The prevalence and prognosis of tricuspid regurgitation in stage A to C heart failure with preserved ejection fraction

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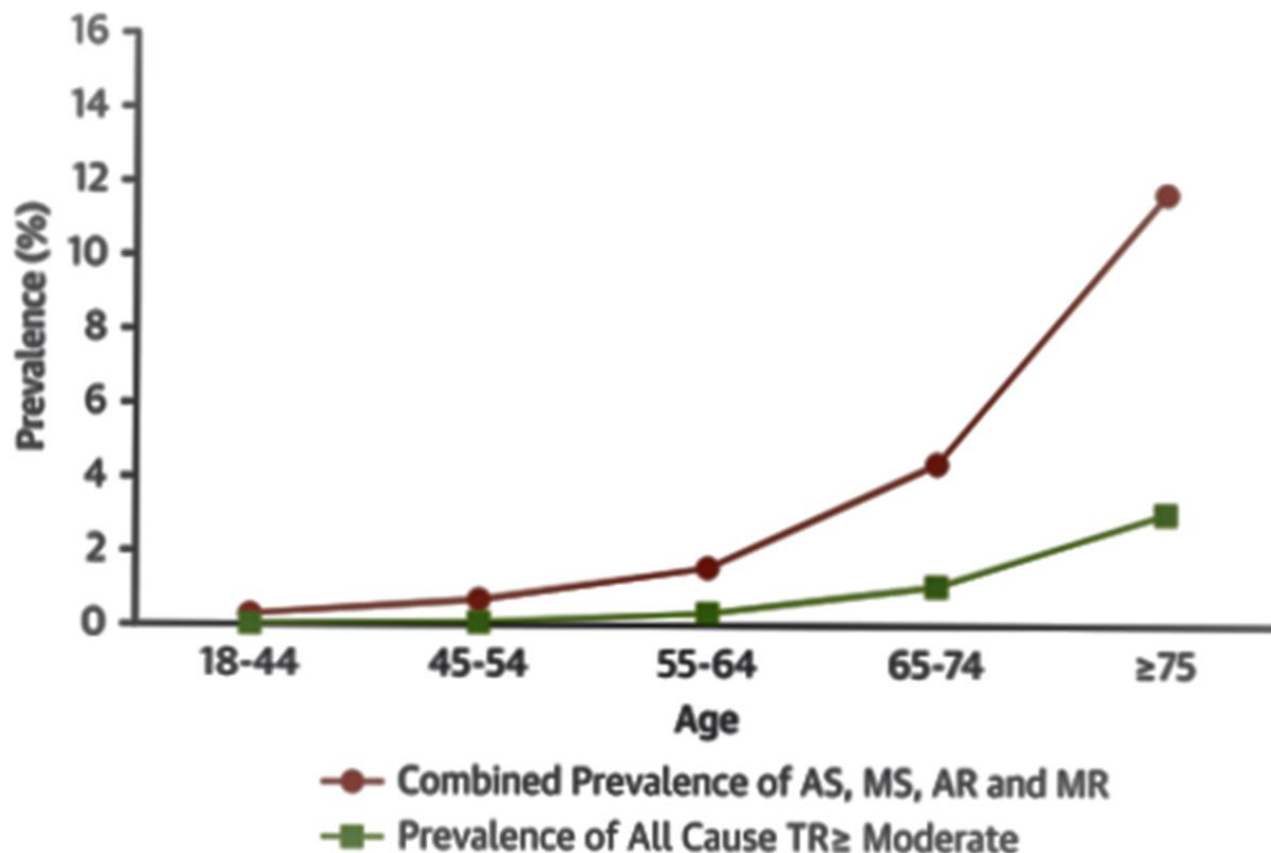Division of cardiology, Department of Medicine, The University of Hong Kong

03.July.2020

Outline

Background

What do we know about tricuspid regurgitation (TR)?

➡ **How common is TR?**

➡ **How important is TR?**

The prevalence of TR compared with the combined prevalence of all left valvular heart disease including :
- aortic stenosis (AS)
- aortic regurgitation (AR),
- mitral stenosis (MS), and
- mitral regurgitation (MR).

