

论著·临床研究

基于超声剪切波弹性成像参数与临床风险因素的术后胰瘘改良预测模型

田晓梵^{1,2}, 董 怡^{1,2}, 楼文晖³, 张 琪¹, 邱艺杰¹, 左 丹¹, 王文平¹

1. 复旦大学附属中山医院超声科, 上海 200032; 2. 上海交通大学医学院附属新华医院超声科, 上海 200092; 3. 复旦大学附属中山医院胰腺外科, 上海 200032

[摘要] **目的**· 基于超声剪切波弹性成像 (shear wave elastography, SWE) 方法定量评估胰腺组织软硬度, 改良现有术后临床胰瘘 (clinically relevant post-operative pancreatic fistula, CR-POPF) 的预测模型。**方法**· 前瞻性纳入拟诊为胰腺肿瘤并计划于复旦大学附属中山医院接受胰腺外科手术的患者, 收集患者相关临床信息。在手术前1周内使用声触诊组织弹性成像与量化技术 (virtual touch tissue imaging and quantification technology, VTIQ) 测量胰腺病灶及门静脉前方胰体部正常腺体实质弹性定量剪切波速度 (shear wave velocity, SWV) 值。术中外科医师通过对胰腺组织的直接接触定性评估组织质地, 并将胰腺触诊结果分为质地软或中等-硬。术后3周随访期内, 根据2016年国际胰瘘研究组织的标准对CR-POPF进行诊断。通过单因素和多因素 Logistic 回归分析围手术期 CR-POPF 的危险因素, 并建立预测模型。通过受试者工作特征曲线 (receiver-operating characteristic curve, ROC 曲线) 与决策曲线分析 (decision curve analysis, DCA) 比较改良模型与现有临床预测模型的诊断效能及临床效益。**结果**· 2021年9月到2022年3月, 共有100名患者被纳入研究, 包括接受胰十二指肠切除术者33例 (33.0%) 及胰体尾切除术者67例 (67.0%)。通过术后3周的随访发现35例 (35.0%) 患者并发CR-POPF。通过 Logistic 回归分析发现, 门静脉前方胰体部实质的低SWV值 [$\lg OR = -2.934$ (95%CI -4.387~-1.479), $P=0.000$], 较窄的主胰管内径 (≤ 3 mm) [$\lg OR = 0.805$ (95%CI 0.274~1.335), $P=0.003$] 为胰腺切除术后并发CR-POPF的独立危险因素。基于SWE定量参数改良的风险评估模型预测CR-POPF的ROC曲线下面积积达0.842, 敏感度、特异度、阳性预测值、阴性预测值及似然比分别为85.7%、64.6%、70.5%、81.8%及2.422。与现有临床预测模型 [胰瘘风险评分 (fistula risk score, FRS) 和改良胰瘘风险评分 (alternative fistula risk score, a-FRS)] 相比, DCA结果显示基于SWE的改良模型具有更好的临床效益。**结论**· 结合SWE定量参数与CR-POPF临床关键危险因素的预测模型具有较高的诊断效能和临床效益, 且能在术前对CR-POPF风险进行无创、定量、客观的评估。

[关键词] 超声剪切波弹性成像; 胰腺切除术; 术后临床胰瘘; 预测模型; 胰瘘风险评分; 改良胰瘘风险评分**[DOI]** 10.3969/j.issn.1674-8115.2023.04.005 **[中图分类号]** R445.1 **[文献标志码]** A

A modified clinically relevant post-operative pancreatic fistula risk evaluation model based on ultrasound shear wave elastography: a prospective study

TIAN Xiaofan^{1,2}, DONG Yi^{1,2}, LOU Wenhui³, ZHANG Qi¹, QIU Yijie¹, ZUO Dan¹, WANG Wenping¹

1. Department of Ultrasound, Zhongshan Hospital, Fudan University, Shanghai 200032, China; 2. Department of Ultrasound, Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200092, China; 3. Department of Pancreatic Surgery, Zhongshan Hospital, Fudan University, Shanghai 200032, China

[Abstract] **Objective**· To modify previous clinically relevant post-operative pancreatic fistula (CR-POPF) risk evaluation models with quantitative evaluation of pancreatic tissue stiffness by ultrasound shear wave elastography (SWE). **Methods**· In this prospective study, the patients who were diagnosed as having pancreatic tumors and scheduled to undergo pancreatotomy at Zhongshan Hospital, Fudan University were initially enrolled, whose clinical information was collected. Virtual touch tissue

[基金项目] 国家自然科学基金面上项目 (82071942, 81972257); 上海市浦江人才计划 (2020PJD008); 申康促进市级医院临床技能与临床创新能力三年行动计划 (SHDC2020CR1031B, SHDC2020CR4060)。**[作者简介]** 田晓梵 (1995—), 男, 中国台湾, 住院医师, 硕士生; 电子信箱: 20211210103@fudan.edu.cn。**[通信作者]** 董 怡, 电子信箱: drdaisydong@hotmail.com。**[Funding Information]** National Natural Science Foundation of China (82071942, 81972257); Shanghai Pujiang Program (2020PJD008); Clinical Research Plan of Shanghai Hospital Development Center (SHDC2020CR1031B, SHDC2020CR4060)。**[Corresponding Author]** DONG Yi, E-mail: drdaisydong@hotmail.com.

