

实时二维剪切波弹性成像评估慢加急性肝衰竭患者的预后

金洁瑛^{1,2}, 郑玉宝^{2,3}, 郑剑⁴, 郭欢仪^{1,2}, 吴莉莉^{1,2}, 高志良^{2,3}, 郑荣琴^{1,2}

(中山大学附属第三医院 1. 超声科, 2. 肝脏疾病研究重点实验室, 3. 感染科, 广东 广州, 510630; 4. 中山大学附属东华医院 超声科, 广东 东莞, 523110)

摘要:【目的】探讨实时二维剪切波弹性成像(2D SWE)评估慢加急性乙型肝炎肝衰竭(ACLF-HBV)患者预后的临床应用价值。【方法】入组对象为2013年10月1日至2015年12月31日我院感染科确诊的312例慢加急性乙型肝炎肝衰竭患者。观察终点为90 d, 根据临床结局分为好转组192例和恶化组120例。入组后3 d内, 应用2D SWE进行肝脏硬度测量, 收集患者血常规、凝血、生化等血清学指标, 观察患者肝实质回声均匀度、肝包膜光滑度、右肝厚度、胆囊壁厚度、脾脏指数、腹水指数、门静脉主干内径、附脐静脉是否重开, 计算终末期肝病评分(MELD)、CTP评分(CTP)、皇家医学院医院评分(KCH), 入组后每2~4周动态检测2D SWE, 直至患者出院或死亡/肝移植。【结果】恶化组的2D SWE高于好转组[(44.0 ± 7.5)kPa vs (36.8 ± 10.3) kPa, $t = -6.5$, $P = 0.000$], 39.2 kPa可作为预后不良的阈值。2D SWE评估ACLF-HBV患者预后的受试者操作特征曲线下面积(AUROC)为0.73, 预后效能高于KCH(AUROC: 0.65, $z = 2.1$, $P = 0.033$)。动态检测2D SWE, 好转组维持在40 kPa以下, 恶化组则一直高于40 kPa, 并有升高趋势。【结论】2D SWE评估ACLF-HBV患者预后的准确性较高, 测值高于39.2 kPa的患者预后较差, 反之预后较好; 动态检测2D SWE的变化对于ACLF-HBV患者的预后评估也有潜在价值。

关键词: 剪切波弹性成像; 慢加急性肝衰竭; 预后; 超声检查

中图分类号: R445.1

文献标志码: A

文章编号: 1672-3554(2017)05-0774-06

Two-dimensional Shear Wave Elastography in Predicting Prognosis of Patients with Acute-on-chronic Liver Failure

JIN Jie-yang^{1,2}, ZHENG Yu-bao^{2,3}, ZHENG Jian⁴, GUO Huan-yi^{1,2}, WU Li-li^{1,2}, GAO Zhi-liang^{2,3},
ZHENG Rong-qin^{1,2}

(1. Department of Ultrasonography, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou 510630, China;
2. Guangdong Key Laboratory of Liver Disease Research, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou 510630, China; 3. Department of Infectious Disease, The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou 510630, China; 4. Department of Ultrasonography, Donghua Hospital Affiliated Sun Yat-sen University of Dongguan, Dongguan 523110, China)
Corresponding to: ZHENG Rong-qin; E-mail: zhengrq@mail.sysu.edu.cn

Abstract: 【Objective】 To evaluate the two-dimensional shear wave elastography (2D SWE) in predicting the prognosis of the patients with acute-on-chronic hepatitis B liver failure (ACLF-HBV). 【Methods】 312 patients diagnosed with ACLF-HBV at the Department of Infectious Diseases in the Third Affiliated Hospital of Sun Yat-sen University from October 1st 2013 to December 31th 2015 were recruited. The baseline data of all patients, including 2D SWE, laboratory data, ultrasonographic data, Model for End-stage Liver Disease score (MELD), Child-Turcotte-Pugh score (CTP), and King's College Hospital score (KCH), were collected when enrolled. All patients were followed up for at least 90 days and their clinical outcomes (recovering or worsening) were recorded. 2D SWE values of all patients were dynamically collected every 2~4 weeks during the follow-up until death, liver transplantation, or discharging from hospital. 【Results】 The worsening patients showed higher 2D SWE values than the recovering ones [(44.0 ± 7.5) kPa vs (36.8 ± 10.3) kPa, $t = -6.5$, $P = 0.000$], 2D SWE value less than 39.2 kPa could be a prediction of the patient's recovery in

