

Validity of different nutritional assessment modalities as indicators of nutritional status in cirrhotic patients

Abstract

Background & Aim: Nutritional assessment in cirrhotic patients is difficult because many of the traditionally measured parameters, such as weight, body mass index (BMI) and biochemical values vary with the severity of liver disease independently of nutritional status. The aim of this study was determination of the best available methods for assessment of malnutrition in cirrhotic patients and to evaluate the impact of malnutrition on occurrence of complications in those patients.

Methods: One hundred cirrhotic patients were enrolled in this cross sectional study. Nutritional status was assessed by Subjective Global Assessment (SGA), Mini-nutritional assessment (MNA), Controlling nutritional status (CONUT), anthropometry, and dominant hand grip strength (HGS). Statistical analysis was performed using Pearson correlation, Kendall's tau-b and Spearman's rho correlation and Receiver Operating Characteristic(ROC curve) with diagnostic test accuracy measurements(sensitivity, specificity, positive and negative predictive values) using SPSS version 16.0. For all used tests, $p < 0.05$ was considered significant.

Results: One hundred patients (57% male) aged 56 ± 10 years, (Child score C 27%, B 51%, A 22%) were included in our study. Using SGA as a reference method of nutritional assessment, there was high prevalence of malnutrition (88%) in our patients. In an attempt to detect diagnostic accuracy of different nutritional assessment modalities using SGA as reference standard, CONUT was an excellent test for detection of malnourished patients ($AUC = 0.91$, 95% CI = 0.79-1, P value = 0.0001). MNA was also excellent for detection of malnourished patients ($AUC = 0.96$, 95% CI = 87-1, P value < 0.0001). Handgrip strength was a very good test for detection of malnourished patients ($AUC = 0.83$, 95% CI = 0.69-0.97, P value < 0.0001). There was a significant increase in degree of decompensation and occurrence of complications with increasing degree of malnutrition. A cut off value of (18.6, 4.5 and 8.5) for HGS, CONUT and MNA respectively were found to be significant in detecting malnourished patients.

Conclusions: HGS, CONUT, MNA, and dried BMI are compatible to SGA in diagnosis of malnutrition in cirrhosis. Key message: Handgrip strength (HGS) is the best method to assess the nutritional status of the cirrhotic patients as it is non-subjective, not lab dependant, cheap and easy method with high accuracy

Keywords: Malnutrition, cirrhosis, subjective global assessment, mini-nutritional assessment, controlling nutritional status, hand grip strength

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Abbreviations: SGA, Subjective global assessment; MNA, Mini-nutritional assessment; CONUT, Controlling nutritional status; HGS, Hand grip strength. body mass index (BMI), spontaneous bacterial peritonitis (SBP), hepato-renal syndrome (HRS, European Society of Enteral and Parenteral Nutrition (ESPEN), complete blood count (CBC), International Normalized Ratio (INR), negative predictive value (NPV) Statistical Package for Social Studies (SPSS), reservoir operator characteristic (ROC)

Introduction

According to the methods of nutritional assessment and degree of severity of liver disease, 65-100% of cirrhotic patients suffer from malnutrition.¹ This is may be attributed to cholestasis, presence of

porto-systemic shunt, pancreatic insufficiency and bile deficiency with inadequate absorption of long-chain fatty acids and metabolic alterations (high protein catabolism, reduced glucose homeostasis due to alterations of gluconeogenesis, low glycogen stores, pro-inflammatory cytokines such as TNF alpha, interleukins).²

Nutritional status is considered to be a predictor of morbidity and mortality in patients with advanced hepatic disease. Malnutrition in those patients is associated with increased incidence of hepatic encephalopathy, variceal bleeding, refractory ascites, spontaneous bacterial peritonitis (SBP), hepato-renal syndrome (HRS), impaired immunity and increased incidence of infection.^{3,4}

The ideal tool for nutritional assessment in patients with cirrhosis is challenging due to variation of the traditional tools of assessment

that vary with the severity of liver disease independently of nutritional status and the gold standard of nutritional assessment in cirrhotic patients has not been established yet.⁵

Assessment of nutritional status consists of combination of history, physical examination, laboratory assessment, anthropometrics, and body composition.⁶