imaging and quantification technology (VTIQ) assessment was applied to the patients within one week before the surgery to measure the shear wave velocity (SWV) of pancreatic lesions and the normal parenchyma of pancreatic body in the superficial layer of the portal vein. During the surgery, the surgeons qualitatively evaluated the stiffness of pancreases *via* direct palpation and divided them into soft pancreases and medium-hard pancreases. During the 3-week follow-up period after pancreatectomy, CR-POPF was diagnosed according to 2016 International Study Group of Pancreatic Fistula (ISGPF) standard. Peri-operative risk factors of CR-POPF were analyzed by univariate and multivariate Logistic regression to build the prediction model. Evaluation and comparison of diagnostic efficacy and clinical benefits among different models were then performed *via* receiver operating characteristic (ROC) curve and decision curve analysis (DCA). **Results** From September 2021 to March 2022, 100 patients were enrolled in this study, including 33 patients (33.0%) who received pancreaticoduodenectomy (PD) and 67 patients (67.0%) who received distal pancreatectomy. CR-POPF was diagnosed in 35 patients (35.0%) during the 3-week post-pancreatectomy follow-up. Multivariate Logistic regression analysis revealed that the SWV value of the body part of pancreatic parenchyma in the superficial layer of the portal vein [$\lg OR = -2.934$ (95%CI -4.387--1.479), $P=0.000$] and the presence of a non-dilated main pancreatic duct (≤ 3 mm) [$\lg OR = 0.805$ (95%CI 0.274--1.335), $P=0.003$] were independent risk factors that significantly correlated with the occurrence of CR-POPF after pancreatectomy. The modified model based on the SWE parameter achieved the area under the ROC curve of 0.842, with the sensitivity, the specificity, the positive predictive value, the negative predictive value and the likelihood ratio of 85.7%, 64.6%, 70.5%, 81.8% and 2.422 in predicting CR-POPF. DCA revealed a better clinical benefit of the modified model compared to the previous prediction models [fistula risk score (FRS) and alternative fistula risk score (a-FRS)]. **Conclusion** The modified model based on the SWE parameter and identified clinical risk factors can make non-invasive, quantitative and objective evaluation of CR-POPF risk before pancreatectomy, and provide sufficient diagnostic efficacy and clinical benefits.

[Key words] ultrasound shear wave elastography; pancreatectomy; clinically relevant post-operative pancreatic fistula (CR-POPF); prediction model; fistula risk score (FRS); alternative fistula risk score (a-FRS)

胰腺切除术 (pancreatectomy) 属于复杂且高风险的普外科手术。胰瘘是胰腺切除术后常见且严重的并发症, 推测其总体发生率在中国内地医院可达近30%, 显著影响胰腺肿瘤患者的预后^[1-2]。根据2016年国际胰瘘研究小组 (International Study Group of Pancreatic Fistula, ISGPF) 提出的胰瘘诊断与分级标准, 术后体液淀粉酶水平大于正常血清阈值3倍以上, 同时伴有相关感染症状或体征时, 即可诊断为术后临床胰瘘 (clinically relevant post-operative pancreatic fistula, CR-POPF), 包括 B/C 级胰瘘^[3]。术前通过高敏感度、无创的影像学方法预测患者胰腺切除术后并发 CR-POPF 的风险, 有助于高危患者的围手术期临床管理, 对于指导术后并发症的处理及改善胰腺肿瘤患者预后具有重要的临床价值^[4-5]。

既往研究^[6-7]回顾性地对胰十二指肠切除术后并发 CR-POPF 的潜在危险因素进行了探索, 并提出基于围手术期临床参数的 CR-POPF 预测模型。目前临床上较为广泛应用的模型包括2013年由CALLERY等^[6]提出的胰瘘风险评分 (fistula risk score, FRS), 其纳入的危险因素包括胰腺质地较软、主胰管内径较窄、术中失血量较多及特定的胰腺肿瘤病理类型 (如胰腺腺癌), 均与 CR-POPF 的发生显著相关。2019年, MUNGROOP 等^[7]提出了改良胰瘘风险评分 (alternative fistula risk score, a-FRS) 模型, 保留了胰腺质地较软与主胰管内径较窄2项高危因素, 同时

增加了患者体质量指数 (body mass index, BMI) 较高作为危险因素; 通过大样本量回顾, 进一步验证了其在预测 CR-POPF 中的诊断效力。胰腺质地较软作为独立的危险因素, 与 CR-POPF 的发生和严重程度显著相关; 既往外科医师多通过术中触诊的方式, 定性评估胰腺质地的软硬度, 但触诊结果无法提供足够的客观性与可重复性^[8], 同时也无法实现术前诊断, 限制了其在临床实践中的进一步应用。

超声剪切波弹性成像 (shear wave elastography, SWE) 是一种可以无创、量化组织弹性的影像学方法, SWE 检测值与胰腺组织纤维化程度存在显著正相关^[9]。我们既往的研究^[2]显示, 通过 SWE 定量评估胰腺肿瘤及其周围正常胰腺实质软硬度, 结果具有良好的可靠性及可重复性, 对于评估胰腺切除术后并发 CR-POPF 具有潜在临床价值。

