

Relevance of Child Pugh Scoring System as Inclusion Criteria in Hepatocellular Carcinoma Management

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Received: 20 May 2021

Accepted: 11 Jun 2021

Published: 18 Jun 2021

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Citation:

Dutta D. Relevance of Child Pugh Scoring System as Inclusion Criteria in Hepatocellular Carcinoma Management. Japanese J Gastro Hepato. 2021; V6(17): 1-3

1. Abstract

Child Pugh scoring system is one of the widely used scoring system to evaluate the liver function status and is used as a criterion for eligibility for an aggressive treatment, like surgery, radiosurgery or transplant. It was Dr. Charles Gardner Child, a surgeon along with Dr. Turcotte who first proposed this scoring system way back in 1964 and published in a textbook for assessing the “hepatic functional reserve” in patients with cirrhosis mostly to stratify them for portosystemic shunt surgery. This scoring system was hence known as Child – Tucotte Criteria (CTC) [1]. They have considered five known factors that represent liver function—1) Serum bilirubin, 2) serum albumin, 3) ascites, 4) neurological status and 5) nutrition. Based on these factors, they categorized patients into A, B, C groups with descending prognosis. CTC scoring criteria was extremely useful in clinical practice at that point of time and several studies have confirmed the prognostic significance of CTC in both short-term and long-term survival after portosystemic shunt surgery.

In the year 1972, Dr. RN Pugh proposed modification of CTC grading system for assessing the feasibility of transection of the esophagus for bleeding esophageal varices in relation to the severity of liver dysfunction. He included secretory functions of liver as well, such as prolongation of the prothrombin time and omitted assessment of body nutrition as this parameter was non-specific [2]. This system makes use of 1, 2, or 3 points scores for increasing abnormality of each of the five parameters measured. Those patients whose aggregate score turned out to be 5 or 6 were considered to be good

operative candidates (grade A), 7, 8, or 9 as moderate (grade B), and patients with 10-15 as poor operative candidates (grade C). Since then, this modified CTC scoring system is popularized as the “Child – Pugh score” (CP). CP scoring system is the most commonly used system for assessing the functioning of liver and to decide on feasibility of liver surgery. It is also taken into consideration in many of the hepatocellular carcinoma (HCC) staging systems like Barcelona Clinic Liver Cancer (BCLC) classification, Cancer of The Liver Italian Program (CLIP) score, Advanced Liver Cancer Prognostic System (ALPCS), China Integrated Score (CIS), Taipei Integrated Score System [3]. The main advantage of CP scoring system is the simplicity and easy accessibility of the scoring system. CP scoring can be done by any physician even in a limited resource setting. Paradoxically, this simplicity of CP scoring system in present era is hindering its wide spectrum usage in newer indications. Let us explain the different factors considered in the Child Pugh scoring system.

2. Total Serum Bilirubin

Once RBC reaches senescence, hemoglobin in it is converted to bilirubin in the spleen which is followed by the process of conjugation to glucuronic acid in liver, making it water soluble and transported into the intestine via the biliary tree for further metabolism into urobilinogen. Since conjugation of bilirubin is an important step in metabolism, serum bilirubin level is taken as a parameter for assessing the liver function. But it has to be kept in mind that there are many other causes of increased bilirubin (increased hemolysis, biliary obstruction) and have to be evaluated adequately before attributing rise in bilirubin to the liver function [4-5].

3. Serum Albumin Levels

This is the most 'non-specific' parameter taken into consideration for liver function assessment. It rather depicts the general condition of the patient and nutritional status. Significant variation can be seen in results due to variation in labs and it is attributed to variation in methods of identifying the albumin and separating it from other serum proteins. Albumin infusion is a common practice for managing patients with cirrhosis and ascites. So, if a patient has been found to be child B8, and is given a 25% albumin infusion for 3-5 days and re-assessed, there is a probability of an improvement in the albumin level and thus will have better Child Pugh Score and Grade. Serum albumin is a 'modifiable' factor. Patient not fit for a radical procedure to liver, either surgery or SBRT due to poor CP score may be taken as fit for the procedure with albumin infusion [6]. This raises some serious questions on credibility of the scoring system.