Note the significant increase in the prevalence of TR with age. All-cause TR is frequent, approximately one-fourth of all left-sided valve disease.
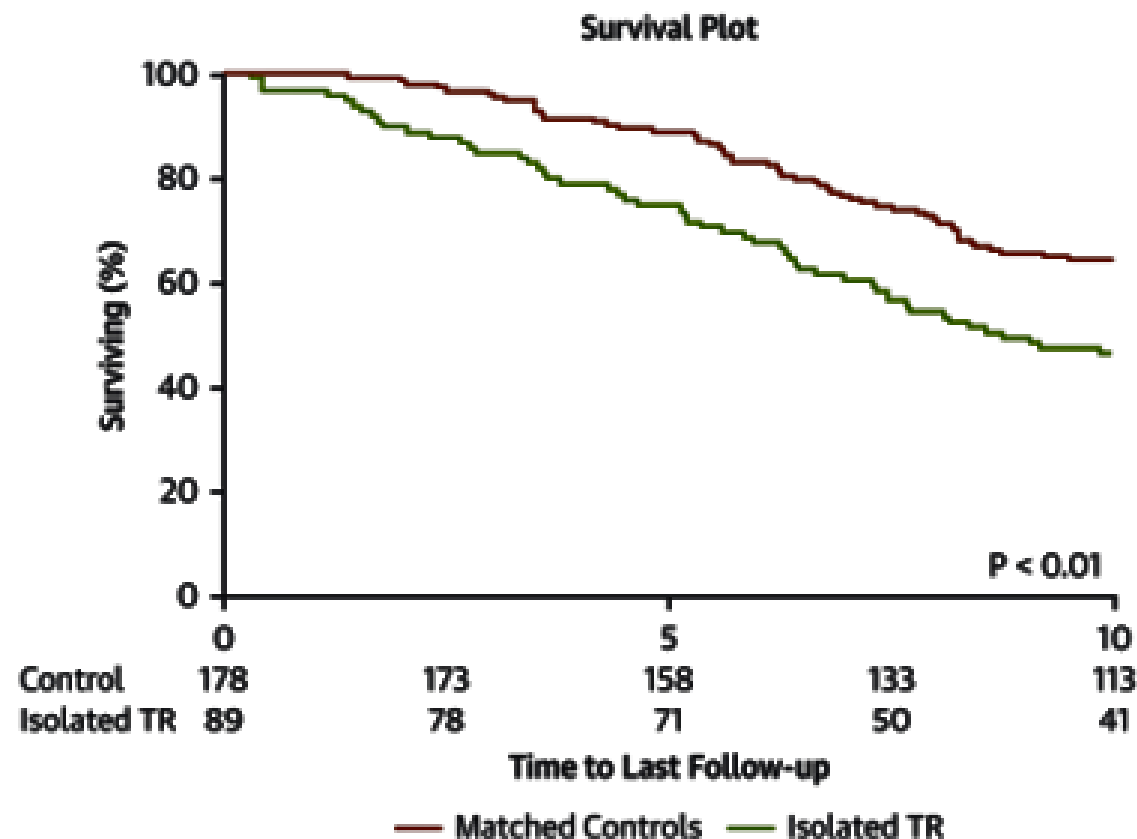
1 in 25 individuals over 75 years old have moderate or severe TR

Topilsky, Yan, et al. *JACC: Cardiovascular Imaging* 12.3 (2019): 433-442.

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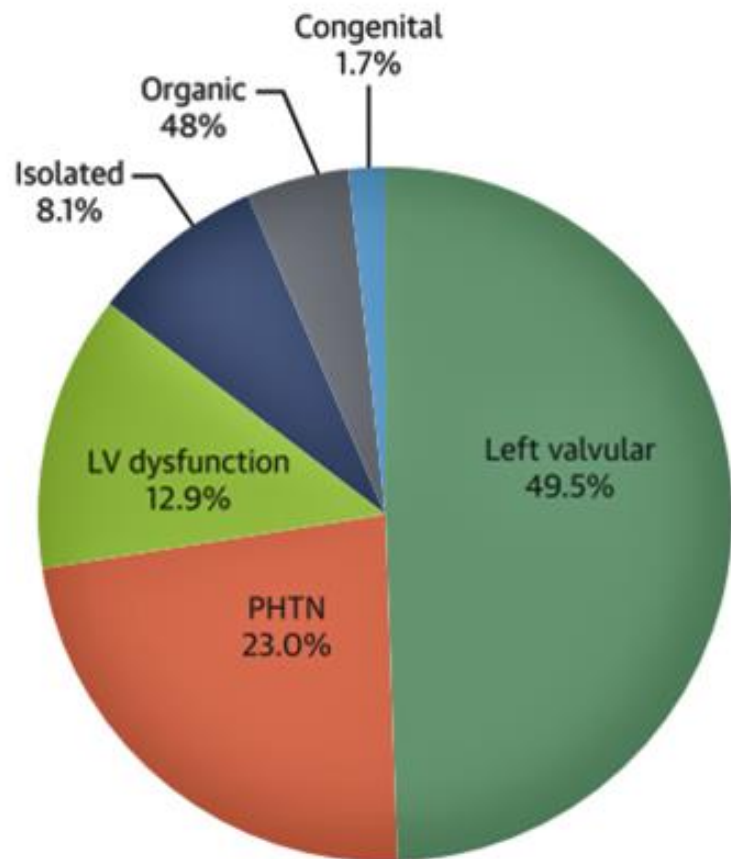
Etiology of TR:
left sided heart disease (most commen)
- Left valvular disease
- Left ventricular dysfunction