本研究的目的是通过结合 SWE 定量参数与临床关键危险因素, 构建改良的 CR-POPF 预测模型, 实现术前无创、定量、客观地评估胰腺切除术后并发 CR-POPF 的风险。

1 对象与方法

1.1 研究对象

本研究为前瞻性研究, 纳入2021年9月至2022年3月复旦大学附属中山医院就诊的胰腺肿瘤患者。

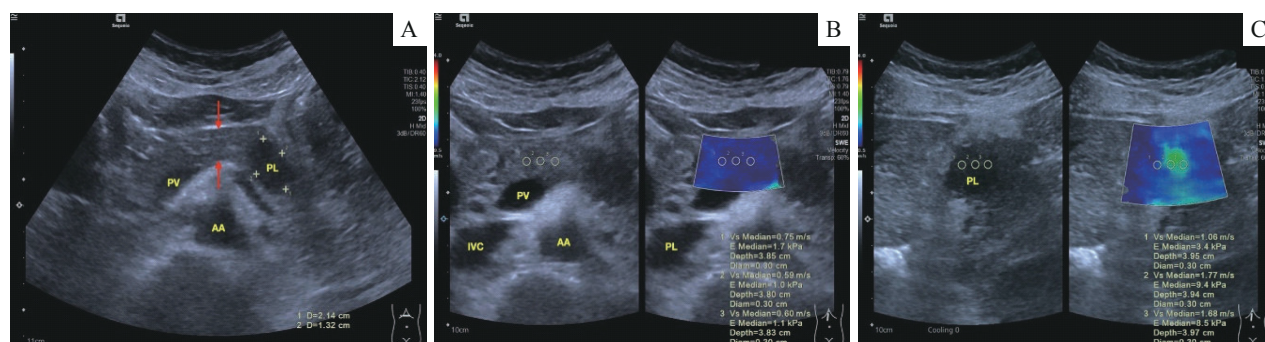
纳入标准:①患者年龄 ≥ 18 岁,充分知情本研究内容并自愿参与。②经影像学诊断为胰腺肿瘤,且评估为手术可切除的病灶,拟于复旦大学附属中山医院接受胰腺切除术(胰十二指肠切除术/胰体尾切除术)者。③手术前未接受放射治疗、化学治疗等其他治疗方式。④胰腺病灶及周边正常腺体实质在二维灰阶超声(B mode ultrasound, BMUS)图像上可清晰显示,病灶与体表深度介于2~10 cm,内部以实质回声为主。排除标准:①患者一般情况较差,存在周围组织或远处转移,或具有其他手术禁忌证者。②患者计划接受姑息性手术、剖腹探查、穿刺活检或内科治疗者。③接受再手术者。④无法配合完成术前超声评估或其他必要检查者。⑤要求退出研究者。

1.2 研究方法

1.2.1 收集患者术前临床资料 收集患者术前的临床特征与指标,包括性别、年龄、BMI和实验室检查结果[血清 γ -谷氨酰转移酶(γ -glutamyltransferase,

γ -GT)、三酰甘油(triacylglycerol, TAG)和胆固醇水平]。

1.2.2 术前BMUS检查与SWE定量评估胰腺质地 术前超声检查使用Siemens ACUSON Sequoia超声诊断及腹部探头5C-1(1~6 MHz)进行,配备声触诊组织弹性成像与量化技术(virtual touch tissue imaging and quantification technology, VTIQ)完成胰腺术前SWE的定量评估(图1)。首先在BMUS清晰显示病灶的情况下,观察并记录病灶大小、边界、形态、内部回声特征、有无囊变/钙化/坏死区及主胰管内径大小,并通过彩色血流成像检测病灶内部血流情况。然后切换至VTIQ模式,在病灶内设置3个相同深度的感兴趣区域(region of interest, ROI)测量组织弹性定量剪切波速度(shear wave velocity, SWV)值(m/s)。重复此步骤3次,计算平均SWV值以代表病灶组织软硬度。最后,在距离病灶边缘至少1 cm的门静脉前方胰体部正常腺体实质内重复上述的测量步骤,以获得正常胰腺组织的SWV参考值。



Note: A. The body part of pancreatic parenchyma (red arrows) in the superficial layer of portal vein was clearly displayed on BMUS with a lesion located in the body-tail part of pancreas (yellow cursors). B. VTIQ assessment makes the visualization of relative elasticity of target tissues. The body part of pancreatic parenchyma appeared in an evenly blue color, which indicated a relatively low elasticity. C. VTIQ revealed an unevenly green color in the pancreatic lesion, which indicated a relatively high elasticity. The circles in B and C indicate the ROIs in the pancreatic parenchyma and the lesions, respectively, and the SWV values were detected. AA—abdominal aorta; IVC—inferior vena cava; PL—pancreatic lesion; PV—portal vein.