收稿日期: 2017-01-24

基金项目: 广东省自然科学基金(2016A030313205, 2015A030313172)

作者简介: 金洁瑛, 博士, 住院医师, E-mail: jinjieyang0214@163.com; 郑荣琴, 通信作者, 教授, E-mail: zhengrq@mail.sysu.edu.cn

90 days. The predictive value of 2D SWE (AUROC = 0.73) was higher than that of KCH (AUROC: 0.65, $z = 2.1$, $P = 0.033$). Among all the dynamically measured patients, 2D SWE rose from (42.1 ± 8.0) kPa to (47.5 ± 9.3) kPa in the worsening group during the 90-day follow-up, while nearly stable in the recovery group. 【Conclusion】 Noninvasive liver stiffness measurement by 2D SWE is a useful method in evaluating the prognosis of ACLF-HBV patients. Taking a cutoff of 39.2 kPa, patients with higher 2D SWE values could have worse clinical outcomes, otherwise better. It seems that dynamically measuring 2D SWE values could also be helpful, but more research in the future should be needed.

Key words: shear wave elastography; acute-on-chronic liver failure; prognosis; ultrasonography

[J SUN Yat-sen Univ (Med Sci), 2017, 38(5): 774-779]

慢加急性肝衰竭 (acute-on-chronic liver failure, ACLF) 是在慢性肝病基础上短时间内因多种因素引起的严重肝脏损害^[1]。乙型肝炎病毒感染是中国引起 ACLF 的首要原因^[2]。慢加急性乙型肝炎肝衰竭 (acute-on-chronic hepatitis B liver failure, ACLF-HBV) 患者发病急骤、进展迅速、死亡率高^[3]。及时、准确评估 ACLF-HBV 患者预后, 从而采取有针对性的治疗十分重要。实时二维剪切波弹性成像 (two-dimensional shear wave elastography, 2D SWE) 可以同时进行肝脏硬度测量以及超声检查, 特别适用于 ACLF 患者。本文拟探讨 2D SWE 检测 ACLF-HBV 患者肝脏硬度的成功率、可靠性, 及其评估 ACLF-HBV 患者预后的应用价值。

1 材料与方法

1.1 病例资料

入组对象为 2013 年 10 月 1 日至 2015 年 12 月 31 日我院感染科确诊的 312 例慢加急性乙型肝炎肝衰竭患者。纳入标准: (1) 符合中华医学会感染病学分会肝衰竭与人工肝学组与中华医学会肝病学会重型肝病与人工肝学组共同颁布的《肝衰竭诊治指南 (2012 版)》^[4] 中 ACLF 诊断标准的患者, 主要为总胆红素 (total bilirubin, TB) 大于正常值上限 10 倍且凝血酶原活动度 (prothrombin time activity percentage, PTA) $\leq 40\%$; (2) 乙型肝炎表面抗原 (hepatitis B surface antigen, HBsAg) 和/或乙型肝炎病毒脱氧核糖核酸 (hepatitis B virus deoxyribonucleic acid, HBV-DNA) 阳性。排除标准: (1) 年龄小于 18 岁的患者; (2) 合并酒精性肝病、代谢性肝病、免疫性肝病或其他病因可导致 ACLF 的患者; (3) 超声提示有肝脏恶性肿瘤的患者。观察终点为 90 d, 根据临床结局分为好转组 192 例和恶

化组 120 例。好转组标准: (1) 患者生存至入组后 90d; (2) 入组后 90 d 病情好转的患者, 即肝功能指标明显好转 (TB 降至正常值的 5 倍以下, PTA $> 40\%$)^[4]。恶化组标准: (1) 患者在入组后 90 d 内死亡或行肝移植手术; (2) 入组后 90 d 病情未见好转的患者, 即肝功能指标未见明显好转 (TB 大于正常值 5 倍, PTA $\leq 40\%$)。患者均经规范内科综合治疗, 包括抗病毒 (根据患者病情应用拉米夫定、恩替卡韦、替诺福韦、替比夫定、阿德福韦酯等核苷 (酸) 类药物)、护肝治疗等, 必要时补充白蛋白、行人工肝支持治疗或行肝移植手术等^[4]。本研究已得到中山大学附属第三医院伦理委员会批准。本研究所涉及的检查均获得受检者的知情同意。

