Reversibility of liver stiffness after tricuspid annuloplasty: a case-control study (abridged secondary publication)

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KEY MESSAGES

1. Patients who underwent combined tricuspid annuloplasty (TA) and left-sided heart valve surgery had higher baseline liver stiffness scores than those who underwent only left-sided heart valve surgery.
2. Liver stiffness significantly improved after TA.
3. Liver stiffness was associated with adverse outcomes in patients who underwent combined TA and left-sided valve surgery. Liver stiffness score of ≥15.5 kPa predicted the 1-year adverse outcome, with sensitivity of 72% and specificity of 62%.

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Introduction

Tricuspid regurgitation (TR) can cause irreversible liver damage. Nonetheless, the reversibility of liver stiffness is unknown after valve surgery, especially after combined tricuspid annuloplasty (TA). The aim of the present study was to evaluate the reversibility of liver stiffness after patients underwent valve surgery and to determine the prognostic role of liver stiffness in patients who underwent combined TA and left-sided heart valve surgery.

Methods

This was a prospective, observational, non-randomised study. Of 369 patients with moderate-to-severe valvular heart disease evaluated, 80 did not undergo surgery, 132 underwent left-sided heart valve surgery, and 157 underwent combined TA and left-sided heart valve surgery (Table 1). Baseline clinical, echocardiographic parameters and liver stiffness were recorded. Adverse outcome after valvular surgery was defined as the occurrence of heart failure requiring admission or all-cause mortality.

Results

Patients who underwent combined TA and left-sided heart valve surgery had the highest liver stiffness score, followed by patients who did not undergo surgery. Patients who underwent TA had higher percentage of combined mitral valve replacement and dual valvular surgery. However, nearly half of those who underwent only left-sided heart valve surgery underwent aortic valve replacement. Of 48 patients who died before 1-year follow-up liver stiffness examination, 21 (43.7%) did not undergo surgery, seven (14.6%) underwent only left-sided heart valve surgery, and 20 (41.7%) underwent combined TA and left-sided heart valve surgery.

Of 321 patients who had fibroscan test, 59 did not undergo surgery, 125 underwent only left-sided heart valve surgery, and 137 underwent combined TA and left-sided heart valve surgery. Liver stiffness improved significantly in patients who underwent combined TA and left-sided heart valve surgery but not in patients who underwent only left-sided heart valve surgery (Table 2). Liver stiffness tended to deteriorate in patients who did not undergo surgery. Improvement in liver stiffness indicated the reversibility of liver stiffness after TA.

After a median follow-up duration of 28 months in patients who underwent combined TA and left-sided heart valve surgery, 25 patients died and 25 patients developed heart failure that required hospital admission. Univariate Cox regression analysis demonstrated that adverse events were associated with age, diabetes mellitus, hypertension, New York Heart Association class III/IV, aortic valve replacement, and liver stiffness score (Table 3). Multivariable Cox regression analysis demonstrated that only age and liver stiffness score were independent predictors of adverse events (Table 3).

Receiver operating characteristic curve was generated to determine the discriminative ability of liver stiffness score in predicting adverse events at 1-year follow-up in patients who underwent combined TA and left-sided heart valve surgery. Liver stiffness score (area under the curve=0.69, P<0.01, Fig) was associated with adverse events and

