Review Article

Liver Functional Volumetry by Tc-99m Mebrofenin Hepatobiliary Scintigraphy before Major Liver Resection: A Game Changer

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Abstract

Future remnant liver function (FRL-F) estimation is important before major liver resection to avoid posthepatectomy liver failure (PHLF). Conventionally, it is estimated by global dynamic liver function tests which assume homogeneous liver function and unable to calculate regional function. Computed tomography is another method to estimate FRL volume but assumes that volume is equivalent to function. Hence, a global and regional non-invasive liver function test is desirable. Studies were identified by MEDLINE, PubMed, and Google Scholar for articles from January 1990 to December 2017 using the following keywords "Mebrofenin, hepatobiliary scintigraphy (HBS), FRL-F, PHLF, portal vein embolization (PVE)." HBS with technetium-99 m galactosyl human serum albumin (Tc-99m GSA) and Tc-99m Mebrofenin is a known test for functional liver assessment. Restricted availability of Tc-99m GSA only in Japan is a main drawback for its global acceptance. However, Tc-99m Mebrofenin is routinely available to the rest of the world. A unique protocol for FRL-F estimation by Tc-99m Mebrofenin is described in detail in this review. Tc-99m Mebrofenin HBS has shown a strong correlation to 15 min indocyanine green clearance. HBS has been reported better in predicting the risk of PHLF with a 2.69%/min/m^2 cutoff of FRL-F. Tc-99m Mebrofenin HBS has been found better in stratification of PVE before major liver surgery as well. We concluded, Tc-99m Mebrofenin HBS was unique in calculating global and regional liver function and takes nonuniformity and underlying pathology in the account. Moreover, a single cutoff might fit in all for PHLF risk assessment and PVE stratification.

Keywords: *Future remnant liver function, gadolinium ethoxybenzyl-diethylenetriaminepentaacetic acid magnetic resonance imaging, hepatobiliary scintigraphy, mebrofenin, portal vein embolization, posthepatectomy liver failure*

Introduction

Liver resection or transplantation is the only curative way for patients with primary liver malignancies. The extent of liver resection mainly relies on estimated future remnant liver function (FRL-F) which may be compromised in pre-existing liver disease and/or prior chemotherapy.[1,2] Insufficient FRL-F will increase the risk of posthepatectomy liver failure (PHLF) which is associated with high mortality.[3-5] Preoperative estimation of FRL-F has become even more important to decide between upfront and staged surgery.[6,7] Various methods have been developed over the years for estimation of FRL-F [Figure 1]. Blood tests and clinical status-based scores are first utilized for prediction of surgical outcome.[8-11] Computed tomography (CT) and magnetic resonance imaging (MRI) volumetry have been the most frequently used preoperative methods for FRL volume (FRL-V) calculation.[12-14] However, these tests assume homogeneous liver function and volume is equivalent to a function which is indeed an exception rather than a rule [Table 1]. Indocyanine green (ICG) clearance and C-13 Methacetin breath test (LiMax) estimate global liver function.[15-17] These functional tests, however, are unable to calculate regional liver function and assume homogeneous liver function [Table 1]. Therefore, there is a need for a test which can calculate global and regional liver function and predict the risk of PHLF in a better way.

Methods

Studies were identified by MEDLINE, PubMed, and Google scholar online search engines for articles from January 1990 to December 2017 using the following keywords "Mebrofenin, hepatobiliary scintigraphy (HBS), FRL-F, PHLF, portal vein embolization (PVE)." Additional

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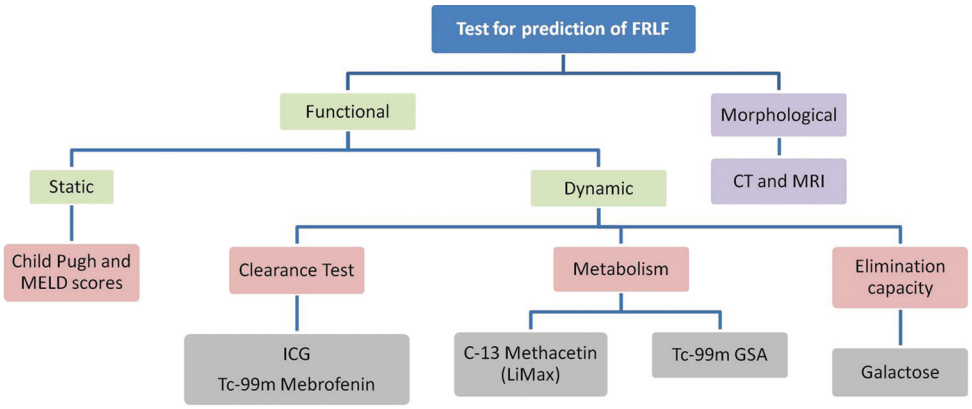