1.2 实验方法

入组后 3 d 内, 应用 2D SWE 对患者进行肝脏硬度测量, 收集患者白细胞 (white blood cell, WBC)、血红蛋白 (hemoglobin, HGB)、血小板 (platelets, PLT)、PTA、国际标准化比值 (international normalized ratio, INR)、谷丙转氨酶 (alanine aminotransferase, ALT)、TB、肌酐 (creatinine, Cr) 等血清学指标, 观察肝实质回声均匀度、肝包膜光滑度、右肝厚度、胆囊壁厚度、脾脏指数、腹水指数、门静脉主干内径、附脐静脉是否重开, 计算终末期肝病评分 (Model for end-stage liver disease scoring system, MELD)^[5-6]、CTP 评分 (Child-Turcotte-Pugh score, CTP)^[7]、皇家医学院医院评分 (King's College Hospital criteria, KCH)^[8]。

2D SWE 由两位均有至少 2 个月以及 500 例 2D SWE 检查经验的医生进行检测, 采用 Supersonic Aixplorer 型超声诊断仪, 选择 SC6-1 型凸阵探头, 参照本中心既往研究发表资料^[9], 仪器条件设置如下: 二维灰阶图像放大至 120%, 深度调节至 8 cm, 聚焦设置于 6 cm; 弹性图像取样框大小选取约 $4 \text{ cm} \times 3 \text{ cm}$, 位于图像中央, 置于肝包膜下 1 ~

3 cm的肝实质处,避开胆囊、大血管、大胆管等结构,ROI直径选取为20 mm,肝脏硬度测量量程调至70 kPa。检测肝脏硬度时要求患者空腹8~12 h,在平静呼吸状态下屏住呼吸3~5秒,冻结图像并确认ROI,采用平均值代表肝脏硬度。每个患者连续测量5次,采用5次的中位数作为检测结果。单次2D SWE检测出现ROI内颜色填充不足1/3或最小值为0 kPa则为无效,5次无效则为检测失败。入组后,每2~4周动态检测2D SWE,直至患者出院或死亡/肝移植。

肝实质回声均匀度参考既往文献标准^[9],均匀计为1分,欠均匀2分,不均匀3分。肝包膜光滑度参考既往文献^[9]观察左肝包膜。光滑计为1分,欠光滑2分,不光滑3分。脾脏指数计为脾脏长径与短径的乘积。腹水指数计为肝前间隙、肝肾隐窝、脾窝、髂窝、盆腔5处位置的液性暗区最大垂直距离之和。附脐静脉是否重开是通过寻找肝圆韧带及其附近是否能观察到离肝静脉样血流^[10],附脐静脉重开计为1分,附脐静脉未重开计为0分。右肝厚度^[11]、胆囊壁厚度^[12]及门静脉主干内径^[12]分别参考文献既往测量方法进行测量。

1.3 统计学方法

计量资料以均数±标准差表示,组间的比较采用t检验;计数资料则以个数(百分比)表示,组间的比较采用卡方检验或Fisher精确检验。采用患者首次2D SWE测值比较好转组与恶化组间2D SWE的差异,构建2D SWE预测患者预后的受试者工作特征(receiver operating characteristic, ROC)曲线,计算受试者操作特征曲线下面积(area under the receiver operating characteristic curve, AUROC)及最大约登指数,根据最大约登指数确定预后阈值。不同AUROC之间的比较采用DeLong检验方法。采用患者首次及随访2D SWE测值评价好转组与恶化组动态变化趋势。 $P < 0.05$ 为差别具有统计学意义。统计分析分别采用SPSS软件(version 13.0, SPSS Inc., Chicago, IL, USA)以及MedCalc软件(version 11.2, MedCalc Software, Mariakerke, Belgium)。