There is decrease in survival with greater or equal to moderate isolated TR even when matched for all comorbidities.

Topilsky, Yan, et al. *JACC: Cardiovascular Imaging* 12.3 (2019): 433-442.

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- **13026 HFrEF patients.**

- **FTR was detected in 88%.**

- **Survival was significantly lower with increasing severity of FTR.**

Benfari, Giovanni, et al. *Circulation* 140.3 (2019): 196-206.
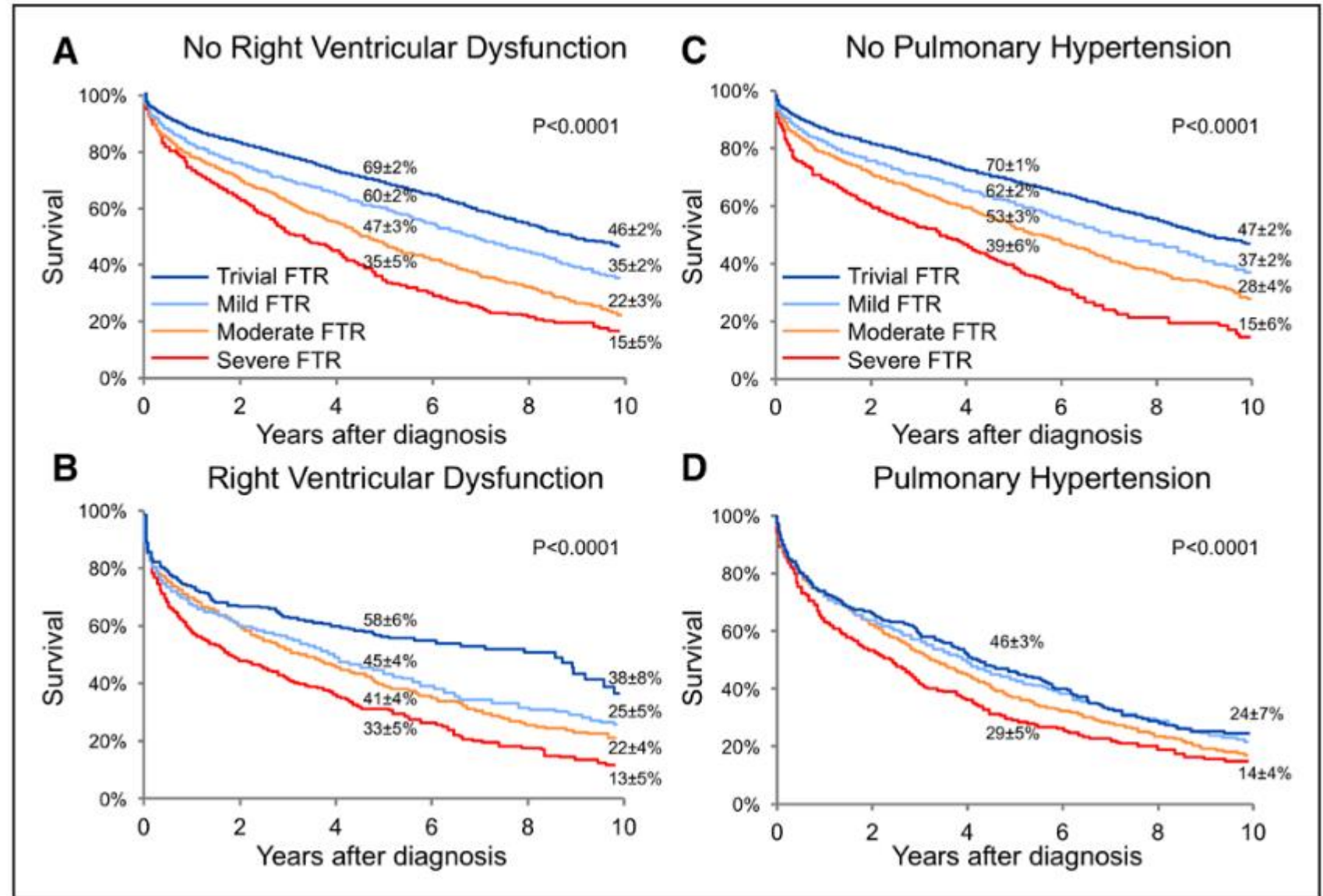
➡ **The presence of trivial and mild TR is often detected during transthoracic echocardiography assessment and has long been thought to be clinically benign.**