Figure 1: Most frequently used clinical tests for estimation of future remnant liver function and prediction of surgical outcome before major liver resection or liver transplantation (MELD: Model for end-stage liver disease, ICG: Indocyanine green, LiMax: Maximum liver function capacity, GSA: Galactosyl human serum albumin, CT: Computed tomography, MRI: Magnetic resonance imaging)

Table 1: Basic advantages and disadvantages of most commonly used test for future remnant liver function estimation and prediction of risk of post hepatectomy liver failure before major liver resection

Tests	Advantages	Disadvantages
ICG[1] and LiMax[2]	Global liver function	No regional calculations, *Assumption: Homogeneous function*
CT[3] and MRI[4]	Global and Regional volumes	Assumption: 1. Homogeneous function 2. Form=Function

[1]ICG: Indocyanine green, [2]LiMax: Maximum liver function capacity, [3]CT: Computed tomography, [4]MRI: Magnetic resonance imaging

papers were identified by a manual search of the references from the key articles. All acronyms with their definition used in this review are described in Table 2.

Results

HBS is a routine nuclear medicine (NM) procedure which exploits its tracer functional capabilities with modern day Gamma cameras for direct calculation of global and regional liver function. Technetium-99m galactosyl human serum albumin (Tc-99m GSA) and Tc-99m Mebrofenin scintigraphy have been used so far successfully for this purpose. In this review, we are describing the protocol for Tc-99m Mebrofenin for FRL-F estimation in detail and analyzing current literature supporting its role in preoperative risk assessment for PHLF and PVE stratification.

Technetium-99 m galactosyl human serum albumin scintigraphy

GSA binds to asialoglycoprotein receptor present only on mammalian hepatocytes on sinusoidal surface.[18] After binding, it undergoes receptor-mediated endocytosis and lysosomal degradation. Hence, it remains within the hepatocytes and does not get excreted into the bile. Due to different receptor-mediated uptake into the hepatocytes, high level of bilirubin will not interfere with GSA uptake.[19] The commercial kit of GSA is available only in Japan for instant labeling and use. Since liver is the only site of uptake and it does not get excreted, Tc-99m GSA produces high-quality images for FRL-F calculation. However, due to unavailability of GSA to the rest of the world is making this study difficult outside Japan.

Tc-99m Mebrofenin scintigraphy

Mebrofenin is a type of iminodiacetic acid (IDA). IDA radiopharmaceuticals were originally synthesized for cardiac imaging due to structural similarity with lidocaine molecule. In view of good hepatic extraction and clearance, soon the potential of these IDA radiopharmaceuticals for hepatic imaging was realized.[20] Food and drug administration has approved three IDA radiopharmaceuticals for clinical use. These are Tc-99m lidofenin (HIDA), Tc-99m disofenin (DISIDA) and Tc-99m mebrofenin (BrIDA) in their chronological order of approval. Out of these, Tc-99m Mebrofenin has the highest hepatic extraction, fastest blood clearance and lowest renal excretion.[21] Mebrofenin is available as a ready to use the kit for radio-labeling with Tc-99m and the product after reconstruction remains stable for at least 6 h. 5 mCi (185MBq) of Tc-99m Mebrofenin will be injected under the camera which gives 1 mSv whole-body radiation dose, and the large bowel remains as a critical organ.

Pharmacokinetics

After injection, IDA binds to protein mainly albumin which minimizes its renal excretion. Organic anion transporter polypeptide (OATP), located on basolateral membrane of hepatocyte, is involved in IDA transport into the hepatocyte. OATP $1B_1$ and $1B_3$ are able to transport Tc-99m Mebrofenin into the hepatocyte.[21] Thereafter, Tc-99m labeled IDA follows the bilirubin pathway within the hepatocyte without undergoing any metabolism or conjugation. IDA radiopharmaceuticals are excreted into the bile canaliculi by multidrug resistance protein 2 (MDRP2) transporters similar to ICG.[22] Due to same receptor uptake mechanism of IDA and bilirubin, there is substrate competition in hyperbilirubinemia state.