2 结果

2.1 2D SWE检测成功率

2D SWE检测总成功率为96.2%(300/312),6

例为肥胖患者(身体质量指数 $> 30 \text{ kg/m}^2$),6例为患者呼吸控制较差而无法配合检测。其中,腹水患者(超声检查提示肝前可见无回声区)的2D SWE检测成功率为100%(218/218),肝脏缩小患者(超声检查提示右肝厚度 $< 100 \text{ mm}$)的2D SWE检测成功率为100%(104/104),肥胖患者的2D SWE检测成功率为93.5%(87/93)。

2.2 好转组与恶化组的比较

由于12例ACLF-HBV患者2D SWE检测不成功,因此纳入统计的患者一共300例,男263例,女37例,年龄(44.3 ± 12.7)岁。ACLF-HBV患者入组时的2D SWE测值、实验室检查、超声指标、预后评分见表1。患者入组时的2D SWE平均值为(39.5 ± 10.0) kPa,其中,好转组患者2D SWE的平均值为(36.8 ± 10.3) kPa,恶化组患者2D SWE的平均值为(44.0 ± 7.5) kPa,好转组低于恶化组,两者比较差异有统计学意义($t = -6.5$, $P = 0.000$)。

2.3 2D SWE评估预后的效能

以临床结局作为金标准,2D SWE评估ACLF-HBV患者预后的AUROC为0.73(图1),预后效能高于KCH评分(AUROC:0.65, $z = 2.1$, $P = 0.033$),而与MELD(AUROC:0.79, $P = 0.135$)、CTP(AUROC:0.69, $P = 0.312$)评分预后效能的差异无统计学意义。

2.4 2D SWE评估预后的阈值

以肝脏弹性模量值39.2kPa作为预后不良的阈值,敏感度为72.3%,特异度为63.8%。

2.5 2D SWE的动态观察

本研究最终入组的300例ACLF-HBV患者中,159例进行了动态的2D SWE检测随访。其中,好转患者为118例,恶化患者为41例。如图2所示,在2D SWE连续检测随访中,好转患者的2D SWE测值则基本维持在40 kPa以下,无明显变化趋势,而恶化患者2D SWE测值一直高于40 kPa,并且由入组时的(42.1 ± 8.0) kPa逐渐升高至随访中的(47.5 ± 9.3) kPa。

3 讨论

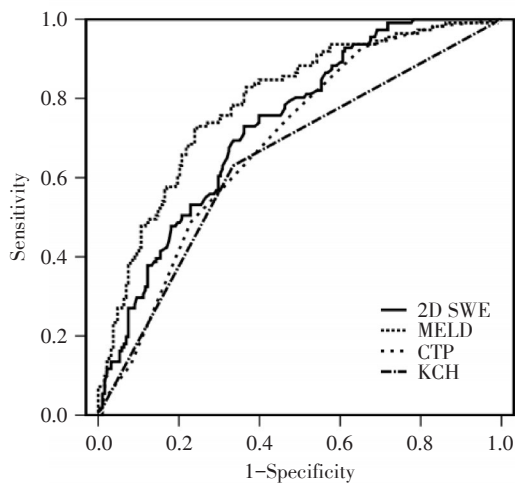
目前,肝脏硬度测量采用的是弹性成像技术,包括TE、2D SWE等。其中应用最早且最广的TE,评估肝纤维化/肝硬化程度的应用价值较

表1 好转组及恶化组患者各项指标的基线资料

Table 1 Baseline characteristics of the patients in the recovering and worsening groups ($\bar{x} \pm s$)

