

Hepatocellular Carcinoma (HCC) Surveillance – Comprehensive Management in Liver Cirrhosis Patients

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Hepatocellular carcinoma (HCC) is the fifth most common cancer and the second leading cause of cancer mortality worldwide.^{1,2} In general prognosis of HCC patient is poor, largely depending on the tumor stage, the severity of underlying liver disease, and treatment modalities. Patients with liver cirrhosis of any aetiology are known to be at increased risk for developing hepatocellular carcinoma (HCC).^{1,3} Chronic infection with hepatitis B and C virus are one of the high risk condition to develop HCC.^{4,6} Diagnosis of this condition is often delayed because no obvious sign or symptom and get noticed till the tumour has become fairly large. Hence, in a majority of symptomatic patients diagnosed with HCC, no effective treatment is possible and survival is short.⁷

World Health Organization (WHO) fact sheet in 2017 stated that 30-50% of cancer, including HCC can be prevented.² In this sense, surveillance of HCC is important part of the management of chronic liver disease patients.^{8,9} There are few method of HCC surveillance and the most widely use is to perform ultrasonography (US) and AFP every 6 months.⁸ Indonesian Association of Study of the Liver (In-ASL) use the same strategy in HCC surveillance.⁹ Asia Pacific Association for Study of the Liver (APASL) suggested the use of other PIVKA-II along with AFP but in Indonesia this test is not yet available. It was estimated that surveillance using AFP and US at 6-month intervals would nearly halve the number of HCC-related deaths.

In the current journal, Putra AP et al describe HCC surveillance in national tertiary referral hospital, Cipto Mangunkusumo.¹⁰ They revealed that from 200 liver cirrhosis patients, 25% of them have been in the HCC surveillance. Ideally all of the cirrhosis patients should be in active surveillance and in their study, only 16.5% in active surveillance. Active surveillance is crucial to make an early diagnosis of HCC because liver cirrhosis condition is high risk for HCC.

Factors that associated with HCC surveillance in their study were HCC education and liver cirrhosis

condition. Patients with worsen liver cirrhosis condition tend to comply better to HCC surveillance compare to patients who has a good liver function. Higher proportion of HCC surveillance was found in patients who received sufficient education about HCC. This data support the previous report by Singa et al that a significant number of patients who undergo HCC surveillance were found in group with adequate education from gastroenterohepatologist.¹¹ Qualitative review by Jin et al from 102 studies revealed that lack of routine surveillance was caused by insufficient education about their disease, prevention plan, and therapy.¹² Patients did not know the risk and benefit from routine HCC surveillance or they thought that their disease can be cured in one time visit to the doctor without further evaluation. Hence, education for the patient is a very important part to improve overall HCC surveillance compliance and must be integrated in the whole HCC management.

Patient education itself is the process of enabling individuals to make informed decisions about their personal health-related behaviour.¹³ A successful behavioural change will improve patient compliance to the treatment. Several theories underlying health-related behavior have been proposed to help us make educational intervention: (1) Self-efficacy, learned helplessness and attribution theory: Self-efficacy is one's own belief in one's ability to cope with certain stresses. It suggests that whether one is able to achieve something is strongly dependent on whether one believes one can do it (Bandura 1977).¹⁴ For example, a patient believes that he/she can give up smoking, then they are more likely to succeed giving up smoking. Learned helplessness is essentially having very low self-efficacy, where one believes that one's own actions will not have any effect on the outcome of an event (Seligman & Maier, 1967; Seligman, 1975).¹⁵ For example patient with heart attack history wont give up smoking because he thought that he will die eventually. Attribution theory recognizes that self-efficacy and learned helplessness are not fixed aspects of personality

(Lewis & Daltroy, 1990);¹⁶ (2) Fear arousal and coping theory: Leventhal (1971) hypothesized that fear is a prime motivator of behaviour.¹⁷ Exposure of fear will change their behaviour to take action that can reduce fear. For example patient with heart attack history should stop smoking or he/she will be at risk of death; (3) Social learning theory: This theory suggest that spcial interactions influence one behavioiur in some way. Rotter (1954) hypothesized that our behaviour is influenced by observing the actions of others. Positive or negative reinforcement of behaviour occurs depending on the outcome of the observed actions.¹⁸

Based on the theories shown before, there are 2 models of health behavior: (1) PRECEDE model (Green et al., 1975; Green, 1979; 1999).¹⁹ This model asses the patient's readiness for behavioural change in 3 phases. 1) predisposing factors, patients believe that their disease will be worsen without enough compliance; 2) enabling factors, patient's must have enough skill and resources; 3) reinforcing factors, patients must believe that this intervention is realistic and can improve their health. They need to fulfill each phase requirement before moving to the next phase; (2) Health belief model: Health belief model depends on individual perception, modifying factor and likelihood of action. Educational models based on behavioral theory can help us to understand patients' actions and to plan effective educational interventions.

An understanding regarding these educational theories will assist healthcare provider in daily basis. Doctor can not be the only person responsible for patient education for HCC and for that reason health personnel such as nurse, laboratory technician, nutritionist must help to educate the patient effectively. Moreover, there should be a clinical manager that evaluate whether the patient comply enough to the treatment plan or lost on follow-up. The whole program will be a system that improve patient compliance to the process of HCC surveillance.