Mebrofenin has the strongest resistance to displacement by high bilirubin and can produce diagnostic image of good quality even with bilirubin level of 20–30 mg/dl.[23] Hypoalbuminemia can hinder mebrofenin uptake because, albumin is the main carrier protein of mebrofenin in the blood.[24] Hypoalbuminemia reduces delivery of mebrofenin to hepatocyte and increases its renal excretion and hence may underestimate the hepatic function. However, hypoalbuminemia may be there due to liver dysfunction. Therefore, reduced mebrofenin uptake in hypoalbuminemia due to liver dysfunction is a matter of research.

Scanning protocol

Tc-99m Mebrofenin scintigraphy for hepatic extraction fraction estimation is simple and can easily be reproduced in any NM center. There is no difference in the scanning protocol for cirrhotic or noncirrhotic patients. Bennink *et al*.[25,26] developed a specific three phase scanning protocol for hepatic extraction fraction estimation [Box 1]. First phase dynamic data set will be used for Tc-99m Mebrofenin uptake rate (MUR) calculation and is presented as total liver function (TL-F). Geometric dataset (Gmean) was generated from anterior and posterior image data set using Gmean formula (Gmean = $\sqrt{\text{anterior} \times \text{posterior}}$). This is done because left lobe of liver is anterior in location in abdomen which leads to overestimation of the left lobe function by anterior projection images alone and underestimation in posterior images alone. Three-time activity curves (TAC) will be generated by drawing region of interest (ROI) over liver, heart (left ventricle), and total field of view [Figure 2]. The same ROIs will be used in the whole data set to have uniformity in calculations. With these 3 TAC, TL-F will be calculated as described by Ekman *et al*.[27,28] and presented as percentage per minute (%/min). Data acquired in between 150–350 s after injection will be used in this calculation considering most homogeneous blood pool activity, most linear hepatic uptake curve and nobiliary excretion. In view of the different metabolic requirement of individuals, TL-F will be normalized with body surface area (BSA) and presented as standardized TL-F (sTL-F) in %/min/m^2. For FRL-F calculation, ROI will be drawn on Gmean summed image of 150–350 s over liver and FRL which will give TL counts (TL-C) and FRL counts (FRL-C), respectively. For the right and left lobe border on Gmean summed image, Cantlie's line (line between middle of gallbladder and inferior vena cava) can be used. Falciform ligament can be used to border segment 3 and 4. FRL-FV can be calculated by dividing FRL-C by TL-C and can be expressed in percentage after multiplying with 100. Thereafter, FRL-FV will be multiplied with normalized TL-F to calculate FRL-F [Box 2].

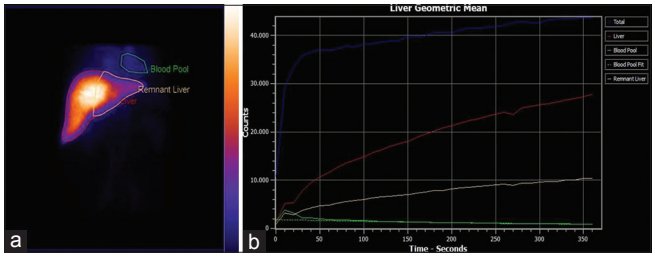

Figure 2: (a) Gmean summed image showing the region of interest over liver, heart, remnant liver, and total field of view. (b) Line graph showing time activity curves of region of interest made in (a) image