➡ **Likewise, the prevalence of moderate and severe TR can be found in 7% to 12%.**

➡ **TR is associated with increasing risk of mortality, heart failure hospitalization in patients with chronic or acute heart failure, HFrEF, pulmonary hypertension, etc.**
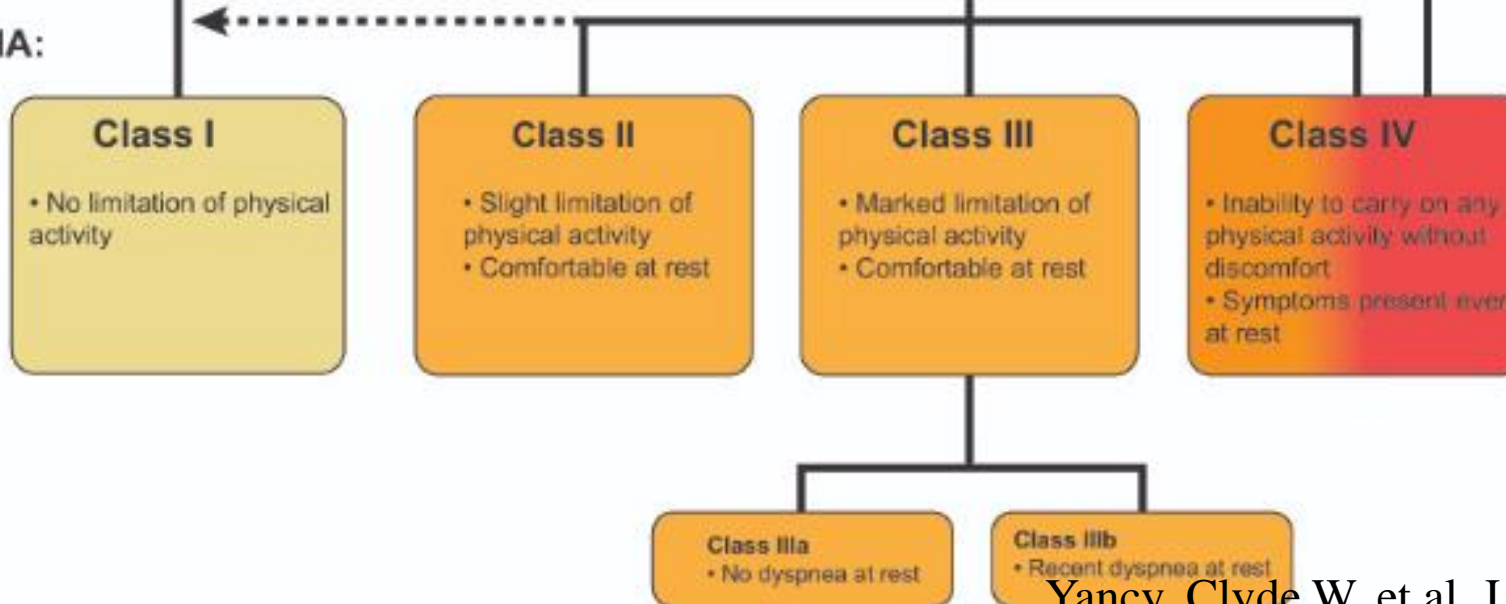
ACC/AHA:

Stage A
- High risk for developing CHF
- No structural disorder of heart

Stage B
- Structural disorder of heart
- Never developed symptoms of CHF

Stage C
- Past or current symptoms of CHF
- Symptoms associated with underlying heart disease

Stage D
- End-stage disease
- Requires specialized treatment strategies

NYHA:

Class I
- No limitation of physical activity

Class II
- Slight limitation of physical activity
- Comfortable at rest

Class III
- Marked limitation of physical activity
- Comfortable at rest

Class IV
- Inability to carry on any physical activity without discomfort
- Symptoms present even at rest

Class IIIa
- No dyspnea at rest

Class IIIb
- Recent dyspnea at rest

Yancy, Clyde W, et al. JACC 62.16 (2013): e147-e239

Definition of Heart Failure with Preserved Ejection Fraction (HFpEF)

Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF <40%	LVEF 40–49%	LVEF ≥50%

	3	_	1. Elevated levels of natriuretic peptides[b];
			2. At least one additional criterion:
			  a. relevant structural heart disease (LVH and/or LAE),
			  b. diastolic dysfunction (for details see Section 4.3.2).
				1. Elevated levels of natriuretic peptides[b];
				2. At least one additional criterion:
				  a. relevant structural heart disease (LVH and/or LAE),
				  b. diastolic dysfunction (for details see Section 4.3.2).