Variable	All(n = 300)	Recovering group(n = 188)	Worsening group(n = 112)	t	P
2D SWE(kPa)	39.5 ± 10.0	36.8 ± 10.3	44.0 ± 7.5	-6.5	0.000
WBC($\times 10^9/L$)	7.4 ± 3.5	7.0 ± 3.2	8.1 ± 3.8	-2.7	0.007
HGB(g/L)	113.4 ± 20.5	116.0 ± 20.5	109.2 ± 19.8	2.8	0.005
PLT($\times 10^9/L$)	115.0 ± 66.3	124.2 ± 65.7	99.5 ± 64.6	3.2	0.002
PTA(%)	33.8 ± 11.2	37.0 ± 11.3	28.4 ± 8.8	7.3	0.000
INR	2.6 ± 0.9	2.3 ± 0.7	3.0 ± 1.1	-6.1	0.000
ALT(U/L)	315.4 ± 429.3	341.3 ± 461.1	271.9 ± 367.7	1.4	0.152
TB($\mu\text{mol/L}$)	401.5 ± 147.5	360.6 ± 140.5	470.0 ± 133.5	-6.6	0.000
CR($\mu\text{mol/L}$)	80.6 ± 44.1	73.0 ± 26.7	93.3 ± 61.5	-3.3	0.001
liver parenchyma	1.6 ± 0.8	1.6 ± 0.8	1.7 ± 0.9	-1.6	0.105
liver surface	1.9 ± 0.7	1.8 ± 0.7	2.0 ± 0.7	-2.6	0.011
right liver lobe diameter	101.7 ± 9.2	103.5 ± 9.0	98.9 ± 8.8	4.3	0.000
gallbladder wall thickness	6.9 ± 3.1	6.4 ± 2.7	7.6 ± 3.5	-2.9	0.004
spleen index	47.0 ± 16.8	46.8 ± 16.7	47.3 ± 16.9	-0.3	0.799
ascites index	60.7 ± 69.3	46.7 ± 59.1	84.1 ± 78.5	-4.4	0.000
portal vein diameter	11.6 ± 1.3	11.5 ± 1.2	11.7 ± 1.4	-1.5	0.125
paraumbilical vein recanalization	0.5 ± 0.5	0.5 ± 0.5	0.6 ± 0.5	-1.8	0.077
MELD	26.1 ± 5.7	24.0 ± 4.7	29.6 ± 5.7	-8.7	0.000
CTP	10.6 ± 1.6	10.2 ± 1.7	11.3 ± 1.3	-6.5	0.000
KCH	0.4 ± 0.5	0.3 ± 0.5	0.6 ± 0.5	-5.2	0.000

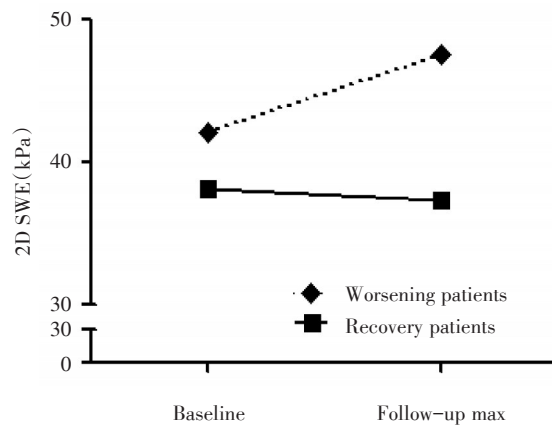
2D SWE: two-dimensional shear wave elastography; WBC: white blood cell; HGB, hemoglobin; PLT: platelet count; PTA: prothrombin activity; INR: international normalized ratio; ALT: alanine aminotransferase; TB: total bilirubin; Cr: serum creatinine; MELD: Model for End-stage Liver Disease; CTP: Child-Turcotte-Pugh; KCH: King's College Hospital



The predictive value of 2D SWE was higher than that of the KCH score ($z = 2.1, P = 0.033$), while there were no significant differences between the 2D SWE and MELD ($P = 0.135$) or CTP ($P = 0.312$)

图1 2D SWE及其他评分评估ACLF-HBV患者预后的ROC曲线

Fig.1 Accuracy of the 2D SWE compared to other prognostic scores in predicting the 90-day mortality of the ACLF-HBV patients



2D SWE values increased from (42.1 ± 8.0) kPa to (47.5 ± 9.3) kPa in the worsening patients, while it stayed stable between (38.1 ± 10.8) kPa to (37.3 ± 12.4) kPa in the recovering patients

图2 好转组与恶化组ACLF-HBV患者2D SWE的动态变化趋势

Fig.2 Dynamic changes in the 2D SWE values of the recovering and worsening patients