Modern day's hybrid gamma cameras are capable of doing fast single-photon emission CT-computed tomography (SPECT-CT).[29] In the second phase of the study, a fast SPECT-CT is acquired because at this time liver activity is at peak and relatively stable. Due to the high count rate with 5 mCi (185MBq) dose during this phase, fast SPECT also has good count statistics. SPECT-CT can be processed similar to CT volumetry data in multimodality workstation by Hermes medical solution [Figure 3]. For automatic SPECT FRL-FV calculation, volume of interest (VOI) will be drawn over the entire liver, and remnant liver using 30% threshold cutoff and taking CT constraints in-account. VOIs can be edited slice by slice by the user for over or under-estimation correction. This will give three-dimensional TL-C and FRL-C for ^{SPECT}FRL-FV calculation [Box 2]. Thereafter, the first phase calculated sTL-F will be multiplied with ^{SPECT}FRL-FV for ^{SPECT}FRL-F calculation. In few patients due to fast excretion, biliary tracer activity can be seen in SPECT images. Activity in biliary radicals will falsely give high counts during SPECT-based functional volume calculation. Hence, this activity in biliary radicals should be replaced by average liver activity during processing. Fusion of separate SPECT and CT acquisitions is technically possible in Hermes, but accurate motion correction will be required for precise attenuation correction and functional volume calculation.

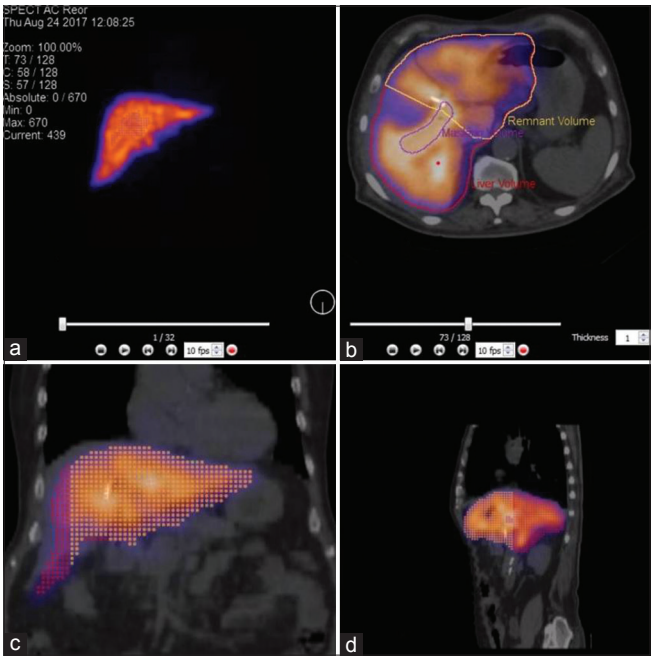

Figure 3: Tc-99m Mebrofenin single photon emission computed tomography-computed tomography functional volumetry. Image (a) showing maximum intensity projection. Image (b-d) showing the volume of interest for liver and remnant in axial, coronal, and sagittal view, respectively. Volume of interest on the right hepatic duct is showing average liver activity now

Table 2: Acronyms used and their definition

Acronyms	Definition
FRL-F	Future remnant liver function
PHLF	Post hepatectomy liver failure
CT	Computed Tomography
MRI	Magnetic resonance imaging
FRL-V	Future remnant liver volume
ICG	Indocyanine green
LiMax	Maximum liver function capacity
HBS	Hepatobiliary scintigraphy
NM	Nuclear medicine
Tc-99m GSA	Technetium-99m galactosyl human serum albumin
IDA	Iminodiacetic acid
OATP	Organic anion transporter polypeptide
MDRP2	Multidrug resistance protein 2
MUR	Mebrofenin uptake rate
TL-F	Total liver function
TAC	Time activity curve
ROI	Region of interest
BSA	Body surface area
sTL-F	Standardized total liver function
TL-C	Total liver counts
FRL-C	Future remnant liver counts
FRL-FV	Future remnant liver functional volume
SPECT-CT	Single photon emission computed tomography-computed tomography
VOI	Volume of interest
3D	3 dimensional
ICG-C_{15}	Indocyanine green clearance rate at 15 min
Mebro-C_{15}	Mebrofinin clearance rate at 15 min
ROC	Receiver operating characteristic
Gmean	Geometric mean
^{Actual}RL-F	Actual remnant liver function
NPV	Negative predictive value
PPV	Positive predictive value
LR+	Likelihood ratio of positive test
LR-	Likelihood ratio of negative test
^{NT}TL-V	Non-tumor total liver volume
eFRL-F	Effective future remnant liver function
PVE	Portal vein embolization
PVO	Portal vein occlusion
ALPPS	Associated liver partition and portal vein ligation for staged hepatectomy
Gd-EOB-DTPA	Gadolinium ethoxybenzyl-diethylenetriaminepentaacetic acid
PHC	Perihilar cholangiocarcinoma
MELD	Model for end stage liver disease
LEHR	Low energy high resolution