TABLE 1. Baseline characteristics of patients

Variable	Patients without surgery (n= 80)*	Patients with only left-sided heart valve surgery (n=132)*	Patients with combined TA and left-sided heart valve surgery (n=157)*	P value (one-way ANOVA)
Age, y	65.6±11.3	62.2±8.7†	63.4±8.6	0.03
Male	26 (32.5)	65 (49.2)†	56 (35.7)‡	0.02
Diabetes mellitus	14 (17.5)	27 (20.5)	31 (19.7)	0.87
Hypertension	21 (26.3)	51 (38.6)	33 (21.0)‡	<0.01
Hyperlipidaemia	9 (11.3)	39 (29.5)†	26 (16.6)‡	0.02
Smoking	10 (12.5)	23 (17.4)	21 (13.4)	0.52
Atrial fibrillation	48 (60.0)	37 (28.0)†	128 (81.5)‡	<0.01
Chronic rheumatic heart disease	46 (57.5)	42 (31.8)†	118 (75.2)‡	<0.01
New York Heart Association class III/IV	21 (26.3)	43 (32.6)	77 (49.0)‡	<0.01
Left ventricular ejection fraction, %	59.7±10.2	56.8±9.1	56.3±8.7‡	0.02
Pulmonary artery systolic pressure, mmHg	43.0±12.7	36.0±11.5†	48.6±13.1‡	<0.01
Moderate-to-severe tricuspid regurgitation	49 (61.3)	17 (12.9)†	138 (87.9)‡	<0.01
Residual moderate-to-severe tricuspid regurgitation after surgery	-	4 (3.0)	13 (8.3)	0.06
Concomitant coronary artery bypass graft	-	21 (15.9)	12 (7.6)	0.03
Valvular surgery detail				<0.01
Mitral valve repair	-	36 (27.3)	28 (17.8)	
Mitral valve replacement	-	16 (12.1)	61 (38.9)	
Aortic valve replacement	-	61 (46.2)	13 (8.3)	
Dual valvular surgery	-	19 (14.4)	55 (35.0)	
Liver stiffness score, kPa	16.1±15.1	8.4±8.2†	18.2±14.5#	<0.01

* Data are presented as mean ± standard deviation or No. (%).
† P<0.05 compared with patients without surgery
‡ P<0.05 compared with patients with the other valve surgery or with TA

TABLE 2. Liver stiffness progression at 1-year follow-up

	Patients without surgery (n=59)	Patients with only left-sided heart valve surgery (n=125)	Patients with combined tricuspid annuloplasty and left-sided heart valve surgery (n=137)
Liver stiffness at baseline, kPa	11.9±9.5	7.7±6.5	17.1±13.3
Liver stiffness at follow-up, kPa	13.3±13.6	8.0±5.9	10.9±8.6
P value	0.25	0.59	<0.01

thus was used to calculate the optimal cutoff value for prediction of outcome. The cutoff value of ≥15.5 kPa predicted the 1-year adverse outcome, with sensitivity of 72% and specificity of 62%.

Discussion

Transient elastography is a reliable and non-invasive ultrasound-based technique for evaluating liver fibrosis according to the European Association for the Study of the Liver guidelines.[1,2] Patients with heart failure have increased liver stiffness as measured by transient elastography.[3] The degree of TR is associated with the degree of liver stiffness.[4] In the present study, baseline liver stiffness was higher in patients who underwent combined TA surgery than those who underwent only left-sided heart valve surgery. This finding indicates that the presence of moderate-to-severe TR may lead to liver function disorder and consequently increasing liver stiffness. Nonetheless, there was reversibility change and significant improvement in liver stiffness after combined TA surgery in those who underwent combined TA and left-sided heart valve

TABLE 3. Factors associated with long-term adverse events in patients who underwent combined tricuspid annuloplasty and left-sided heart valve surgery

Variable	Univariate		Multivariable	
	Hazard ratio (95% confidence interval)	P value	Hazard ratio (95% confidence interval)	P value
Age	1.07 (1.03-1.11)	<0.01	1.05 (1.00-1.09)	0.03
Male	1.48 (0.85-2.59)	0.17	-	
Diabetes mellitus	1.92 (1.05-3.53)	0.03	1.29 (0.66-2.51)	0.46
Hypertension	1.97 (1.09-3.58)	0.03	1.25 (0.61-2.56)	0.54
Hyperlipidaemia	1.45 (0.74-2.84)	0.27	-	-
Smoking	0.75 (0.30-1.88)	0.54	-	-
Atrial fibrillation	1.27 (0.60-2.71)	0.53	-	-
Chronic rheumatic heart disease	0.81 (0.43-1.52)	0.51	-	-
New York Heart Association class III/IV	1.89 (1.08-3.34)	0.03	1.65 (0.90-3.04)	0.11
Left ventricular ejection fraction	1.00 (0.97-1.04)	0.94	-	-
Pulmonary artery systolic pressure	1.01 (0.99-1.03)	0.48	-	-
Moderate-to-severe tricuspid regurgitation	2.11 (0.66-6.77)	0.21	-	-
Residual moderate-to-severe tricuspid regurgitation after surgery	1.18 (0.50-2.77)	0.71	-	-
Concomitant coronary artery bypass graft	1.43 (0.57-3.60)	0.45	-	-
Combined valvular surgery during tricuspid annuloplasty				
Mitral valve repair	0.49 (0.19-1.23)	0.13	-	-
Mitral valve replacement	0.88 (0.50-1.57)	0.67	-	-
Aortic valve replacement	2.50 (1.18-5.34)	0.02	1.25 (0.49-3.18)	0.65
Dual valvular surgery	1.12 (0.63-1.98)	0.70	-	-
Liver stiffness score	1.03 (1.01-1.04)	<0.01	1.02 (1.00-1.04)	0.038

