Relation of Tricuspid Regurgitation to Liver Stiffness Measured by Transient Elastography in Patients With Left-Sided Cardiac Valve Disease

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The aim of the study was to evaluate the relation between tricuspid regurgitation (TR) severity and liver stiffness (LS) in patients with TR. A total of 131 patients with various degrees of TR secondary to left-sided heart valve disease were enrolled. Severity of TR was quantitatively assessed by proximal isovelocity surface area−derived effective regurgitant orifice (ERO). Patients were divided into 2 groups: 48 with mild−moderate TR (ERO <0.4 cm^2) and 83 with severe TR (ERO ≥0.4 cm^2). Transient elastography was used to measure the level of LS, an established marker of liver fibrosis, with the threshold of significant LS set at ≥12.5 kPa. Patients with severe TR had a higher LS and prevalence of significant LS than those with mild −moderate TR. Furthermore, LS and significant LS independently correlated with TR-ERO, right atrial pressure and inferior vena cava (IVC) diameter. The presence of a large TR-ERO (≥0.4 cm^2) and IVC diameter (>2.15 cm^2) provided a high specificity of 78% for significant LS. In conclusion, the present study demonstrates that TR-ERO, right atrial pressure, and IVC diameter are important parameters associated with LS in patients with TR. **(Am J Cardiol 2016;117:640−646)**

Significant tricuspid regurgitation (TR) is not uncommon[1] and is often found in patients with left-sided heart valvular disease.[2,3] In addition to causing right-sided heart failure, the presence of TR can lead to irreversible liver derangement and cirrhosis.[4−6] Accurate assessment of the degree of liver dysfunction in patients with TR is also difficult because significant liver injury may develop well in advance of abnormal serum liver biochemistry.[6,7] Consequently, the relation between TR severity and liver dysfunction has not been evaluated in detail. The proximal isovelocity surface area (PISA) method enables accurate quantitative assessment of TR and is superior to the conventional estimation by regurgitant jet area that provides only a semiquantitative assessment.[8] In addition, transient elastography (TE) is an ultrasound-based, noninvasive, and reliable technique to measure liver stiffness (LS) and has been universally recognized as a quantitative marker for liver fibrosis assessment.[9,10] Therefore, the aim of the present study was to innovatively evaluate the relation between TR severity evaluated by the PISA method and detailed echocardiography parameters and LS as measured by TE in patients with TR.

Methods

From November 2012 to August 2014, 143 consecutive Chinese patients with variable degrees (mild to severe) of TR secondary to left-sided heart valvular disease, aged >18 and referred to the Department of Cardiology at Queen Mary Hospital were recruited. A total of 12 patients with the following condition were excluded: poor quality echocardiography images (n = 2), congenital heart disease (n = 3), viral hepatitis B or C (n = 5), excessive alcohol intake (n = 2), acute liver failure, or other terminal illness. Accordingly, 131 patients were included in the final analysis. The study was part of the Chinese Valvular Heart Disease Study to evaluate Chinese patients with valvular heart disease in an attempt to evaluate the pattern of disease, pathophysiology, and clinical outcome in these patients.[11] The local institutional ethics board approved the study, and all subjects gave written informed consent.

Data on baseline clinical demographics and fasting blood samples were obtained on the same day from all study subjects. The cause of valvular heart disease was recorded. New York Heart Association classification was given as class I/II and class III/IV, and the status of valvular atrial fibrillation (AF) was also recorded for each subject. Laboratory blood tests including complete blood count, liver function, renal function, and hepatitis B and C virology were measured. Body mass index and conventional cardiovascular risk factors were also documented.

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See page 646 for disclosure information.

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Table 1
Clinical and echocardiographic parameters in patients with mild−moderate and severe tricuspid regurgitation