图1 1例胰导管腺癌患者的术前BMUS影像及SWE定量评估

Fig 1 Preoperative BMUS imaging and quantitative evaluation of SWE in a patient with pancreatic ductal adenocarcinoma

1.2.3 收集患者术中临床信息 术中的临床信息包括手术类型(胰十二指肠切除术/胰体尾切除术)、手术持续时间、术中失血量和通过外科医师直接触诊定性评估的胰腺质地(软、中等-硬)。术中触诊由一位经验丰富的高年资外科医师进行,且外科医师术前未被告知SWE结果。术后经组织病理学检查,确定胰腺肿瘤的最终诊断。

1.2.4 CR-POPF的诊断与分级 术后胰瘘的诊断与分级是根据ISGPF于2016年制定的标准^[3]。在本研究中,只有当术后引流液淀粉酶水平达到正常血清值

上限的3倍以上,同时出现感染相关症状/体征时,诊断为B级胰瘘;若出现严重术后出血、多器官衰竭或患者需要再手术,甚至死亡时,则诊断为C级胰瘘。B/C级胰瘘均属于CR-POPF。

1.3 统计学分析

应用SPSS 26.0软件进行统计分析。定量资料用 $\bar{x} \pm s$ 表示,2组之间比较采用 t 检验;定性资料用频数(百分比)表示,2组之间比较采用 χ^2 检验。通过单因素和多因素Logistic回归分析建立CR-POPF预测模

型, 通过受试者工作特征曲线 (receiver-operating characteristic curve, ROC 曲线) 和决策曲线分析 (decision curve analysis, DCA) 评估模型的诊断效力及临床效益。所有检验均为双侧检验, 当 $P < 0.05$ 时表示有统计学意义。

2 结果

2.1 患者一般信息

2021年9月至2022年3月, 按纳排标准本研究共纳入100名胰腺肿瘤患者, 包括57名男性和43名女性, 年龄为 (59.3 ± 13.2) 岁, BMI 为 (23.2 ± 3.2) kg/m^2 ; 其中33例 (33.0%) 患者接受了胰十二指肠切除术,

67例 (67.0%) 患者接受了胰体尾切除术, 术后病理结果示于表1。通过术后3周的临床随访, 58例 (58.0%) 患者并发POPF, 包括23例 (39.7%, 23/58) 无症状A级胰瘘 (生化瘘)、35例 (60.3%, 35/58) 例B级胰瘘, 无患者发生C级胰瘘。对于CR-POPF的处理包括引流、抗生素和胰酶抑制剂的应用、营养支持治疗, 所有患者预后良好。

CR-POPF 阳性组和阴性组的性别、年龄、BMI, 以及实验室检查结果和术后病理诊断为胰腺腺癌 [包括胰腺导管腺癌 (pancreatic ductal adenocarcinoma, PDAC) 和胰腺腺鳞癌 (pancreatic adeno-squamous cancer, PASC)] 的患者比例差异均无统计学意义 (均 $P > 0.05$, 表1)。

表1 CR-POPF 阳性和阴性的胰腺肿瘤患者临床特征的比较

Tab 1 Comparison of clinical characteristics between CR-POPF-positive and -negative pancreatic tumor patients

| Index | CR-POPF positive (n=35) | CR-POPF negative (n=65) | t/χ^2 value | P value |
|--|-------------------------|-------------------------|------------------|---------|
| Gender/n(%) | | | 0.396 | 0.529 |
| Male | 16 (45.7) | 34 (52.3) | | |
| Female | 19 (54.3) | 31 (47.7) | | |
| Age/year | 57.7 ± 14.4 | 60.1 ± 12.5 | 0.887 | 0.378 |
| BMI/($\text{kg} \cdot \text{m}^{-2}$) | 23.5 ± 2.9 | 23.1 ± 3.3 | -0.702 | 0.484 |
| γ -GT>150 $\text{U} \cdot \text{L}^{-1}/\text{n}(\%)$ | 4 (11.4) | 16 (24.6) | 2.473 | 0.116 |
| TAG>1.7 $\text{mmol} \cdot \text{L}^{-1}/\text{n}(\%)$ | 10 (28.6) | 18 (27.7) | 0.009 | 0.926 |
| Cholesterol>5.2 $\text{mmol} \cdot \text{L}^{-1}/\text{n}(\%)$ | 6 (17.1) | 12 (18.5) | 0.027 | 0.870 |
| Diabetes mellitus/n(%) | 4 (11.4) | 16 (24.6) | 2.473 | 0.116 |
| Lesion size/mm | 29.6 ± 14.8 | 29.8 ± 14.1 | 0.081 | 0.935 |
| MPD diameter ≤ 3 mm/n(%) | 29 (82.9) | 36 (55.4) | 7.547 | 0.006 |
| SWV value/($\text{m} \cdot \text{s}^{-1}$) | | | | |
| Pancreatic parenchyma | 0.86 ± 0.18 | 1.24 ± 0.45 | 5.941 | 0.000 |
| Lesion | 1.42 ± 0.60 | 1.41 ± 0.64 | -0.078 | 0.938 |
| Lesion-parenchyma ratio | 1.69 ± 0.72 | 1.24 ± 0.68 | -3.044 | 0.003 |
| Surgery type/n(%) | | | 1.293 | 0.256 |
| Pancreaticoduodenectomy | 9 (25.7) | 24 (36.9) | | |
| Distal pancreatectomy | 26 (74.3) | 41 (63.1) | | |
| Surgery duration/min | 178.3 ± 66.7 | 195.7 ± 80.6 | 1.091 | 0.278 |
| Blood loss/mL | 138.3 ± 131.0 | 119.2 ± 139.8 | -0.664 | 0.508 |
| Palpation of pancreas/n(%) | | | 1.876 | 0.171 |
| Soft | 19 (54.3) | 26 (40.0) | | |
| Medium-hard | 16 (45.7) | 39 (60.0) | | |
| Pathological diagnosis of PDAC/PASC/n(%) | 13 (37.1) | 37 (56.9) | 3.560 | 0.059 |
| FRS/point | 4.9 ± 1.3 | 3.8 ± 1.8 | -2.891 | 0.005 |
| a-FRS/% | 60.6 ± 27.2 | 21.3 ± 23.2 | -7.593 | 0.000 |

Note: MPD—main pancreatic duct; FRS—fistula risk score (CALLERY et al, 2013); a-FRS—alternative fistula risk score (MUNGROOP et al, 2019).

