated with aflatoxin (a toxin found in some food such as mouldy peanuts and grains).[5,7]

Other risk factors include diabetes, obesity, smoking, and certain hereditary conditions such as haemochromatosis, glycogen storage disease and Wilson's disease.[4,7,8,9]

Primary prevention

4. Some preventive measures can help reduce the risk of HCC which is the major type of liver cancer:

(a) Vaccinate against HBV[10]
(b) Do not drink
(c) Do not smoke
(d) Avoid unprotected sexual intercourse or sharing needles
(e) Avoid food source of aflatoxins such as mouldy peanuts and grains
(f) Maintain healthy diet and body weight

Early detection

5. Early stage liver cancer can be asymptomatic. Common signs and symptoms of liver cancer include unexplainable weight loss, jaundice, dark urine, pale stool, abdominal pain and swelling. Individuals with these signs and symptoms should be investigated for liver cancer.

Screening

6. There is a lack of strong randomized controlled trial evidence for the effectiveness of HCC screening by Alpha-fetoprotein (AFP) test and Ultrasonography (USG).

Screening tests

7. Alpha-fetoprotein (AFP) remains widely used for screening HCC although it has never been adequately studied as a single screening tool.[8,11] Apart from HCC, increased levels of AFP are seen in some germ cell tumours and inflammation of the liver (such as in chronic hepatitis), regenerating nodules and pregnant women.[10,12] Whereas around 20% of HCC do not secrete AFP, at a cut-off of 20 ng/mL, the sensitivity of AFP is about 39% to 64% and the specificity ranges from 76% to 91%.[13]

8. Ultrasonography (USG) has been used for clinical surveillance to patients with

chronic HBV for HCC. The pooled sensitivity for HCC is estimated at 94%, with a lower sensitivity of 63% for early disease with smaller tumours. Specificity is estimated at between 92% and 98%.[14] USG is highly-observer dependent and is of limited value in patients with obesity and ascites. Interpretation can be difficult in patients with cirrhosis and regenerative nodules. USG can be used in conjunction with AFP.

9. Computed tomography (CT) and magnetic resonance imaging (MRI) have higher sensitivities and specificities, but the radiation exposure (for CT), high cost, and availability of machines preclude the use of these imaging techniques for regular surveillance. For patients with high-riding liver or obesity, where the whole liver cannot be reliably examined by USG, CT and MRI would have obvious benefits.[15]

10. Newer techniques such as microbubble contrast enhancement and harmonic imaging techniques may significantly improve detection rates by demonstrating the arterialization of HCC, allowing differentiation from other liver tumours that are fed by the portal vein. These emerging techniques are only available in specialized centres and their role in screening has not been studied in randomised clinical trials.[16]

Effectiveness of liver cancer screening for people at high risk

11. To date, studies on liver cancer screening on high risk groups are few. The two community trials on patients with chronic HBV infection conducted in Qidong[17] and Shanghai[18] did not show consistent effect of HCC screening by AFP and USG on mortality reduction and survival. A systematic review in 2014[19] concluded that, due to methodological flaws in existing studies, there was only very-low-strength evidence from which to draw conclusions about the effectiveness of liver cancer screening in high-risk patients with chronic liver disease. A local retrospective cohort study[20] showed that HCC screening in chronic HBV patients by AFP and /or USG could identify tumours at an early stage, thereby increasing the chance of receiving curative treatment. A meta-analysis performed in 2014[21] also showed that HCC screening in patients with cirrhosis was associated with improved early stage detection (OR 2.08, 95% CI1.80-2.37) and curative treatment rates (OR 2.24, 95% CI 1.99-2.52).

12. After taking into consideration local epidemiology, emerging scientific evidence, local and overseas screening practices, the Cancer Expert Working Group on Cancer Prevention and Screening (CEWG) made the following recommendations on liver

cancer screening at its 27th meeting on 23 November 2017:

For persons at average risk	
1.	Routine screening with alpha-fetoprotein (AFP) or ultrasonography (USG) for asymptomatic persons at average risk is not recommended.
For persons at high risk	
2.	People with chronic hepatitis B virus (HBV) or hepatitis C virus (HCV) infection, or liver cirrhosis regardless of the cause are at increased risk of hepatocellular carcinoma (HCC). Depending on certain criteria such as age, family history, presence of cirrhosis and other clinical parameters, some subgroups are at higher risk and should consider receiving periodic cancer surveillance (e.g. every 6-12 months) with AFP and USG. People with chronic HBV or HCV infection, or liver cirrhosis should thus seek advice from doctors to determine their need for and approach of cancer surveillance.

Cancer Expert Working Group on Cancer Prevention and Screening
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