^{99m}Tc-GSA SPECT/CT fused images for assessment of hepatic function and hepatectomy planning

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Abstract: To assure safe hepatectomy, accurate estimation of the functional reserve of the future remnant liver is crucial. The combination of indocyanine green retention rate at 15 min and CT volumetry is widely used in deciding on the extent of hepatectomy. On the other hand, there are quantitative indices calculated from ^{99m}Tc-GSA scintigraphy that reflect the number and function of hepatocytes. Therefore, there are many indices calculated from ^{99m}Tc-GSA scintigraphy that have been reported. In recent *Annals of Surgical Oncology* on Oct. 2014 the Uptake Index (UI) calculated from ^{99m}Tc-GSA scintigraphy was reported to be useful for hepatectomy planning and postoperative liver failure prediction. In this paper, we report on the usefulness and limits of quantitative indices calculated from ^{99m}Tc-GSA SPECT/CT for preoperative simulation.

Keywords: ^{99m}Tc-GSA SPECT/CT fused image; Uptake Index (UI); hepatectomy planning

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In order to realize a successful surgical outcome, it is necessary to estimate before hepatectomy the whole liver function and hepatic functional reserve of the future remnant liver. ^{99m}Tc-labeled diethylenetriaminepenta—acetic acid galactosyl human serum albumin (GSA) scintigraphy is a widely used scintigraphy for the quantitative assessment of preoperative liver functional reserve (1). Recently, Du *et al.* reported the Uptake Index (UI) as a new index calculated from ^{99m}Tc-GSA scintigraphy (2). UI was useful for evaluating the whole liver function. Moreover, Mao *et al.* reported the UI values calculated by combining UI and ^{99m}Tc-GSA SPECT/CT fused imaging on Annals of Surgical Oncology on Oct. 2014 (3).

There are various models for assessing the hepatic function using ^{99m}Tc-GSA scintigraphy. The receptor index (LHL15) and clearance index (HH15) are the most commonly used parameters and are reported to be useful for assessment of both the function and functional reserve of the liver. We have previously demonstrated that the combination of LHL15 and ICG R15 proved useful for the risk stratification of postoperative liver failure, and LHL15 was more associated with the postoperative liver function than indocyanine green retention rate at 15 min (ICG R15) (4). Although HH15 and LHL15 are useful indices for preoperative evaluation, the anatomical information of these indices is not sufficient to accurately assess the function of the future remnant liver. Therefore, HH15 and LHL15 are usually corresponded with the CT volumetry just the same as ICG R15. UI was also calculated from ^{99m}Tc-GSA dynamic scintigrams. Although UI has the same weaknesses as the HH15 and LHL15, the UI values that are calculated from the combination of UI and ^{99m}Tc-GSA SPECT/CT fused images overcome the lack of anatomical information. Moreover, SPECT/CT fused imaging was constructed by SPECT image and contrast enhanced CT image. UI values of regional liver are based on vascular tributaries. However, it was not clarified what kind of machines was used to obtain ^{99m}Tc-GSA SPECT/CT. The SPECT/CT integrated system is now commercially available. The registration error of SPECT and CT fused imaging becomes very small

when using the SPECT/CT integrated system. From our experience, the registration error is not small when the SPECT and CT images obtained by separate machines. Therefore, we suggest that it should be clearly describe machines of SPECT/CT fused imaging to prove the quantitatively of the UI values.

The quantitative index calculated from ^{99m}Tc-GSA SPECT/CT imaging is known to be useful for predicting postoperative liver failure. Although many different parameters can be calculated from different kinetic models, they are highly complex and therefore not widely used in the clinical setting. We have introduced a functional liver volume calculated from ^{99m}Tc-GSA SPECT/CT imaging that is a simple and convenient index. We showed that this functional volume was useful to evaluate the functional distribution of liver after portal vein embolization (5). We reported that the functional liver volume was better indicator to predict postoperative morbidity, liver-related morbidity and mortality than CT volumetry (6). Therefore, accurate assessment of functional distribution of liver functional volume is a very important. In addition, based on our observations, we have introduced other quantitative indices that reflected the hepatic function, namely, Liver Uptake Value (LUV) (7). LUV is linked with hepatic function and histopathological damage of liver. UI values are based on the ^{99m}Tc-GSA SPECT/CT fused imaging as same as the functional volume. Then UI values can reflect functional distribution accurately. Moreover, the predictive UI values are strongly related with not only preoperative liver function but also postoperative liver function. Therefore, UI values are useful to evaluate the functional distribution of liver and regional function of liver quantitatively. Although UI values reflect the Child Pugh score, we want to know the relation between UI values and histopathological damage of liver.

The prediction of postoperative failure is important for hepatectomy planning. Serum hyaluronate and CT volumetry are reported to be useful for predicting the postoperative failure. Using the receiver operating characteristic (ROC) analysis, area under curve (AUC) of both indices are 0.80 and 0.65, respectively (8,9). On the other hand, there were various reports that present the usefulness of ^{99m}Tc-GSA SPECT for predicting postoperative liver failure. We previously described the merit of predicting the postoperative function by using LUV of the future remnant liver (10). In that study, AUC of the LUV of the future remnant liver was 0.89. As the negative predictive value was 99%, we suggested LUV is expedient for safe hepatectomy. The R max calculated from dynamic scintigram of ^{99m}Tc-GSA showed high diagnostic performance for predicting postoperative liver failure (AUC is 0.97) (11). UI values also showed high diagnostic performance for predicting postoperative liver failure (AUC was 0.95) (3). From these results, UI values and R max seem to give an almost perfect diagnostic performance. On the other hand, the diagnostic performance of LUV seems to be worse than these indices. However, we suggest there are two reasons for the discrepancy. The first, the definitions of postoperative liver failure are not standardized. The 50-50 criteria (12,13), modified 50-50 criteria, or international study group of liver surgery (ISGLS) criteria (14) are used in many studies. Although UI values are evaluated to predict postoperative Child Pugh grade C as the postoperative liver failure, when the clinical and laboratory data were obtained is not presented fully. The second, we suggested the postoperative liver failure is not related to the functional reserve of the remnant liver alone. In fact, patients with low hepatic function do not always experience postoperative liver failure. In previous studies, bile leakage (15), intraoperative blood loss (16) and venous congestion (17) have been reported to be risks of postoperative liver failure. We suggest that among patients with marginal hepatic function of suspicious liver failure, there were cases with these complications that showed a poor outcome. Therefore, when only using a quantitative index for predicting postoperative liver failure, it is easy to set the cut-off value for high negative predictive values but it is difficult to do so for high positive predictive values. Finally, we think that it is rather improbable to accurately predict postoperative liver failure based solely on one index related to hepatic function obtained before hepatectomy. We consider that for better prediction of postoperative liver failure, clinical information such as the complexity of the surgical procedure or predictive blood loss is needed.

Conclusions

We are convinced the quantitative indices calculated from ^{99m}Tc-GSA scintigraphy are reliable for safe hepatectomy. Moreover, using the SPECT/CT integrated system, it is possible to accurately evaluate the function of regional liver. Especially, UI values have possibility of high accurate prediction of postoperative liver failure. However, the diagnostic procedures for predicting postoperative liver failure may not be regarded as perfect. For a much more

accurate method of predicting postoperative liver failure, the appropriate combination of indexes based on the ^{99m}TcGSA SPECT/CT and other risk factors needs to be determined.

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