2.2 术前超声影像学特征与剪切波弹性成像

术前BMUS检查显示,CR-POPF阳性组和阴性组之间病灶大小差异无统计学意义($P=0.935$)。CR-POPF阳性组中,主胰管内径 ≤ 3 mm的患者比例显著高于CR-POPF阴性组($P=0.006$)。VTIQ测量结果显示:CR-POPF阳性组中门静脉前方胰体部正常腺体实质测得的SWV值显著低于CR-POPF阴性组($P=0.000$);2组间病灶内SWV值差异无统计学意义($P=0.938$);CR-POPF阳性组病灶与周围胰腺实质的SWV比值显著高于CR-POPF阴性组($P=0.003$)。见表1。

2.3 患者术中相关临床信息

在CR-POPF阳性组和阴性组之间,接受胰十二指肠切除术或胰体尾切除术的患者比例差异无统计学

意义($P=0.256$)。通过外科医师术中对胰腺的直接触诊,术者定性评估为质地软和质地中等-硬的比例在CR-POPF阳性组与阴性组间差异无统计学意义($P=0.171$)。2组的平均手术时间和术中失血量之间差异也无统计学意义(均 $P>0.05$)。见表1。

2.4 改良CR-POPF模型的建立

先对术前VTIQ测得的SWE定量值与围手术期临床上可能相关的因素进行单因素Logistic回归分析,然后将 $P<0.05$ 的变量纳入多因素Logistic回归分析;结果显示,门静脉前方胰体部实质的低SWV值[lgOR=-2.934(95%CI -4.387~-1.479), $P=0.000$]和较窄的主胰管内径(≤ 3 mm)[lgOR=0.805(95%CI 0.274~1.335), $P=0.003$]是CR-POPF的独立危险因素(表2)。

表2 单因素和多因素Logistic回归分析CR-POPF发生的相关因素

Tab 2 Univariate and multivariate Logistic regression analysis of related factors of CR-POPF

| Variables | Univariate | | Multivariate | | |
|----------------------------------|------------------------|---------|--------------|------------------------|---------|
| | lgOR (95%CI) | P value | B value | lgOR (95%CI) | P value |
| Gender (female) | 0.115 (-0.243~0.473) | 0.530 | — | — | — |
| Age | -0.006 (-0.020~0.007) | 0.375 | — | — | — |
| BMI | 0.020 (-0.036~0.077) | 0.480 | — | — | — |
| Diabetes mellitus | 0.043 (-0.111~0.918) | 0.124 | — | — | — |
| γ -GT level (>150 U/L) | 0.403 (-0.111~0.918) | 0.124 | — | — | — |
| Lesion size | -0.001 (-0.013~0.012) | 0.935 | — | — | — |
| MPD diameter (≤ 3 mm) | -0.590 (-1.027~-0.153) | 0.008 | 1.852 | 0.805 (0.274~1.335) | 0.003 |
| SWV of pancreatic parenchyma | -2.441 (-3.635~-1.248) | 0.000 | -6.755 | -2.934 (-4.387~-1.479) | 0.000 |
| Palpation of pancreas (soft) | -0.251 (-0.611~0.110) | 0.173 | — | — | — |
| Surgery type (PD) | 0.228 (-0.167~0.623) | 0.258 | — | — | — |
| Constant | — | — | 4.737 | 2.057 | 0.002 |

CR-POPF的发生概率可基于以下公式计算获得:

$$\text{发生概率} = \frac{1}{(1 + e^{-1.852[\text{MPD}] + 6.755[\text{SWV}] - 4.737})}。$$

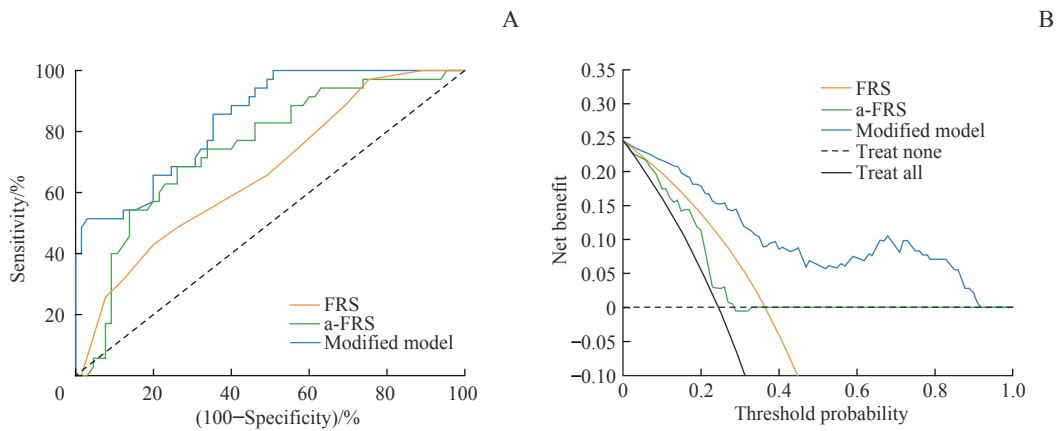
当主胰管内径 ≤ 3 mm时,[MPD]=1;当主胰管内径 >3 mm时,[MPD]=0;[SWV]=门静脉前方胰体部实质SWV值(m/s)。