Atherton, John James, et al. Eur J Heart Fail 18 (2016): 891-975.

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% HFpEF

- EF cut-off ≥50%
- EF cut-off ≥40%

UK-Heart	GTWG	ADHERE	OPTIMIZE-HF	ADHERE-I	JCARE-CARD
31.2	36	50.4	51.2	45.7	52.3
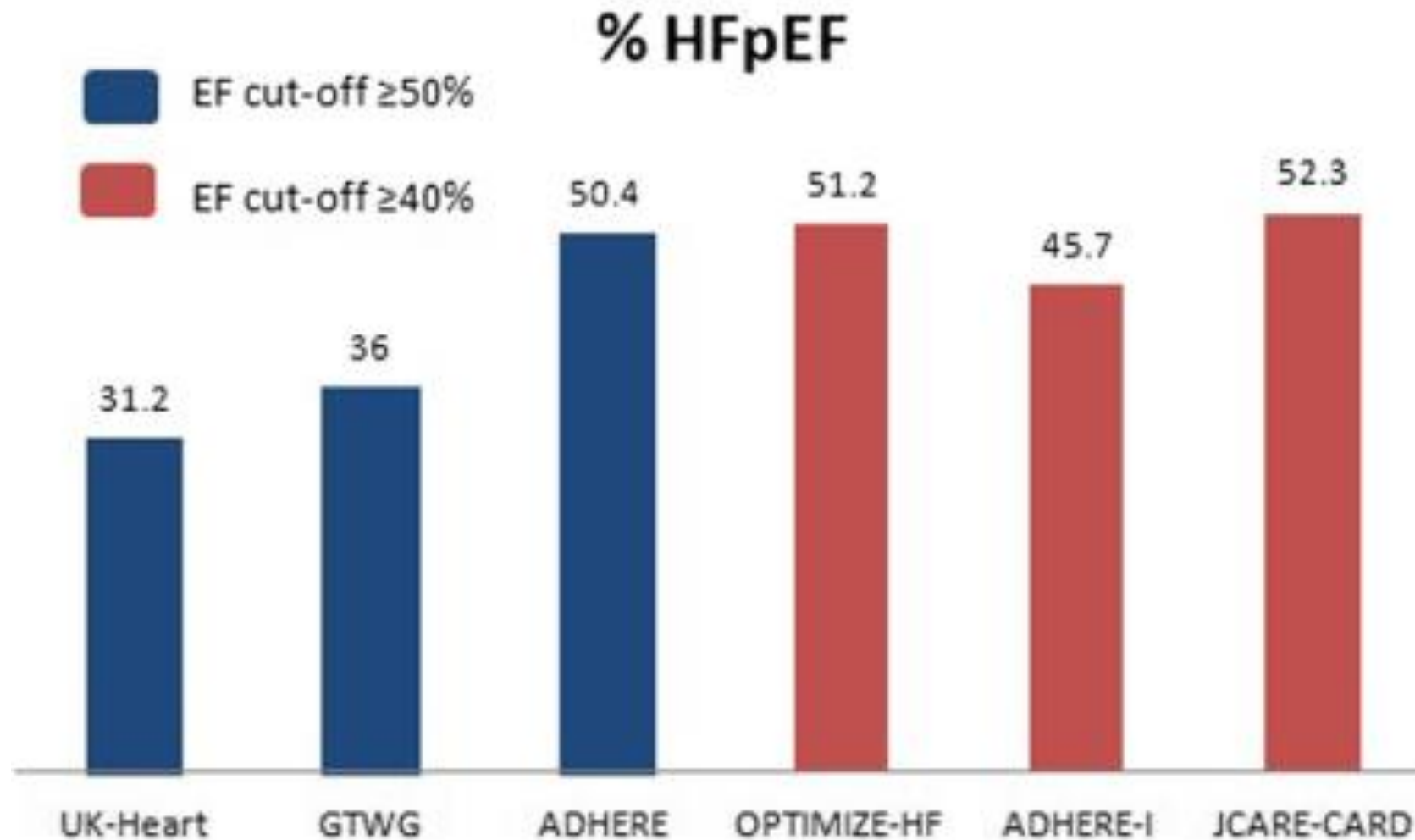
The prevalence of HFpEF amongst patients hospitalised for HF varies widely from 31 to 52 %.

