衞生防護中心
Centre for Health Protection

Cancer Expert Working Group on Cancer Prevention and Screening

2016 Recommendations on Prevention and Screening for Liver Cancer For Health Professionals

Local epidemiology

1. In 2014, liver cancer was the fourth commonest cancer in men and the seventh commonest cancer in women. A total of 1,847 liver cancer cases were recorded, accounting for 6.2% of all newly diagnosed cancer cases. The age-standardised incidence rate (ASIR) was 23.8 for male and 6.9 for female per 100,000 standard population. The median age at diagnosis was 64 for males and 72 for females.[1]

2. There were 1571 deaths due to liver cancer in 2015, ranking third as leading cause and constituting 11% of all cancer deaths. The age-standardised mortality rates (ASMR) of liver cancer were 18.4 for male and 5.4 for female per 100,000 standard population. After adjusting for population ageing, both the ASIR and ASMR for men and women showed a downward trend in the past three decades. 62% of its deaths were registered under hepatocellular carcinoma (HCC) in 2014.[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, long term use of oral contraceptives and certain hereditary conditions such as haemochromatosis, glycogen storage disease and Wilson's disease. [4,7,8,9]

Primary prevention

(a) 4. Some preventive measures can help reduce the risk of HCC which is the major type of liver cancer: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 to screen 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. A Cochrane systemic review in 2012 concluded that there was insufficient evidence to recommend for or against screening for HCC with USG or AFP, or both, among patients with chronic HBV infection. More and better designed randomised trials are required to compare screening against no screening.[11]

12. A meta-analysis in 2014 examined the potential impact of HCC surveillance in patients with cirrhosis.[17] The meta-analysis included 47 studies with a total of 15,158 patients, of whom 6,284 (41.4%) had HCC detected by surveillance. Result showed that HCC screening was associated with improved early stage detection and curative treatment rates, and prolonged survival. Limitations of the analysis of current data included many studies having insufficient duration of follow-up to assess survival, and the majority not adjusting for liver function or lead-time bias.

13. 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 26th meeting in June 2016:

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 at higher risk of hepatocellular carcinoma (HCC), namely carriers of hepatitis B virus (HBV) or hepatitis C virus (HCV), and those with cirrhosis regardless of cause, may consider receiving periodic screening (e.g. every 6-12 months) with AFP and USG in consultation with doctors with relevant expertise.

Cancer Expert Working Group on Cancer Prevention and Screening
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