Box 1: Tc-99m Mebrofenin scintigraphy protocol for hepatic extraction fraction

Patient preparation:

4 h fasting

Radiopharmaceutical:

Tc-99m Mebrofenin 5 mCi (185MBq)

Instrumentation:

Camera: Large field of view gamma camera

Collimator: Low energy high resolution (LEHR)

Window: 15% over 140-KeV photopeak

Matrix: 128×128

Views: Both anterior and posterior

Patient positioning:

Supine; heart and liver in the field of view

Imaging protocol:

Take patient height (Ht) and weight (Wt)

Calculate body surface area (Mosteller formula):

$$BSA\ (m^2) = \sqrt{\frac{Ht\,(cm) \times Wt\,(Kg)}{3600}}$$

Inject Tc-99m Mebrofenin intravenously as a bolus and start computer program as per following protocol:

First phase (Hepatic uptake): 36 frames @ 10 sec/frame

Second phase (Fast SPECT-CT): 60 frames @ 8 sec/frame followed by a low dose CT scan

Third Phase (Excretion Phase): 15 frames @ 1 min/frame

Box 2: Most common parameters generated in Tc-99m Mebrofenin scintigraphy for future remnant liver function calculation

Total liver function (TL-F) or Mebrofenin uptake rate (MUR): %/min

Total liver function normalized to body surface area (sTL-F): %/min/m^2

Future remnant liver functional volume (FRL-FV):

$$\frac{\text{Future remnant liver counts (FRL}-\text{C)}}{\text{Total liver counts (TL}-\text{C)}}$$

Future remnant liver function (sFRL-F): FRL-FV x sTL-F (%/min/m^2)

Clinical use of Tc-99m Mebrofenin hepatobiliary scintigraphy in preoperative estimation of future remnant liver function and risk assessment for posthepatectomy liver failure before major liver resection

Various clinical studies in the last two decades have shown a notable impact of Tc-99m Mebrofenin HBS in preoperative workup before major liver resection. Ekman *et al*. first described the method for measuring hepatocytes function by IDA clearance rate.[27] He later reported a strong correlation in IODIDA blood clearance rate and hepatic uptake rate by scintigraphy in healthy (r = 0.92) and liver transplant (r = 0.93) patients.[28] Heyman also proposed HBS as a liver function test in 1994.[29,30] Erdogan *et al*. reported the first clinical study on the assessment of liver function in 54 patients with Tc-99m Mebrofenin and compared it with the 15 min ICG clearance rate (ICG-C_{15}). There was a significant correlation (r = 0.81) between ^{99m}Tc-Mebrofenin blood clearance rate at 15 min (Mebro-C_{15}) and ICG-C_{15}.

A significant correlation (r = 0.76) between Tc-99m Mebrofenin uptake (%/min) by scintigraphy and Mebro-C_{15} was reported. A significant correlation (r = 0.73) between Tc-99m MUR (%/min) and ICG-C_{15} was also reported.[31] In a small study, Bennink *et al*. reported that HBS was an easily reproducible technique and a strong positive association (r = 0.95) between the remnant liver function determined preoperatively and the actually measured value 1-day postoperatively.[32] Besides functional information, HBS can also be utilized to see the segmental difference, biliary clearance and postoperative biliary complications which makes this technique unique.

Dinant *et al*. investigated the role of preoperative Tc-99m Mebrofenin HBS in the prediction of PHLF and compared it with CT volumetry.[33] Preoperative FRL-F was found to be significantly low in patient suffered from PHLF and liver failure-related mortality. However, CT volume of the future remnant was not able to predict any of the outcome parameters. On receiver operating characteristic (ROC) analysis, patients with uptake above 2.5%/min/BSA had a 3% chance of liver failure and uptake below 2.5%/min/BSA had a 56% chance of liver failure. On multivariate analysis, uptake % was very reliable indicator which could help in predicting outcome.