2.5 CR-POPF风险评估模型的比较

基于SWE的改良模型在预测胰腺切除术后并发CR-POPF的ROC曲线下面积为0.842,敏感度、特异度、阳性预测值、阴性预测值和似然比分别为85.7%、

64.6%、70.5%、81.8%和2.422(图2,表3)。

与既往基于围手术期CR-POPF危险因素的临床模型^[6-7]相比,基于SWE的改良模型显示出良好的诊断效能。通过DCA分析,改良模型的应用对比既往模型可以提供更好的临床预测效益(图2)。图3显示了本研究中的CR-POPF阳性组和阴性组患者分别采用3种CR-POPF预测模型计算发生概率/风险评分后的频数分布,结果表明改良模型的临界预测概率可以有效预测CR-POPF($P=0.000$)。其中,门静脉前方胰体部实质的SWV值作为连续变量,对CR-POPF风险预测的敏感度更高。



Note: A. ROC curves of 3 models. B. Decision curves of 3 models.

图2 基于SWE的改良模型和既往临床模型对于预测CR-POPF的ROC曲线和决策曲线

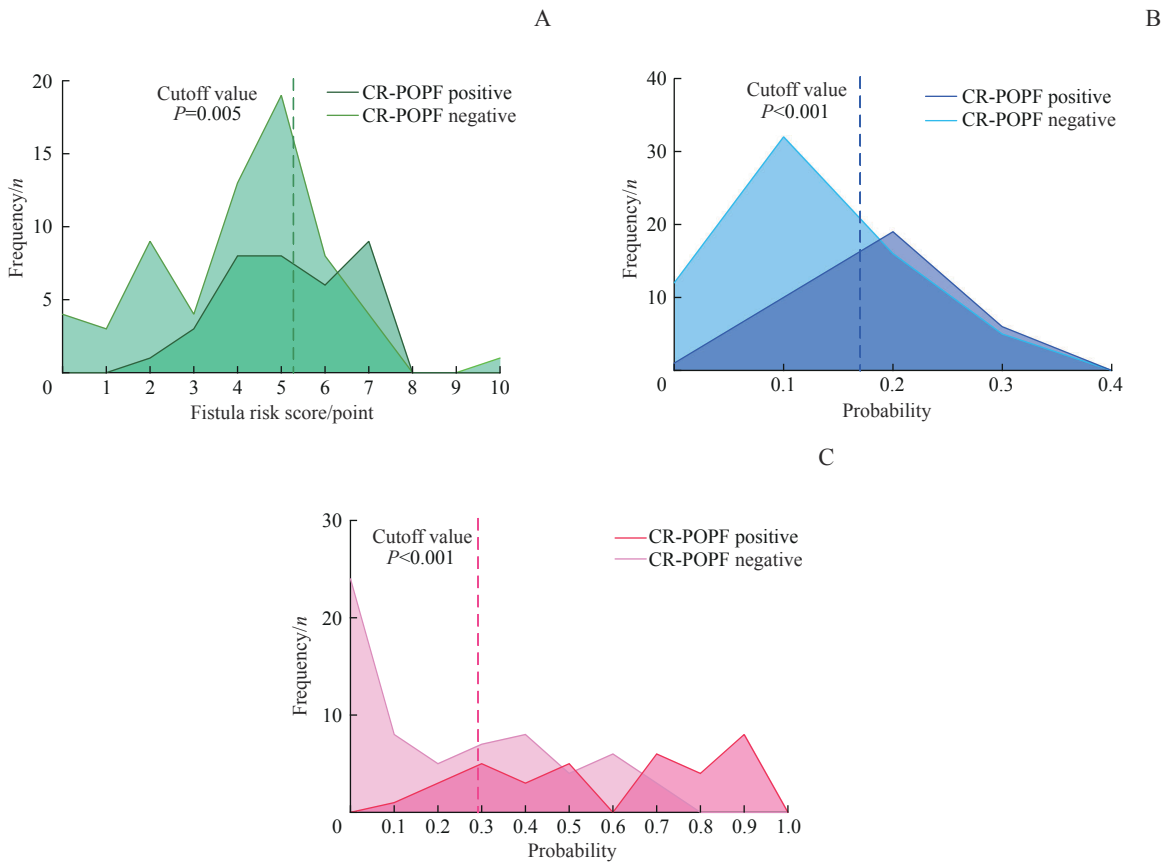
Fig 2 ROC curves and decision curves of the modified model based on SWE and previous clinical models in the prediction of CR-POPF