Variables	Tricuspid regurgitation		*P*
	Mild-moderate (n=48)	Severe (n=83)	
Clinical characteristics			
Age (years)	64±10	65±10	0.51
Male	19(40%)	30(36%)	0.70
Body mass index (kg/m^2)	21.7±3.0	21.6±2.8	0.86
Systolic blood pressure (mmHg)	131±17	126±20	0.39
Diastolic blood pressure (mmHg)	75±9	69±15	0.11
Liver stiffness measurement (kPa)	9.4±7.6	20.1±13.4	<0.01
Platelet (10^9/L)	221±80	174±69	<0.01
Haemoglobin (g/dL)	13±2.0	11±2.0	<0.01
Creatinine (umol/L)	88±27	95±48	0.34
Total protein (g/L)	76±6	74±8	0.09
Albumin (g/L)	42±4	39±5	<0.01
Globulin (g/L)	34±6	35±7	0.63
Bilirubin (umol/L)	17±13	22±13	0.03
Alkaline phosphatase (u/L)	93±65	97±44	0.67
Alanine aminotransferase (u/L)	23±13	24±17	0.73
Aspartate aminotransferase (u/L)	33±23	40±22	0.11
Hypertension	7(15%)	15(18%)	0.61
Diabetes mellitus	7(15%)	18(22%)	0.32
Hypercholesterolemia	8(17%)	8(10%)	0.24
Atrial fibrillation	28(58%)	72(87%)	<0.01
Native valvular lesion (n = 77)			
Mitral stenosis	12(33%)	18(44%)	0.68
Mitral regurgitation	17(47%)	14(34%)	
Aortic stenosis	5(14%)	7(17%)	
Aortic regurgitation	2(6%)	2(5%)	
Surgical details (n = 54)			
Mitral valve replacement	6(50%)	19(45%)	0.59
Mitral valve repair	1(8%)	2(5%)	
Aortic valve replacement	2(17%)	3(7%)	
Dual valvular replacement	3(25%)	18(43%)	
New York Heart Association			
I	21(44%)	28(34%)	0.34
II	20(42%)	33(40%)	
III	7(14%)	20(24%)	
IV	0	2(2%)	
Echocardiographic parameters			
Left ventricular end-diastolic septal wall thickness (cm)	11.6±2.3	11.7±2.4	0.82
Left ventricular end-diastolic diameter (cm)	48.9±9.5	49.3±9.3	0.78
Left ventricular end-diastolic posterior wall thickness (cm)	10.9±2.1	11.4±1.9	0.20
Left ventricular end-diastolic volume (ml)	92.5±44.0	92.5±41.8	0.99
Left ventricular end-systolic volume (ml)	37.3±21.6	39.8±26.2	0.57
Left ventricular ejection fraction (%)	60.8±7.9	58.6±9.2	0.16
Right ventricular end-diastolic area (cm^2)	13.8±3.4	20.4±8.1	<0.01
Right ventricular end-systolic area (cm^2)	7.6±2.6	11.2±4.6	<0.01
Right ventricular fractional area change (%)	46.1±8.8	44.8±9.7	0.45
Tricuspid annular plane systolic excursion (cm)	1.8±0.4	1.6±0.4	<0.01
Right ventricular systolic pressure (mmHg)	42.4±12.7	50.6±15.1	<0.01
Tricuspid regurgitation- effective regurgitant orifice (cm^2)	0.19±0.07	1.05±1.08	<0.01
Right atrial pressure (mmHg)	7.3±4.0	12.3±3.7	<0.01
Inferior vena cava (cm)	1.9±0.4	2.5±0.7	<0.01

Values are mean ± SD or n (%).

Detailed transthoracic echocardiography was performed in all subjects using a commercially available echocardiography system (Vingmed E9, General Electric Vingmed Ultrasound, Milwaukee). Left ventricular (LV) and right-sided heart echocardiographic parameters were measured according to the current recommendations.[12,13] From the apical 4-chamber views, right ventricular end-diastolic area (RVEDA) and RV end-systolic area (RVESA) were measured by manually tracing the RV endocardial border, and RV fractional area change was calculated from the following equation: (RVEDA−RVESA)/RVEDA × 100%.[13] Tricuspid annular plane systolic excursion (TAPSE) was measured by the M mode. From the subcostal view, the long-axis diameter of the inferior vena cava (IVC) was measured at end expiration. Then, specific values of right atrial pressure (RAP) were estimated from the IVC diameter and respiratory changes according to the current recommendations.[13] Finally, RV systolic pressure (RVSP) was determined from peak TR velocity by continuous-wave Doppler using simplified Bernoulli equation and combining this value with an estimate of the RAP: $RVSP = 4(V)^2 + RAP$, where V indicates peak velocity of tricuspid regurgitation.

The severity of TR was quantified by effective regurgitant orifice (ERO) using PISA method.[8] The PISA method, as previously described,[8,14,15] allows accurate calculation of ERO, combining the measurement of tricuspid flow and its velocity by continuous-wave Doppler. Briefly, color Doppler images of TR proximal flow convergence were obtained from apical 4-chamber views and zoomed to the region of interest. The color-flow velocity scale was maximized, and the baseline was shifted downward until the flow convergence region was visualized clearly. The Nyquist velocity range (color scale) was selected from 0.39 to 0.60 m/s for TR. Radial distance between the first aliasing velocity (red/blue interface) and the center of the tricuspid orifice was measured to calculate regurgitant flow in mid systole. The ERO area was then calculated as the ratio of regurgitant flow to the peak velocity of the TR jet. Patients were further divided into 2 groups on the basis of their TR severity: 48 patients with mild−moderate TR (ERO <0.4 cm^2) and 83 with severe TR (ERO ≥ 0.4 cm^2).[15]

TE was used to estimate the level of LS and performed by a professionally trained operator, blinded to clinical data, with a FibroScan (Echosens, Paris, France) using an M probe. Details of the technique and examination procedure