de Graaf *et al*. analyzed Tc-99m Mebrofenin HBS with SPECT for assessment of hepatic function and liver functional volume before partial hepatectomy in 36 patients.[34] Due to the anterior location of the left lobe of the liver, anterior projections result in overestimation of the left lobe liver function, hence geometric mean (Gmean) of anterior and posterior data sets was suggested. In addition, both ^{Gmean}FRL-F and ^{SPECT}FRL-F demonstrated a strong correlation with actual remnant liver function (^{actual}RL-F), but only ^{SPECT}FRL-F showed no significant difference in preoperative estimates and ^{actual}RL-F. ROC analysis in 55 high-risk patients undergoing major liver resection, a cutoff value for FRL-F of 2.69%/min/m^2 identified patients who developed postoperative liver failure with sensitivity 89%, specificity 87%, negative predictive value (NPV) 97.6%, and positive predictive value (PPV) 57%.[26] Hence, a high-risk patient underwent major liver resection with FRL-F more than 2.69%/min/m^2 had 2.4% risk of liver failure. The likelihood ratio for a positive test (LR +) was 6.8 while LR for a negative test (LR −) was 0.12. Further, it was found that total hepatic function by HBS was significantly lower in a patient with the parenchymal liver disease while nontumor TL volume (^{NT}TL-V) was significantly larger in compromised liver patients. This equation suggested that volume is not equal to function. In correlation of FRL-F and FRL-V, patients with normal liver showed good correlation (r = 0.71) while patients with compromised liver showed moderate (r = 0.61) correlation. Chapelle *et al*. compared 88 patients future liver remnant volume (^{MRI}FLR-V) measured on MRI and effective FRL-F (eFRL-F) calculated by multiplying ^{MRI}FLR-V by TL-F by ^{99m}Tc-Mebrofenin scintigraphy.[35] eFLRF cut off of 2.3%/min/m^2 was the only independent predictive factor for PHLF with sensitivity, specificity, NPV, PPV, LR−, and LR + of 92%, 98%, 99%, 92%, 0.84%, and 71%, respectively.

Clinical role of Tc-99m Mebrofenin hepatobiliary scintigraphy for portal vein embolization stratification before major liver resection

PVE is a well-accepted procedure to increase the FRL-F before major liver resection. PVE not only reduces the chance of PHLF but also helps in fast recovery.[36-39] Cieslak *et al*. reported 163 patients' data who underwent major liver resection with the inclusion of Tc-99m Mebrofenin HBS in preoperative workup, with a cutoff 2.7%/min/m^2 in decision-making. 29/163 patients underwent PVE due to FRL-F <2.7%/min/m^2 while other 134 patients underwent upfront surgery with no PVE due to sufficient FRL-F. 8/29 patients underwent PVE due to insufficient FRL-F despite sufficient FRL-V.[40] There was no significant difference noted in postoperative outcome in both groups. In comparison to a historical cohort (n = 55) before implementation of HBS in preoperative work up to patient cohort (n = 134) who underwent upfront surgery due to sufficient FRL-F with no PVE, there was significant difference seen in the postoperative outcome in terms of morbidity and mortality due to liver failure. Hence, it was concluded that implementation of HBS in preoperative workup before major liver resection added functional orientation to PVE decision and led to the better postoperative outcome.

A prospective interventional study investigated management strategy to avoid PHLF in 100 patients.[41] eFRL-F cutoff of 2.3%/min/m^2 as described by Chapelle *et al*.[35] was used to decide management. Patients with eFRL-F ≥2.3%/min/m^2 underwent surgery upfront while <2.3%min/m^2 underwent portal vein occlusion with re-evaluation after 4–6 weeks and underwent surgery if the response was sufficient. No significant difference was seen in postoperative outcome of these two groups. However, in comparison to historical observational patients group (n = 88) in which FRL-V (>25%) was used as a sole criteria, postoperative outcome in terms of grade B/C PHLF and related mortality was significantly low.