Many methods of assessment of nutritional status have been developed to identify malnourished patients or the risk for malnutrition. Most of the methods of assessment like, subjective global assessment (SGA), Mini Nutritional Assessment (MNA), Nutritional Risk screening (NRS) and Malnutrition Universal Screening Tool included blends of information as medical history, dietary intake, amount of weight loss, biochemical variables, and anthropometric measurements.⁷

The BMI is well known anthropometric measure that is basic in assessment of nutritional state of healthy and diseased persons. It is a cheap and convenient objective tool dependent on height and weight. But, presence of cirrhosis and oedema make it non accurate tool as it overestimate the actual body mass. Campillo⁸ used the "Dry BMI" as a corrected BMI values interpretation according to amount of ascites.⁸ They considered these values (Dry BMI) as a valid method of nutritional assessment in cirrhotic patients with sensitivity of 90% and specificity of 86% in their studies Campillo⁸ Campillo⁹ Using the interpretation values of dry BMI in our study improved the sensitivity of BMI from 17%-89%, but still with 66% specificity.

Subjective global assessment (SGA) is the most popular method used in evaluation of nutritional state in hospitalized patients.^{10,11} The use of the SGA was recommended by the 2006 guidelines of the European Society of enteral and parenteral Nutrition (ESPEN) together with anthropometric analysis and handgrip strength test (HGS) for identifying patients with cirrhosis who are at risk of malnutrition.¹² Lacking gold standard nutritional assessment tool in cirrhotic patients renders SGA widely accepted tool for evaluation in such patients despite its limitations in predicting clinical outcomes.^{13,14} So, our study aimed to identify the most efficient tool to assess nutritional state in cirrhotic patients as well as to evaluate the impact of malnutrition on occurrence of complications in those patients.

Methods

Our study was designed as a descriptive cross sectional study of 100 patients with cirrhosis, admitted to [removed for blind peer review] starting between June 2016 and February 2017. The diagnosis of cirrhosis was based on the medical history, physical examination, biochemical findings and imaging methods (ultrasound and / or computed tomography). The patients aged 18 years or more with documented liver cirrhosis in a stable hemodynamic condition were invited to enter in our study. Those who accept to share were included. Patients with hepatic encephalopathy grade III-IV, active gastrointestinal bleeding, ongoing alcoholism, sepsis, liver failure, suspected hepatocellular carcinoma (using alpha fetoprotein AFP and / or abdominal ultrasound), chronic diarrhoea, on haemodialysis or with renal failure, patients with chronic debilitating diseases (e.g. DM, T.B) were excluded from the study.

The protocol was approved by the ethical committee of [removed for blind peer review]. A written informed consent was obtained from all participants in the study.

The laboratory data collected included complete blood count (CBC), bilirubin, albumin, prothrombin time (PT), International Normalized Ratio (INR), serum urea, serum creatinine and serum cholesterol; all markers were measured by standard laboratory methods. The ultrasound evaluation included the signs of cirrhosis and portal hypertension. For all patients CTP score was calculated based on clinical examination, laboratory findings and U/S data.

Nutritional status of the patients was determined for each patient by means of:

- a. Anthropometric measurement: including weight and height BMI was calculated by dividing weight in kg/(height in meters)². To correct for overweight estimation due to ascites, dry BMI was interpreted to have under nutrition as follow; No ascites, BMI \leq 22 kg/m², Mild ascites, BMI \leq 23 kg/m², Tension ascites, BMI \leq 25 kg/m².
- b. Body fat and body water contents were measured using Body composition analyzer (Model: X-contact 350 F, Measurement Range:100-950 Q).
- c. Subjective Global Assessment (SGA): The features of SGA are history, physical evaluation and SGA rating. The history includes weight change, dietary intake, gastrointestinal symptoms, and functional capacity of work. Physical examination includes detection of ankle oedema and ascites. Based on this evaluation, patients were classified into three groups: well nourished, moderately malnourished and severely malnourished.¹⁵
- d. Mini-nutritional assessment (MNA): The features of MNA are change in food intake, weight loss and psychological stress in the last 3 months, mobility of the patient, neuropsychological problems and BMI (Calf circumference if BMI is not available) based on this evaluation, patients were defined as normal nutritional status, at risk of malnutrition and malnourished.¹⁶
- e. Handgrip strength(HGS): HGS was measured with the subject in the seated position, shoulders adducted and neutrally rotated, elbow flexed at 90° with the forearm and wrist in a neutral position. Every patient squeezed the dynamometer (Haoyue brand) with as much force as possible, 3 trials were performed on dominant hand and the average of the measurements used for comparison with age- and sex-adjusted standards.¹⁷
- f. Controlling nutritional status (CONUT): it is consisted of three parameters, serum albumin, cholesterol, and total lymphocytic count.¹⁸

Based on this evaluation, patients were defined as normal, light, moderate and severe degree of under nutrition.