Dunlay et al. *Nature Reviews Cardiology* 14.10 (2017): 591-602.

➡ **Little is known about the prevalence of tricuspid regurgitation.**

➡ **Whether TR has predictive impact on patients with stage A to C heart failure with preserved ejection fraction is unclear.**

Flow chart

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Patients who underwent detailed out-patient echocardiography (2013 to 2017) N=4942

LVEF<50% (N=1794)
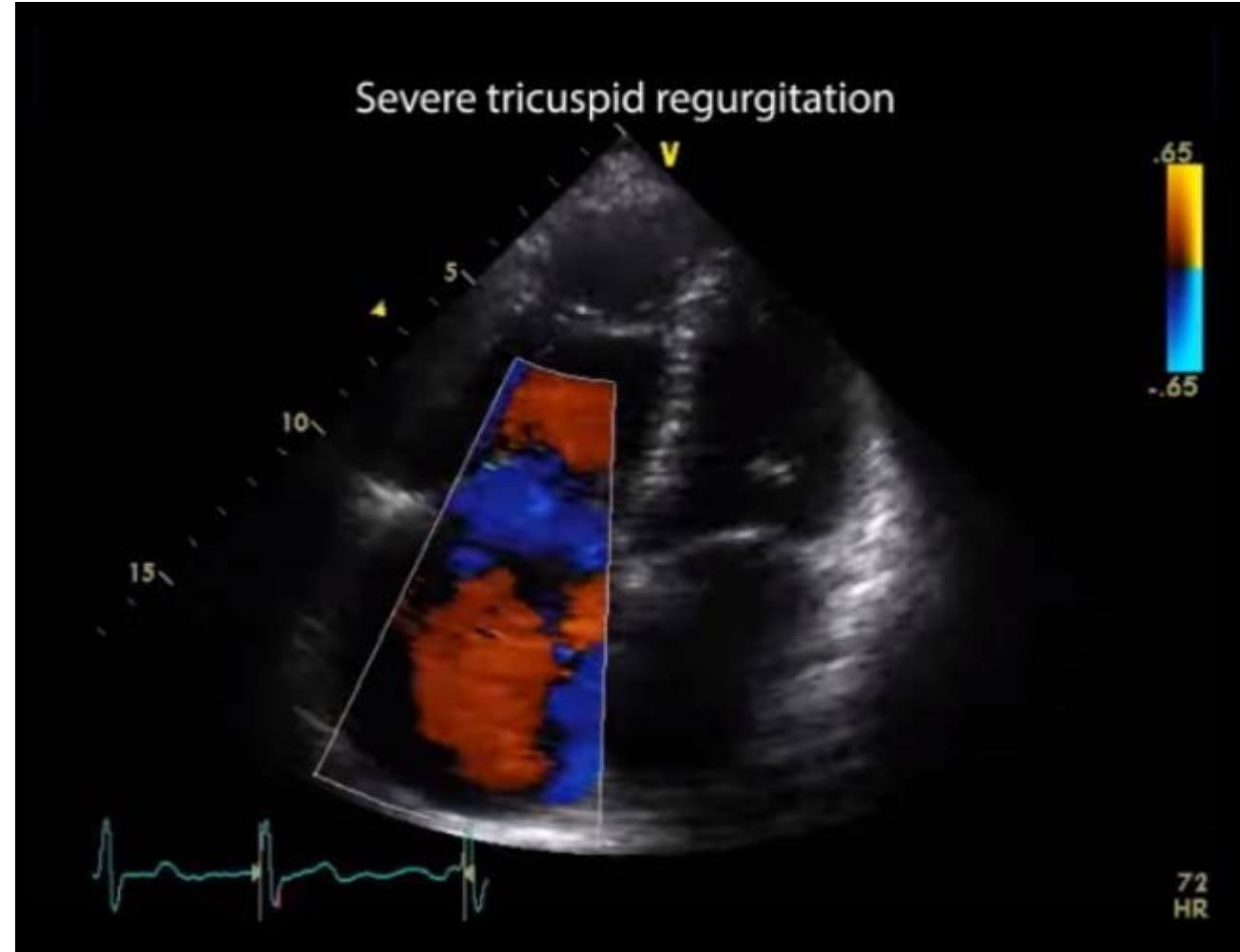
N=3148

Incomplete data (N=106)

N=3042

Stage D HF (N=37)