FRL-F was also being investigated for hypertrophy response following PVE by Cieslak *et al*.[42] Post-PVE FRL-F cutoff of 2.7%/min/m^2 was considered as sufficient function. On ROC analysis, 33 chemotherapy naïve patients with a pre-PVE FRL-F cutoff of ≥1.72%/min/m^2 was considered safe to identify sufficient hypertrophy response 3 weeks after PVE with sensitivity of 81.3% and specificity 82.4%. Thirty-three patients who received neoadjuvant chemotherapy, a cutoff of 1.92%/min/m^2 was able to distinguish responder from nonresponder with sensitivity of 62.5% and specificity 71.4%. Overall PVE led to 1.00%/min/m^2 median increase in FRL-F in 3 weeks with a median increase of 0.32%/min/m^2 per week. By identifying PVE nonresponder, patients may be considered for

associated liver partition and portal vein ligation for staged hepatectomy which has better hypertrophy response.

Gadolinium-ethoxybenzyl-diethylenetriaminepentaacetic acid (Gd-EOB-DTPA) is a paramagnetic hepatobiliary-specific MRI contrast agent. It is actively taken up hepatocytes by OATP $1B_1$ and $1B_3$ receptor and excreted into the bile by MDRP2 receptor similar to mebrofenin. MRI is the investigation of choice for identification and characterization of liver lesion. Due to better temporal and spatial resolution, researchers started using Gd-EOB MRI for assessment of FRL-F. In a recent study (n = 14) comparing Tc-99m Mebrofenin HBS and Gd-EOB-DTPA-enhanced MRI for evaluation of right and left lobe liver function in post-PVE patients has claimed a significant correlation.[43] However, we need to remember that only 50% of Gd-EOB-DTPA is taken up by the normal hepatocytes and the rest get excreted through the kidney. In hyperbilirubinemic state, renal excretion will be increased further, and its accuracy can be reduced. Routine clinical availability is another concern for Gd-EOB-DTPA enhanced MRI.

Clinical role of Tc-99m Mebrofenin hepatobiliary scintigraphy in perihilar cholangiocarcinoma before major liver resection

Liver resection and biliary reconstruction is the only way for a long-term survival in perihilar cholangiocarcinoma (PHC). However, this procedure has a high morbidity and mortality. Sufficient FRL-V is one of the major requirements for good outcome of surgery and to reduce the risk of PHLF. In a recent study by Olthof *et al*., the role of FRL-F and FRL-V was compared in 116 PHC patients.[44] In comparison to a patient group who suffered from PHLF (n = 27) to those who did not develop PHLF (n = 89), a significant difference in FRL-F was seen while the FRL-V difference was insignificant. The diagnostic power of FRL-F (%/min) and BSA normalized FRL-F (%/min/m^2) for PHLF prediction was almost similar. It was observed that high bilirubin had a negative association with TLF by HBS and a bilirubin value above 50 μmol/L (2.92 mg/dl) results in a sharp decrease in TL-F by HBS. They concluded a new FRL-F cutoff of 8.5%/min for better prediction of PHLF in PHC with NPV of 94%. So far FRL-F by Tc-99m Mebrofenin HBS has been proved to be better than CT FRL-V in PHLF risk assessment in many studies. However, all these studies were retrospective in nature, with a small sample size and from single center. Consequently, a prospective clinical trial for assessing the risk of postoperative liver failure by HBS (Hepatobiliary Scintigraphy to assess the risk of postoperative liver failure hepatectomies, SCINTIVOL Trial, NCT02753517) was started in December 2015 which will finish in October 2019. A clinical trial comparing the HBS role with liver-specific contrast-enhanced MRI for FRL-V estimation definitely needs attention and action since both have shown a great potential individually. We have started doing Tc-99m Mebrofenin HBS for FRL-F calculation before major liver resection in recent time. In our experience, we have found that this technique can become a routine NM procedure and can easily be reproduced in any center with a dual head gamma camera; however, SPECT-CT is preferred for more accurate calculations. We follow a FRL-F cutoff value of 2.7%/min/m^2 for HBS in conjunction with other methods in our clinical practice and decision-making.

Conclusion

Tc-99m Mebrofenin HBS is a unique procedure for calculation of global and regional liver function. This takes into account the nonuniformity of liver function and underlying liver pathology. Moreover, a single cutoff might fit in all for PHLF risk assessment and PVE stratification. Results of SCINTIVOL trial will strengthen the currently available mostly retrospective data. However, further studies will be required to see the impact of hyperbilirubinemia and hypoalbuminemia on its accuracy.

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Conflicts of interest

There are no conflicts of interest.

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