4. Ascites

Ascitis is another 'modifiable' parameter. A bedside paracentesis is the most common procedure in any primary health care center for a patient with ascites. Further, development of ascites depends on other factors like albumin, sodium, renal function. There is a wide inter-observer variation in quantification of the ascites also. Same imaging is not followed in all the institutes for quantification. Use of diuretics to manage ascites may further lead to hypoalbuminemia and electrolyte abnormalities.

5. Hepatic Encephalopathy

Altered level of consciousness due to liver failure is termed as hepatic encephalopathy. It is graded from 0-4 by West Haven Criteria. Grade 0 which includes no obvious changes other than potentially mild decrease in intellectual ability, and grade 4 is coma unresponsive to verbal and noxious stimulus. However, duration of altered consciousness is not considered in this staging. When there is a single episode of altered consciousness, whether it should be considered as a manifestation of liver failure or should it be attributed to any underlying electrolyte abnormality becomes an uncertain.

6. Prothrombin Time / INR

Prothrombin Time (PT) evaluates the ability of the blood to clot. The INR is a calculation that adjusts for changes in the PT reagents and allows for results from different laboratories to be compared. Liver is the main source of coagulation factor I (fibrinogen), II (prothrombin), V, VII, IX, X XI and also protein C, protein S and anti-thrombin. These coagulation factors have very short half-life (eg: factor V have only 5 hours' half-life). Prothrombin time evaluates the extrinsic pathway of coagulation. Any change in liver function and production of coagulation factors immediately affects the prothrombin time. Hence, prothrombin time represents the 'real time' or 'immediate' liver function (hepatocytes) status. Serum albumin (secretory function) and bilirubin (excretory function) value change take some time and represent 'long-term' insult or impairment of liver function. PT /INR alone leaving all other factors as a criterion

for liver functioning might not be an ideal test.

Child Pugh scoring system is 'easy to do' scoring system for liver function status which is used for case selection for various treatment procedures (shunt surgery, radiosurgery) [7-8]. CP scoring system is also used for evaluation of the effectiveness and toxicity of any treatment procedure. This system is used to assess the improvement or deterioration of liver function status after treatment. Main use of CP score is for case selection for surgery, TACE or radiosurgery. However, main issue with this scoring system is that the scores are 'modifiable'. Albumin level can be improved with albumin infusion, ascites can be improved by peritoneal drainage and INR may be modified by Vitamin-K injection. A patient with Child-Pugh B8 score can be improved to Child A with these modifications. Main concern is that this 'improved' score may not represent the 'real' liver function status.

Hence, baseline Child Pugh score which is the main case selection factor for various procedures may not truly represent the clinical situation. On the other hand, patients with poor CP score not considered for more aggressive treatment may also have been erroneously excluded when the Child Pugh score could have been improved with simple measures.

Child Pugh score has not included few pertinent factors, such as volume of disease, degree of cirrhosis, infective status, duration of disease and most importantly performance status [8-9]. Child Pugh score is an ideal grading system in the 1970s when it was proposed requiring only bedside assessments and basic blood tests. Even in the present era Child Pugh scoring system is a useful and 'easy to do' scoring system for bedside practice. In SBRT, case selection is based on Child Pugh scoring system. Patients suffering from HCC with CP score more than B7 are not considered for SBRT. Modifying the 'modifiable factors', a proportion of patients may be eligible for the treatment (3,8). But, there is a need for prospective studies to evaluate the impact of modifying these factors before recommendation for aggressive treatment such as SBRT or liver resection. In the present era, with safer treatment delivery techniques and advancements in modification of liver function status, there is a need for a scoring system which includes both the variable and non-variable factors, a scoring system representing both the liver function as well the extent of the disease status.

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