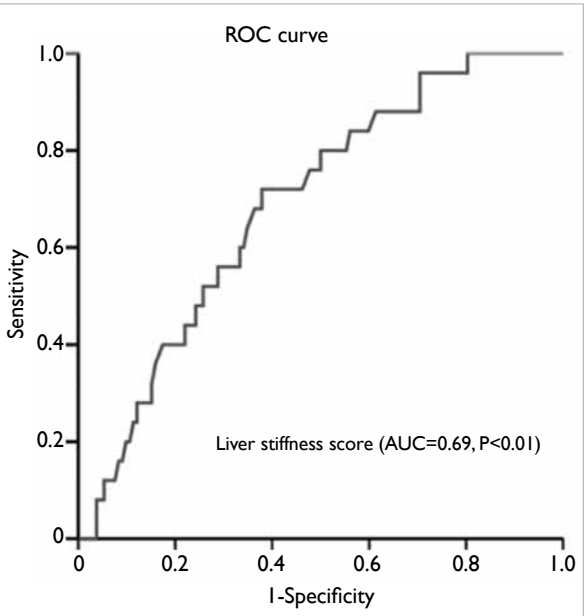

FIG. Receiver operator characteristic curve analysis to determine the accuracy of liver stiffness score associated with adverse events at the 1-year follow-up in patients who underwent combined tricuspid annuloplasty and left-sided heart valve surgery.

surgery but not in those who underwent only left-sided heart valve surgery. A possible explanation may be that moderate-to-severe TR is a major contributor of congestive hepatopathy, and liver congestion subsequently leads to increased liver stiffness. Another possible explanation may be that TA can reduce right-sided filling pressure that reflects the comprehensive status of right heart failure and liver congestion, which will relieve liver congestion and improve liver stiffness. In addition, liver stiffness tended to increase in patients who did not undergo surgery. This finding confirmed that liver dysfunction was common in patients with moderate-to-severe valvular heart diseases, and liver stiffness increased very quickly in patients who were denied surgery. Moderate-to-severe valvular heart diseases have a causative role in the development of liver dysfunction, and medical treatment alone is not sufficient to slow the progress. Therefore, combined TA and left-sided valve surgery is necessary for patients with moderate-to-severe valvular heart diseases to improve liver stiffness.

Liver stiffness can predict adverse outcomes in patients with heart failure.[3] In patients who

underwent combined TA and left-sided heart valve surgery, liver stiffness was associated with adverse outcomes during long-term follow-up. Combined surgical correction of valvular status is effective to prevent progression of liver stiffness in patients with moderate-to-severe valvular heart diseases.

At present, there are no guidelines that incorporate liver stiffness into risk stratification or that suggest the optimal time for combined TA and left-sided heart valve surgery. In the present study, liver stiffness score of ≥15.5 kPa predicted the 1-year adverse outcome, with sensitivity of 72% and specificity of 62%. Therefore, surgical intervention before increase of liver stiffness (liver congestion or right-sided filling pressure/central venous pressure[3,5]) may reduce adverse events. The cut-off value of ≥15.5 kPa may be used for pre-operative risk stratification.

Fibroscan examination should be evaluated frequently in patients with moderate-to-severe valvular heart diseases, especially in patients with moderate-to-severe TR. Liver stiffness should be considered an important indication for early TA surgery. Early identification of increased liver stiffness may improve risk stratification and clinical management.

Conclusion

There were reversibility change and significant improvement in liver stiffness among patients who underwent combined TA and left-sided heart valve surgery. Liver stiffness score can provide useful information to predict adverse outcomes in patients undergoing TA.

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Disclosure

The results of this research have been previously published in:

1. Chen Y, Liu YX, Seto WK, et al. Prognostic value of hepatorenal function by Modified Model For End-Stage Liver Disease (MELD) score in patients undergoing tricuspid annuloplasty. J Am Heart Assoc 2018;7:e009020.

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