Statistical analysis: The collected data were organized, tabulated and statistically analyzed using Statistical Package for Social Studies (SPSS) version 16. Chicago. SPSS Inc. Categorical data were presented as number and percent while numerical data were presented by mean \pm standard deviation for normally distributed data. For skewed data, median and inter-quartile range was used. Association between different parameters and degree of malnutrition was tested using Kendall's tau-b and Spearman's rho correlation to obtain correlation coefficient(r). For evaluation of diagnostic accuracy of different modalities used to test malnutrition in our patients, we perform reservoir operator characteristic (ROC) curve using SGA as

the best available reference test. The area under the curve(AUC) with 95%CI were used to get the optimal cutoff values, and sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and test accuracy were calculated accordingly. For all used tests P value <0.05 was considered significant. As SPSS doesn't allow for comparison of ROC curves, we used MedCalc for Windows, version 18.6 (MedCalc Software, Ostend, Belgium) for all pair wise comparison between ROC curves with standard error (SE) calculated according to DeLong et al., 1988. to calculate the Z score. P value <0.05 was considered significant.

Results

A series of 100 hospitalized cirrhotic patients, 57 (57%) male and 43 (43%) female, median age 56 (range 18-76 years) were included. The etiology of liver disease was HCV in 97 (97%), one patient had primary biliary cirrhosis and 2 patients had autoimmune hepatitis. Twenty two patients (22%) were classified as Child A, 51 patients (51%) Child B and the rest 27 patients (27%) were Child C.

By clinical examination of the patients it was found that about 57% of them had ascites in the form of mild, moderate, marked and tense ascites, 64% of them had lower limb oedema, 9% had reducible umbilical hernia, 34% were jaundiced, 54% with pallor, 19% had hepatic encephalopathy grade I & II—in whom nutritional assessment was done after recovery from encephalopathy- and 22% had ecchymosis. The biochemical tests and anthropometric measurements of the studied patients were shown in (Table 1).

The studied patients admitted to the hospital with infection were 52% (16 patients) with chest infection, 15 with spontaneous bacterial peritonitis, 9 with urinary tract infection, 3 with typhoid and 9 with cellulitis affecting the lower limbs.

Number of malnourished patients according to SGA was 88%, MNA was 88%, CONUT was 95%, handgrip strength was 81%, BMI was 17% and dry BMI was 79% (Figure 1).

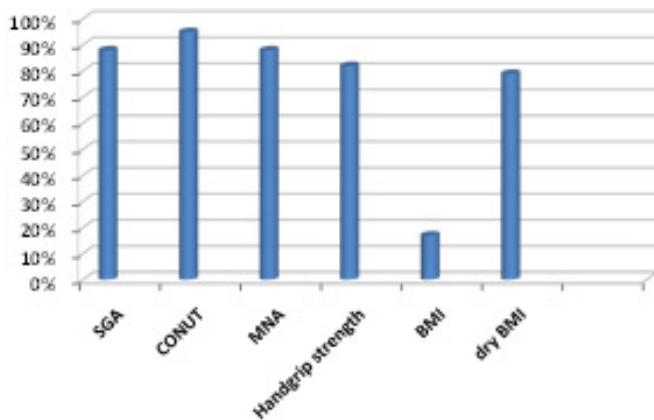


Figure 1: Number of malnourished patients as measured by different modalities of nutritional assessment.

In an attempt to detect diagnostic accuracy of different nutritional assessment modalities using SGA as reference standard, dry BMI was a very good test for detection of malnourished patients (AUC = 0.81, 95% CI = 0.66-0.95, P value < 0.0001). CONUT was an excellent test for detection of malnourished patients (AUC = 0.91, 95% CI =

0.79-1, P value = 0.0001). MNA was an excellent test for detection of malnourished patients (AUC = 0.96, 95% CI = 0.87-1, P value < 0.0001). Handgrip strength was a very good test for detection of malnourished patients (AUC = 0.83, 95% CI = 0.69-0.97, P value < 0.0001) (Table 2) (Figure 2).