表3 基于SWE的改良模型和既往临床模型对于预测CR-POPF的诊断效能

Tab 3 Diagnostic efficacy of the modified model based on SWE and previous clinical models in predicting CR-POPF

| Model | AUROC | Sensitivity/% | Specificity/% | PPV/% | NPV/% | Likelihood ratio |
|----------------|-------|---------------|---------------|-------|-------|------------------|
| FRS | 0.665 | 42.9 | 80.0 | 68.2 | 58.4 | 2.143 |
| a-FRS | 0.744 | 68.6 | 73.9 | 72.4 | 70.2 | 2.622 |
| Modified model | 0.842 | 85.7 | 64.6 | 70.5 | 81.8 | 2.422 |

Note: AUROC—area under the receiver operating characteristic curve; PPV—positive predictive value; NPV—negative predictive value.



Note: A. FRS. B. a-FRS. C. Modified model.

图3 CR-POPF阳性组和阴性组患者采用基于SWE的改良模型和既往临床模型计算后的频数分布

Fig 3 Frequency distributions of CR-POPF-positive group and -negative group calculated by the modified model based on SWE and previous clinical models

3 讨论

术前预测 CR-POPF 可以确保高危患者在围手术期获得及时有效的临床干预,避免手术相关腹腔内感染、大出血甚至是患者死亡的情况发生;改善胰腺肿瘤患者的预后,一直以来得到外科医师的广泛关注。2013 年 CALLERY 等^[6]提出的 FRS 模型及 2019 年 MUNGROOP 等^[7]提出的 a-FRS 模型是目前临床使用较为广泛的 CR-POPF 预测模型,通过综合评估围手术期 CR-POPF 的危险因素,为临床提供了预测 CR-POPF 的可行方法。然而,FRS 中的许多危险因素,例如胰腺质地软硬度及术后病理诊断,难以在术前被有效地定量评估,影响了其临床实际应用的价值^[10]。另外术中通过外科医师触诊定性评估的胰腺质地,对于操作者的经验依赖性高,触诊结果在不同术者间存在较大差异,导致预测值的偏差及不可重复性^[11]。因此,亟需一种术前无创、定量的 CR-POPF 改良风险模型预测方法,这将有助于提高临床术前预测的客观性与准确性。

作为一种无创超声定量触诊的影像学方法,SWE 可以实现对胰腺病灶及其周围正常胰腺实质弹性无创、定量的评估^[12]。VTIQ 技术作为新一代的超声剪切波技术,不仅可以直观地用颜色显示局部组织的相对软硬度,而且可以设置多个 ROI,定量测量组织内的 SWV 值。在实时显示组织相对弹性图像的条件下,SWV 值具有高度的可重复性,有助于标准化测量结果;其或可作为既往术中直接接触胰腺的替代方案,在预测胰腺切除术后并发 CR-POPF 中具有潜在的临床价值^[2,9]。

既往的研究^[13-14]曾应用 CT 或 MRI 的方法定量评估胰腺的纤维化程度或脂肪浸润,并探讨其在评估胰十二指肠切除术后并发 CR-POPF 的可能性。CT 根据靶组织的造影剂积聚程度评估组织纤维化程度,从而间接推测组织软硬度,评估的结果可能无法提供足够的准确性与可重复性^[13]。此外,胰腺实质的其他弥漫性改变,如扩张主胰管的支持作用,也可直接影响胰腺组织的软硬度^[15]。MRI 弹性成像虽然可以客观地定量评估靶组织弹性,敏感度与特异度均可达 70% 以上,但其检查过程十分耗时且费用昂贵^[14]。两者均不适合作为常规术前检查项目。与 CT 或 MRI 定量方法相比,超声 SWE 检测具有实时成像、可定量、观察角度灵活多变、无创、无辐射等诸多优势,

适合在临床推广应用。

我们基于超声 SWE 定量测值和术前临床关键危险因素,构建了改良的 CR-POPF 预测模型,实现了影像学对胰腺切除术前 CR-POPF 风险定量、客观的评估。ROC 曲线分析结果显示其预测 CR-POPF 的 ROC 曲线下面积达 0.842,敏感度、特异度、阳性预测值、阴性预测值及似然比分别为 85.7%、64.6%、70.5%、81.8% 及 2.422,具有足够的诊断效能。DCA 显示,相较于既往的临床预测模型,改良模型可以提供更好的临床效益。最终被纳入改良模型的参数包括主胰管内径(是否 ≤ 3 mm)以及门静脉前方胰体部正常实质的超声弹性定量 SWV 值。两者均可通过术前常规 BMUS 影像学表现,结合 SWE 准确定量评估,对于高危患者的围手术期管理可以提供重要的参考信息。

本研究的局限性为样本量较小,以及缺乏外部验证。在未来的研究中,我们计划通过持续增加样本量来进一步验证改良模型的预测效力,并通过多中心队列研究进行外部验证。

综上所述,基于 SWE 对胰腺组织质地的定量评估,并结合临床关键危险因素的改良胰瘘风险评估模型,可以提高 CR-POPF 术前评估的客观性及可靠性,为临床决策提供有效的参考。

利益冲突声明/Conflict of Interests

所有作者声明不存在利益冲突。

All authors disclose no relevant conflict of interests.