N=3005

Others (N=123)

All stage A, B and C HF patients N=2882 with a median follow-up of 3.8 years

Parameters

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➡ **Demographic variables were collected.**

➡ **Detailed echocardiography was performed.**

➡ **TR was graded as none, mild, moderate, or severe.**


Severe tricuspid regurgitation

Clinical characters	Overall (N=2882)	No TR (N=1465)	Mild TR (N=1195)	Moderate TR (N=168)	Severe TR (N=54)	P value
Age, y	65.2±14.6	62.2±14.5	67.4±14.3	72.8±11.7	74.5±12.0	**<0.01**
Male, n (%)	1411(47)	785(50)	529(43)	77(45)	20(35)	**<0.01**
Hb, g/dL	12.8±2.1	12.8±2.1	12.9±2.1	12.4±2.3	12.4±2.2	0.12
Cr, umol/L	88.9±39.0	88.5±38.9	88.7±39.3	89.7±35.3	101.7±44.6	0.14
Clinical history						
HT, n (%)	1757(58)	916(59)	724(59)	87(51)	29(50)	0.07
DM, n (%)	991(33)	594(38)	344(28)	38(22)	14(24)	**<0.01**
HL, n (%)	1273(42)	671(43)	539(44)	47(27)	15(26)	**<0.01**
AF, n (%)	542(18)	169(11)	238(19)	92(54)	42(72)	**<0.01**
IHD, n (%)	604(20)	292(19)	260(21)	39(23)	13(22)	0.39
HF stage						
HF stage A, n (%)	904(31)	510(35)	358(30)	36(21)	0(0)	**<0.01**