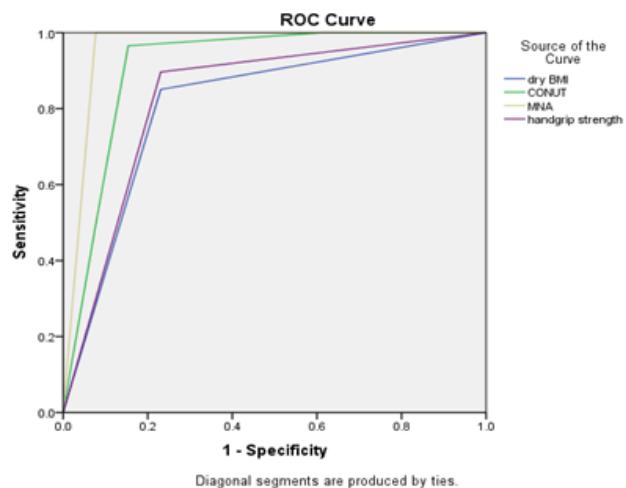


Figure 2: Diagnostic accuracy of different nutritional assessment modalities.

We compared the areas under ROC curves using SGA as classification variable to calculate Z score. The result of pair wise comparison of all ROC curves shows that area under ROC curve was significantly higher for MNA in comparison to HGS (P=0.0189) and dry BMI (P=0.0107). All other tests had comparable area under the curve (P>0.05), (Table 3) (Figure 2).

There was a significant positive correlation between degree of malnutrition assessed with Handgrip strength, Dry BMI and presence of infection at time of admission ($r= 0.214, 0.212$ and $P=0.033, 0.035$ respectively) while assessment with SGA, CONUT and MNA lacks this correlation ($P= 0.225, 0.091, 0.225, 0.237$ respectively). There was a significant positive correlation between degree of malnutrition as assessed by scores of CONUT and Handgrip strength and presence of ascites at time of admission ($r= 0.190, 0.227$ and $P= 0.047, 0.024$ respectively), while assessment with SGA, MNA and Dry BMI lacks such correlation ($P= 0.796, 0.08$ and 0.053 respectively) as shown in (Table 4).

Considering severity of liver disease, The degree of malnutrition assessed with SGA, CONUT, MNA, Handgrip strength, Dry BMI had a significant positive correlation to Child score ($r= 0.479, 0.292, 0.479, 0.478$ and 0.484 respectively), significant negative correlation to serum albumin ($r= -0.491, -0.756, -0.491, -0.558$, and -0.443 respectively) with $P < 0.0001$ for them all, but significant positive correlation to INR for the first 3 methods ($r= 0.205, 0.205, 0.279$ and $P= 0.04, 0.005$ and 0.04 respectively) and significant positive correlation to total bilirubin for the first 4 methods ($r= 0.376, 0.392, 0.376, 0.288$ and $P= 0.0001, 0.0001, 0.0001$ and 0.004 respectively) as shown in Table 4.

Table 1: Biochemical tests and anthropometric measurements of the studied patients (n=100)

Item	Mean	SD	MIN	MAX	Median	IQR
Hb gm/dl	10.33	1.97	6.1	17.2	10.1	11.1
Platelets /cu mm	134170	82006.17	20000	430000	108000	410000
WBCs /cu mm	6099	2930.88	2500	13900	4950	11400
TB mg/dl	2.68	2.94	0.4	13	1.65	12.6
ALT U/L	39.35	35.29	10	188	27	178
AST U/L	64.3	51.35	15	274	45.5	259
S. albumin mg/dl	2.83	0.56	1.4	4.3	2.8	2.9
INR	1.49	0.39	1.05	3.91	1.42	2.86
S.creatinine mg/dl	0.98	0.3	0.21	2.04	0.995	1.83
Urea mg/dl	36.83	17.31	13.2	92	32.5	78.8
S. cholesterol mg/dl	109.55	39.15	43	256.4	104.05	213.4
ESR1 mm	37.34	22.61	5	85	31	80
ESR2 mm	63.99	31.48	10	130	60	120
CRP mg/L	8.16	11.8	0	48	6	48
RBS mg/dl	113.08	31.44	65	197	103.5	132
Height	164.5	8.04	144	189	164	45
Weight	78.08	14.13	40.7	121.4	76.7	80.7
BMI	28.95	5.47	18.1	46.3	28.25	28.2
Dry BMI	1.77	0.42	18.1	46.3	2	28.2
Body fat	22.13	10.45	1.1	51.5	21.65	50.4
Body water	39.89	7.17	13.7	55.7	39	42