高^[13-14]。但是,TE仅为一维检查,无法实时观察肝脏形态、大小,并且TE无法应用于腹水患者,所以有一定局限性。最新的肝脏硬度测量技术2D SWE,评估肝纤维化/肝硬化程度的诊断价值与TE相当,甚至在诊断早期肝纤维化时更加准确。本团队的前期研究^[9,15],分别对303例和198例慢性肝病患者进行2D SWE肝脏硬度测量评估肝纤维化程度,并以肝脏组织穿刺活检结果作为金标准,所得结论为2D SWE应用于肝纤维化分期 \geq F2(AUROC, 0.862 ~ 0.917)以及 $=$ F4(AUROC, 0.925 ~ 0.967)的诊断价值均高,这有助于临床进一步的诊断和治疗。同时,2D SWE通过实时二维的超声图像引导,可以准确定位,避免了TE的盲目性,更加稳定、可靠,并且2D SWE可以应用于腹水患者。本研究结果证实,2D SWE应用于ACLF-HBV患者的总成功率为96.5%,其中,2D SWE应用于腹水患者的成功率为100%。在ACLF-HBV的患者中,有高达69.9%的患者合并腹水,这些患者如应用TE则受到较大限制;而2D-SWE则可充分发挥其不受腹水影响的优势,提高检测的成功率。

肝脏硬度测值不仅与肝纤维化程度高度相关,同时也受肝脏炎症/坏死的影响,与之有一定的相关性。欧洲超声医学与生物学联合会《超声弹性成像临床应用指南与建议(2013版)》^[13]、世界超声医学与生物学联合会《超声弹性成像临床应用指南与建议(2015版)》^[14]以及《弹性成像评估肝纤维化专家共识(2015版)》^[16]均有提出,肝脏硬度测量数值与炎症/坏死程度相关,患者肝脏的炎症/坏死程度越重则测值相应越高。Sharma等^[17]对45例ACLF患者进行TE肝脏硬度测量,发现入院时患者的肝脏硬度测量数值高达 (61 ± 18) kPa,并且提出检测肝脏硬度可用于鉴别ACLF与急性肝炎患者,其敏感性及特异性均达到90%以上。本研究结果显示,2D SWE评估ACLF-HBV患者预后的效能较高,AUROC为0.73,与MELD评分及CTP评分的预后效能相当,优于KCH评分。经过动态检测所知,2D SWE测值有升高趋势的患者预后较差。理论上而言,肝脏炎症/坏死明显时,肝细胞明显肿胀,炎症细胞广泛浸润,肝组织显著水肿,这均可能导致肝

脏硬度增大;另一方面,一部分ACLF-HBV患者是在肝硬化的基础上发生的肝衰竭,其肝纤维化程度已较重,故肝脏硬度测值高。本研究结果提示,2D SWE肝脏硬度测量能较好地反映ACLF-HBV患者的病情变化,当病情恶化时,2D SWE测值升高;反之,2D SWE测值降低或趋于稳定。2D SWE能客观、量化地反映ACLF-HBV患者的预后,用于评估ACLF-HBV患者预后具有重要的临床价值。

对于ACLF患者,准确的评估预后有助于选择合适的治疗手段、判断是否需要进行肝移植并指导肝移植时机的选择,从而最大程度地改善患者近/远期预后乃至挽救其生命。目前,主要采用MELD评分评估ACLF患者的预后。MELD评分包含了TB、INR、Cr及病因等四个指标,评分越高者病情越重、生存率越低^[5-6]。CTP评分是目前判断肝功能及肝脏疾病严重程度的常用指标^[7],KCH评分是评估急性肝衰竭患者预后较为常用的标准^[8],这两者对于ACLF患者的预后评估也有文献提及。不可否认,临床综合评分评估ACLF患者预后有其应用价值,但是,这些评分也有不足之处。MELD评分计算复杂,所纳入指标的影响因素较多,并未纳入门静脉高压等指标;CTP评分仅是通过临床症状及体格检查评定,评价主观,纳入指标有限,准确性一般;KCH评分中部分为定性指标,评价较为主观,且准确性欠佳。对于ACLF患者,临床需要一种无创、快捷、简便、准确的方法评估预后。2D SWE肝脏硬度测量无创伤性,检测过程仅数分钟,操作简单易学,可行床边检测,并可同步行肝脏普通超声检查,临床应用价值较高。

ACLF是肝脏乃至全身多个器官功能损害的综合征,对这类患者应进行多角度、多方面的观察及评估。今后,我们将进行更大样本、更多病种的研究,并尝试将2D SWE与现有临床综合评分相结合,构建一个更加准确、实用的预后模型。

综上所述,2D SWE评估ACLF-HBV患者预后的准确性较高,测值高于39.2 kPa的患者预后较差,反之预后较好;动态检测2D SWE的变化对于ACLF-HBV患者的预后评估也有潜在价值。