Many studies suggest that patients with cirrhosis lack the knowledge to effectively manage their disease. The introduction of a leaflet resulted in a statistically significant improvement in understanding.²⁰ It seems that a patient information leaflet might offer a cost-effective and simple method to improve knowledge despite its small size and limited follow-up period in the study. Longitudinal studies are required to confirm whether this intervention can make improvement in overall disease outcome.

The use of modern technology such as multimedia can also improve the understanding of liver cirrhosis

and its complication. Multimedia education is a recent effective method to improve patients understanding of liver disease.²¹ When education was delivered by screencast, a large increase in knowledge questionnaire scores was observed at one month interval follow up. This suggests that this form of education enabled sustained retention of the knowledge. This method can also be easily adopted in many centres and used in wide range of other diseases.

Holistic management in cirrhosis and HCC will still become challenging issues for the next couple years. Patient education regarding HCC surveillance should be included in the management of liver cirrhosis patients as a whole. Education about liver cirrhosis patient should include understanding about how their liver can be damage by long standing process in chronic liver disease and unnoticed because no obvious symptoms or signs. Understanding theories underlying health-related behavior and health education model can help us to make effective educational intervention. Given the rising prevalence of cirrhosis and HCC, the necessity for a more holistic approach to the management of liver disease will become inevitable.

HCC surveillance must be done for all liver cirrhosis patients to find early liver cancer. Also to avoid complications of decline liver function which can put the patient into a difficult situation if liver cancer should be treated. The most reliable factor for HCC surveillance is to educate the patients on the importance of the program and how the program can help them to achieve longer survival.

REFERENCES

1. Tsukuma H, Hiyama T, Tanaka S, Nakao M, Yabuuchi T, Kitamura T, et al. Risk factors for hepatocellular carcinoma among patients with chronic liver disease. *N Engl J Med* 1993;328:1797-801.
2. Fact Sheet WHO 2017.
3. Velazquez RF, Rodriguez M, Navascues CA, Linares A, Pérez R, Sotorriós NG, et al. Prospective analysis of risk factors for hepatocellular carcinoma in patients with liver cirrhosis. *Hepatology* 2003;37:520-7.
4. Beasley RP, Hwang LY, Lin CC, Chien CS. Hepatocellular carcinoma and hepatitis B virus: a prospective study of 22,700 men in Taiwan. *Lancet* 1981;2:1129-33.
5. Kew MC, Houghton M, Choo QL, Kuo G. Hepatitis C virus antibodies in South African blacks with hepatocellular carcinoma. *Lancet* 1990;335:873-4.
6. Colombo M, Kuo G, Choo Q, Donato MF, Del Ninno E, Tommasini MA, et al. Prevalence of antibodies to hepatitis C virus in Italian patients with hepatocellular carcinoma. *Lancet* 1989;2:1006-8.
7. Stuart KE, Anand AJ, Jenkins RL. Hepatocellular carcinoma in the United States. Prognostic features, treatment outcome, and survival. *Cancer* 1996;77:2217-22.

8. Omata M, Cheng A, Kokudo N, Kudo M, Lee JM, Jia J, et al. Asia-Pacific clinical practice guidelines on the management of hepatocellular carcinoma: a 2017 update. *Hepatol Int* 2017;11:317-370.
9. Hasan I, Loho IM, et al. *Konsensus Nasional Penatalaksanaan Karsinoma Sel Hati*. Jakarta: PPHI. 2017
10. Putra AP, Sulaiman AS, Kurniawan J, Harimurti K. Factors Associated with Surveillance for Early Detection of Hepatocellular Carcinoma in Liver Cirrhosis Patients. *J Gastroenterol Hepatol Dig Endosc* 2017;18:153-8.
11. Singal AG, Conjeevaram HS, Volk ML, Fu S, Fontana RJ, Askari F, et al. Effectiveness of hepatocellular carcinoma surveillance in patients with cirrhosis. *Cancer Epidemiol Biomarkers Prev* 2012;21:793-9.
12. Jin J, Sklar GE, Oh VM, Li SC. Factors affecting therapeutic compliance: a review from the patient's perspective. *Therapeutics and Clinical Risk Management* 2008;4:269-86.
13. Bellamy R. An introduction to patient education: theory and practice. *Medical Teacher* 2004;26:359-65.
14. Bandura A. Self-efficacy: toward a unifying theory of behavior change. *Psychol Rev* 1977;84:191-215.
15. Seligman M, Maier S. Failure to escape traumatic shock. *J Exp Psychol* 1967;74:1-9.
16. Lewis FM, Daltroy LH. How causal explanations influence health behavior, in: K. Glanz, F.M. Lewis & B.K. Rimer (Eds). *Health Behavior and Health Education: Theory, Research and Practice*. San Francisco, Jossey Bass 1990;92-114.
17. Leventhal H. Fear appeals and persuasion: the differentiation of a motivational construct. *American Journal of Public Health* 1971;61:1208-1224.
18. Rotter JB. *Social Learning and Clinical Psychology*. New Jersey, Prentice-Hall. 1954.
19. Green LW, Levine DM, Deeds SG. Clinical trials of health education for hypertensive patients: design and baseline data. *Preventive Medicine* 1975;4:417-425.
20. Beg S, Curtis S, Shariff M. Patient education and its effect on self-management in cirrhosis: a pilot study. *Eur J Gastroenterol Hepatol* 2016;28:582-587.
21. Goldsworthy MA, Fateen W, Thygesen H, Aldersley MA, Rowe IA, Jones RL. Patient understanding of liver cirrhosis and improvement using multimedia education. *Frontline Gastroenterol* 2017;8:214-219.