Table 2: Diagnostic accuracy of different nutritional assessment modalities

	Cutoff	Sensitivity	Specificity	PPV	NPV	Accuracy
Dry BMI	18.6 kg/m ²	89%	66%	89%	57%	100%
handgrip strength	18.6	100%	64%	65.80%	100%	100%
MNA	8.5	14.20%	100%	100%	98%	100%
CONUT	4.5	90%	100%	100%	35%	91%

Table 3: Pair wise comparison of ROC curves using SGA as classification variable

Compared tests	Difference	SE	95% CI	Z score	P
BMI ~ CONUT	0.0992	0.0589	-0.0162–0.215	1.684	0.0921
BMI ~ MNA	0.148	0.0516	0.0259–0.243	2.637	0.0107
BMI ~ handgrip	0.0288	0.0213	-0.0129–0.0706	1.353	0.1759
CONUT ~ handgrip	0.0842	0.0597	-0.0142–0.207	1.613	0.0798
CONUT ~ MNA	0.0498	0.0456	-0.0134–0.0912	1.534	0.0975
handgrip ~ MNA	0.128	0.0546	0.0211–0.235	2.347	0.0189

Table 4: Correlation between malnutrition detected by different methods of nutritional assessment and Child score, presence of infection, degree of ascites, serum albumin, INR and total bilirubin

	SGA		MNA		HGS		CONUT		Dry BMI	
	r	P	r	P	R	P	r	P	r	P
Child score	0.47	0.0001	0.47	0.0001	0.47	0.0001	0.29	0.0001	0.484	0.0001
Infection	0.114	0.255	0.114	0.255	0.214	0.033	0.162	0.091	0.212	0.035

Table Continued

	SGA		MNA		HGS		CONUT		Dry BMI	
	r	P	r	P	R	P	r	P	r	P
Ascites	0.173	0.08	0.173	0.173	0.227	0.024	0.190	0.047	0.194	0.053
Serum albumin	-0.49	0.0001	-0.49	0.0001	-0.55	0.0001	-0.75	0.0001	-0.44	0.0001
INR	0.205	0.04	0.205	0.04	0.188	0.061	0.279	0.005	0.121	0.229
Total bilirubin	0.376	0.0001	0.376	0.0001	0.288	0.004	0.392	0.0001	0.192	0.055

Discussion

In this study, we aimed firstly to identify the most efficient tool to assess nutritional state in cirrhotic patients. SGA is the most popular method used in evaluation of nutritional state in hospitalized patients.^{10,11} Considering that there is no gold standard test, we used SGA as a reference test.

Using Subjective global assessment (SGA), 88% of our cirrhotic patients were malnourished. This was higher than prevalence reported by Reyes¹⁹ (77%) and García-Rodríguez²⁰ (50.9%). This higher prevalence may be attributed to the difference in nutritional habits and lacking regular nutritional evaluation of cirrhotic patients in Egypt.

The severity of chronic liver disease, according to the Child–Pugh classification is correlated to their degree of malnutrition.²¹ This was true for our patients as a significant positive correlation was found between the degree of malnutrition according to SGA and the child score.

To overcome the long questioner of SGA, reduced forms were developed. Among them Mini-nutritional assessment (MNA) is the commonest. It is the most-established tool internationally to evaluate nutritional status in older people.⁷ We had used it to assess nutritional status in cirrhotic patients. It was reported that MNA correlated well with nutritional intake and with anthropometric and biological nutritional parameters in tested individuals.²² According to MNA, it was found that the number of malnourished patients was 88%. In our study MNA was able to detect 100% of SGA diagnosed malnourished patients. It was very useful to get the same results obtained with SGA with shorter and easier tool. Our results were in accordance with Yasutake²³ who found MNA equal or better than SGA. The severity of liver disease generally correlates with the severity of malnutrition, and protein-calorie malnutrition correlates with worsening of clinical outcome.²⁴ This was in accordance with our study, results which showed as we find a significant positive correlation between the degrees of malnutrition according to MNA the severity of chronic liver disease, according to the Child–Pugh classification.