伦理批准和知情同意/Ethics Approval and Patient Consent

本研究涉及的所有操作均已通过复旦大学附属中山医院科学伦理委员会的审核批准(文件号 B2020-309R)。所有过程均遵照《赫尔辛基宣言》的条例进行。受试对象或其亲属已经签署知情同意书。All experimental protocols in this study were reviewed and approved by Ethics Committee of Zhongshan Hospital, Fudan University (Approval Letter No. B2020-309R), and all experimental protocols were carried out by following Declaration of Helsinki. Consent letters have been signed by the research participants or their relatives.

作者贡献/Authors' Contributions

董怡、楼文晖、田晓梵、王文平参与了研究设计;田晓梵负责实施研究、搜集并整理数据;田晓梵、左丹参与了数据分析;田晓梵、张琪、邱艺杰参与了论文的写作和修改。所有作者均阅读并同意了最终稿件的提交。

The study was designed by DONG Yi, LOU Wenhui, TIAN Xiaofan, and WANG Wenping. TIAN Xiaofan conducted the research, and collected and organized the original data. Data analysis was conducted

by TIAN Xiaofan and ZUO Dan. The manuscript was drafted and revised by TIAN Xiaofan, ZHANG Qi, and QIU Yijie. All the authors have read the last version of paper and consented for submission.

• Received: 2022-10-10
• Accepted: 2023-03-14
• Published online: 2023-04-28

参 · 考 · 文 · 献

- [1] AOYAMA T, MURAKAWA M, KATAYAMA Y, et al. Impact of postoperative complications on survival and recurrence in pancreatic cancer[J]. *Anticancer Res*, 2015, 35(4): 2401-2409.
- [2] TIAN X F, KUANG T T, DONG Y, et al. Prediction of pancreatic fistula after pancreatectomy by virtual touch tissue imaging and quantification (VTIQ) technology[J]. *Pancreatol*, 2021, 21(8): 1498-1505.
- [3] BASSI C, MARCHEGANI G, DERVENIS C, et al. The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 years after[J]. *Surgery*, 2017, 161(3): 584-591.
- [4] KAWAIDA H, KONO H, HOSOMURA N, et al. Surgical techniques and postoperative management to prevent postoperative pancreatic fistula after pancreatic surgery[J]. *World J Gastroenterol*, 2019, 25(28): 3722-3737.
- [5] WILLIAMSSON C, ANSARI D, ANDERSSON R, et al. Postoperative pancreatic fistula-impact on outcome, hospital cost and effects of centralization[J]. *HPB (Oxford)*, 2017, 19(5): 436-442.
- [6] CALLERY M P, PRATT W B, KENT T S, et al. A prospectively validated clinical risk score accurately predicts pancreatic fistula after pancreatectomy[J]. *J Am Coll Surg*, 2013, 216(1): 1-14.
- [7] MUNGROOP T H, VAN RIJSSEN L B, VAN KLAVEREN D, et al. Alternative fistula risk score for pancreatectomy (a-FRS): design and international external validation[J]. *Ann Surg*, 2019, 269(5): 937-943.
- [8] HATANO M, WATANABE J, KUSHIHATA F, et al. Quantification of pancreatic stiffness on intraoperative ultrasound elastography and evaluation of its relationship with postoperative pancreatic fistula[J]. *Int Surg*, 2015, 100(3): 497-502.
- [9] KUWAHARA T, HIROOKA Y, KAWASHIMA H, et al. Quantitative evaluation of pancreatic tumor fibrosis using shear wave elastography[J]. *Pancreatol*, 2016, 16(6): 1063-1068.
- [10] 罗海峰, 高雪, 杜渐, 等. 胰十二指肠切除术后胰瘘发生的危险因素分析[J]. *中华消化外科杂志*, 2017, 16(10): 1036-1041.
- [11] LUO H F, GAO X, DU J, et al. Analysis of risk factors of postoperative pancreatic fistula after pancreaticoduodenectomy[J]. *Chinese Journal of Digestive Surgery*, 2017, 16(10): 1036-1041.
- [12] TAJIMA Y, KAWABATA Y, HIRAHARA N. Preoperative imaging evaluation of pancreatic pathologies for the objective prediction of pancreatic fistula after pancreaticoduodenectomy[J]. *Surg Today*, 2018, 48(2): 140-150.
- [13] LEE T K, KANG C M, PARK M S, et al. Prediction of postoperative pancreatic fistulas after pancreatectomy: assessment with acoustic radiation force impulse elastography[J]. *J Ultrasound Med*, 2014, 33(5): 781-786.
- [14] SHI H Y, LU Z P, LI M N, et al. Dual-energy CT iodine concentration to evaluate postoperative pancreatic fistula after pancreatectomy[J]. *Radiology*, 2022, 304(1): 65-72.
- [15] YOON J H, LEE J M, LEE K B, et al. Pancreatic steatosis and fibrosis: quantitative assessment with preoperative multiparametric MR imaging[J]. *Radiology*, 2016, 279(1): 140-150.
- [16] FUJITA Y, KITAGO M, ABE T, et al. Evaluation of pancreatic fibrosis with acoustic radiation force impulse imaging and automated quantification of pancreatic tissue components[J]. *Pancreas*, 2018, 47(10): 1277-1282.

[本文编辑] 瞿麟平