参考文献:

- [1] WHO. Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection [M]. 2015.
- [2] Sarin SK, Kedarisetty CK, Abbas Z, et al. Acute-on-chronic liver failure: Consensus recommendations of the Asian Pacific Association for the Study of the Liver (APASL) 2014[J]. *Hepatology*, 2014,8(4):453-471.
- [3] Bernal W, Jalan R, Quaglia A, et al. Acute-on-chronic liver failure[J]. *Lancet*, 2015, 386(10003):1576-1587.
- [4] 中华医学会感染病学分会肝衰竭与人工肝学组, 中华医学会肝病学会重型肝病与人工肝学组. 肝衰竭诊治指南(2012年版)[J]. *中华移植杂志(电子版)*, 2013,1(7):48-56.
Liver Failure and Artificial Liver Group, Chinese Society of Infectious Diseases, CMA; Severe Liver Disease and Artificial Liver Group, Chinese Society of Hepatology, CMA. Guideline for diagnosis and treatment of liver failure[J]. *Chin J Transplant(Elect Ed)*, 2013, 1(7):48-56.
- [5] Malinchoc M, Kamath PS, Gordon FD, et al. A model to predict poor survival in patients undergoing transjugular intrahepatic portosystemic shunts [J]. *Hepatology*, 2000,31(4):864-871.
- [6] Kamath P. A model to predict survival in patients with end-stage liver disease[J]. *Hepatology*, 2001, 33(2):464-470.
- [7] Pugh RNH, Murray-Lyon IM, Dawson JL, et al. Transection of the oesophagus for bleeding oesophageal varices[J]. *Brit J Surg*, 1973,8(60):646-649.
- [8] Grady JGO, Alexander GJM, Hayllar KM, et al. Early indicators of prognosis in fulminant hepatic failure [J]. *Gastroenterology*, 1989,97(2):439-445.
- [9] Zheng J, Guo H, Zeng J, et al. Two-dimensional shear-wave elastography and conventional US: The optimal evaluation of liver fibrosis and cirrhosis [J]. *Radiology*, 2015,275(1):290-300.
- [10] Zhang C, Xu J, Li J, et al. Predict esophageal varices via routine trans-abdominal ultrasound: A design of classification analysis model [J]. *J Gastroen Hepatol*, 2016,31(1):194-199.
- [11] 郭万学, 燕山, 杨浣宜, 等. 超声医学 [M]. 6. 北京: 人民军医出版社, 2011, 1694.
Guo WX, Yan S, Yang HY, et al. *Ultrasonic Medicine* [M]. 6. People Military Medical Press, 2011, 1694.
- [12] 中国医师协会超声医师分会. 腹部超声检查指南 [M]. 北京: 人民军医出版社, 2015, 136.
Ultrasonic Physician Branch of the Chinese Medical Doctor Association. *Guideline for abdominal ultrasonography* [M]. People Military Medical Press, 2015, 136.
- [13] Cosgrove D, Piscaglia F, Bamber J, et al. EFSUMB guidelines and recommendations on the clinical use of ultrasound elastography. Part 2: Clinical applications [J]. *Ultraschall Med*, 2013,34(03):238-253.
- [14] Ferraioli G, Filice C, Castera L, et al. WFUMB guidelines and recommendations for clinical use of ultrasound elastography: Part 3: Liver [J]. *Ultrasound Med Biol*, 2015,41(5):1161-1179.
- [15] Zeng J, Liu G, Huang Z, et al. Diagnostic accuracy of two-dimensional shear wave elastography for the non-invasive staging of hepatic fibrosis in chronic hepatitis B: A cohort study with internal validation [J]. *Eur Radiol*, 2014,24(10):2572-2581.
- [16] Barr RG, Ferraioli G, Palmeri ML, et al. Elastography assessment of liver fibrosis: Society of radiologists in ultrasound consensus conference statement [J]. *Radiology*, 2015,276(3):845-861.
- [17] Sharma P, Bansal R, Matin A, et al. Role of transient elastography (fibroscan) in differentiating severe acute hepatitis and acute on chronic liver failure [J]. *J Clin Exp Hepatol*, 2015,5(4):303-309.

(编辑 王晓鹰)