However, both SGA and MNA had limitations of subjectivity. This is considered a true limitation of the test especially makes the test useless when the patient has some difficulty in reporting their nutritional history adequately.²⁵ This may necessitate the use of more objective tests.

Controlling nutritional status (CONUT) is considered to be an objective tool to assess the degree of malnutrition in cirrhotic patients. It has sensitivity of 90% and specificity of 100% for detection of malnutrition in our patients. This was in accordance with García-Rodríguez²⁰ who considered CONUT a very good test to assess degree of malnutrition in cirrhotic patients with sensitivity 75% and specificity 78.57%.

Cholongitas²⁶ considered the value of CONUT closely associated with severity of chronic liver disease, and one of the most predictive

factors for prognosis in cirrhotic patients. In our study there was positive correlation between degree of malnutrition as assessed by CONUT score and severity of chronic liver disease according to Child–Pugh classification. This was in accordance with Taniguchi²⁷ who reported similar results.

Controlling nutritional status (CONUT) was an objective test, relatively cheap, had no sophisticated parameters, easily performed and interpreted. All these factors added to its high accuracy render it a very useful tool in assessment of male nutrition in our patients.

However, CONUT may be affected in cirrhotic patients due to the pathology of liver itself which affects the values of albumin and cholesterol (2 of its 3 parameters). This makes lymphocytes the main parameter related to protein depletion and malnutrition indicator.²⁰

Figueiredo²⁸ suggested that screening for body cell mass (BCM) depletion and attenuated muscle function can be measured by Hand grip strength (HGS). In our study, handgrip strength measurement was a very good test for detection of malnourished patients with sensitivity 100% and specificity 64% at cut off value 18.6 kg when compared with SGA. This was in accordance with Daphnee²⁹ who considered HGS a reliable, non-invasive and cost-effective tool to identify malnutrition in cirrhotic patients at cut off value 19.5 kg with sensitivity and specificity 67% and 75% respectively. The difference in cut off value of this study and our results may be due to difference in type of handgrip dynamometer used, as Daphnee used Hydraulic Hand Grip Dynamometer while we used portable handgrip Dynamometer.

Our results were in agreement with another study where handgrip strength had a sensitivity and specificity of 86.7% and 70.2%, respectively, for identifying cirrhotic patients with malnutrition.³⁰ HGS has been found to identify 63% of malnourished cirrhotic patients, which is superior to the SGA in the same patients.³ The test is simple and a significant advantage is that the grip strength value is an independent predictor of cirrhosis decompensation.³¹

In our study, the presence of malnutrition as assessed by HGS was positively correlated to severity of chronic liver disease. Similar results were obtained by Sharma³². It was also associated with increased incidence of infection. This was in accordance with Johnson et al who stated that HGS can predict complications like infection better than the BMI and the SGA.³³ This may be attributed to the augmented effect of cirrhosis and infection which both produce sarcopenia with subsequent weakness of handgrip strength. This explanation is supported by Reid³⁴ who stated that Infection affects muscle metabolism (inflammatory cytokines and endotoxemia results in increased muscle proteolysis) which resulted in muscle weakness. Handgrip strength is objective, cheap, easy to perform, does not necessitate skilled personnel, and lastly it is considered another quantitative method to assess malnutrition.

So, in conclusion, in our study; using SGA as reference standard: MNA, CONUT, and handgrip strength were the best alternative tests to be used in cirrhotic patients. BMI was not accurate, but using the interpretation values of dry BMI increased its accuracy. There was

strong association between the degree of malnutrition and the degree of decompensation.

However, this study has some limitations. The sample size was small, the study was conducted on a selected group of patients with cirrhosis limiting its generalizing ability to all cirrhotic patients especially those with grade III and IV hepatic encephalopathy.

We recommend the use of Handgrip strength (HGS) to evaluate the nutritional status of the cirrhotic patients as it is non-subjective, not lab dependant, cheap and easy method with high accuracy.

Acknowledgment

None.

Conflict of interest

The authors declare that they have no competing interests.

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