HF-stage A

HF-stage B

HF-stage C
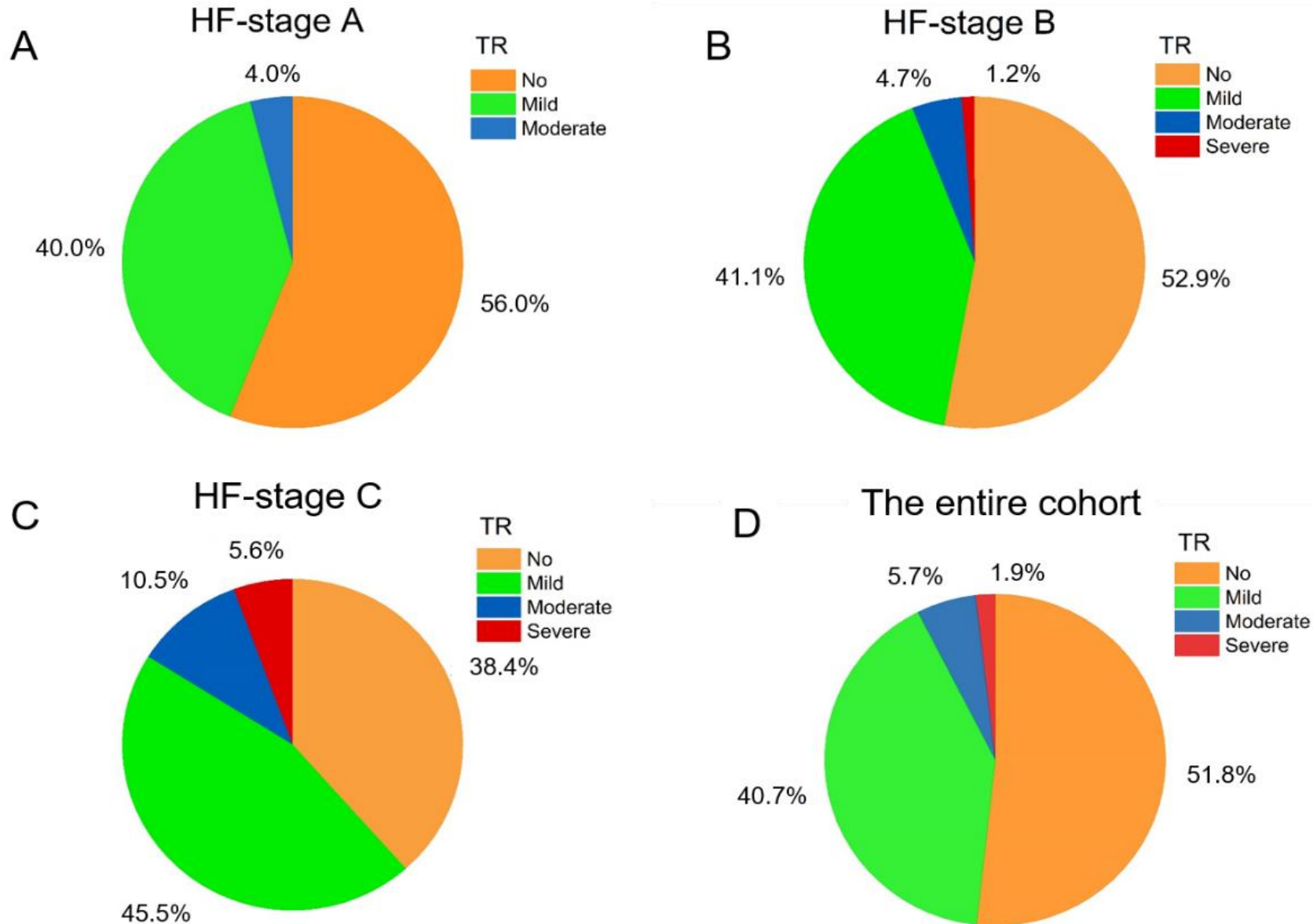
The entire cohort

Patients were stratified as:
- no TR (n=1465, 52%)
- mild TR (n=1195, 41%)
- moderate TR (n=168, 6%)
- severe TR (n=54, 2%)
in the entire cohort.

In particular, the prevalence of
- Moderate TR (4.0% vs. 4.7% vs. 10.5%, P<0.01)
- Severe TR (0% vs. 1.2% vs. 5.6%, P<0.01)
increased from HF stage A, B and C, respectively.

The impact of TR on endpoints

TR grade	Unadjusted Model		Adjusted for Age and Sex		Adjusted for Age, Sex, EF, AF and HF stage	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
All-cause mortality and HF hospitalization						
No TR	Reference		Reference		Reference	
Mild TR	1.4(1.2-1.7)	<0.01	1.2(1.0-1.4)	0.07	1.1(0.9-1.3)	0.51
Moderate TR	2.8(2.1-3.7)	<0.01	2.0(1.5-2.7)	<0.01	**1.6(1.2-2.1)**	0.01
Severe TR	6.1(4.3-8.6)	<0.01	4.2(2.9-5.9)	<0.01	**2.4(1.6-3.4)**	<0.01

When compared with those with no TR, moderate/severe TR was independently associated with all-cause mortality, and HF requiring hospitalization.

All cause mortality

No TR	Reference		Reference		Reference	
Mild TR	1.4(1.2-1.7)	<0.01	1.2(1.0-1.5)	0.06	1.1(0.9-1.4)	0.24
Moderate TR	2.6(1.9-3. 6)	<0.01	1.9(1.4-2.6)	<0.01	**1.6(1.1-2.2)**	0.07
Severe TR	4.7(3.0-7.3)	<0.01	3.3(2.1-5.1)	<0.01	**2.1(1.3-3.4)**	0.01

HF Hospitalization

No TR	Reference		Reference		Reference	
Mild TR	1.6 (1.2-2.1)	0.02	1.3(0.9-1.7)	0.12	1.0 (0.9-1.3)	0.65
Moderate TR	4.3(2.9-6.4)	<0.01	2.8(1.9-4.2)	<0.01	**1.5(1.1-1.9)**	0.01
Severe TR	12.7(8.3-19.5)	<0.01	7.5(4.8-11.6)	<0.01	**2.2(1.5-3.3)**	<0.01

When compared with those with no TR, moderate/severe TR was independently associated with all-cause mortality, or HF requiring hospitalization, respectively.

CV death

No TR	Reference		Reference		Reference	
Mild TR	2.8 (1.8-4.3)	<0.01	2.0(1.3-3.1)	<0.01	**1.8(1.2-2.9)**	0.01
Moderate TR	6.0(3.2-11.0)	<0.01	3.5(1.9-6.3)	<0.01	**2.5(1.3-4.7)**	<0.01
Severe TR	13.3(6.3-28.2)	<0.01	7.6(3.8-15.5)	<0.01	**3.9(1.8-8.4)**	<0.01

Non-CV death

No TR	Reference		Reference		Reference	
Mild TR	1.3 (1.1-1.7)	0.02	1.2 (0.9-1.5)	0.02	1.1(0.9-1.4)	0.34
Moderate TR	1.9(1.2-2.9)	<0.01	1.5(1.0-2.3)	<0.01	1.3(0.8-2.0)	0.24
Severe TR	2.5(1.3-5.0)	<0.01	1.9(0.9-3.7)	<0.01	1.4(0.7-2.8)	0.37

Moderate/severe TR was independently associated with CV death while no such association was noted for non-cardiovascular mortality.
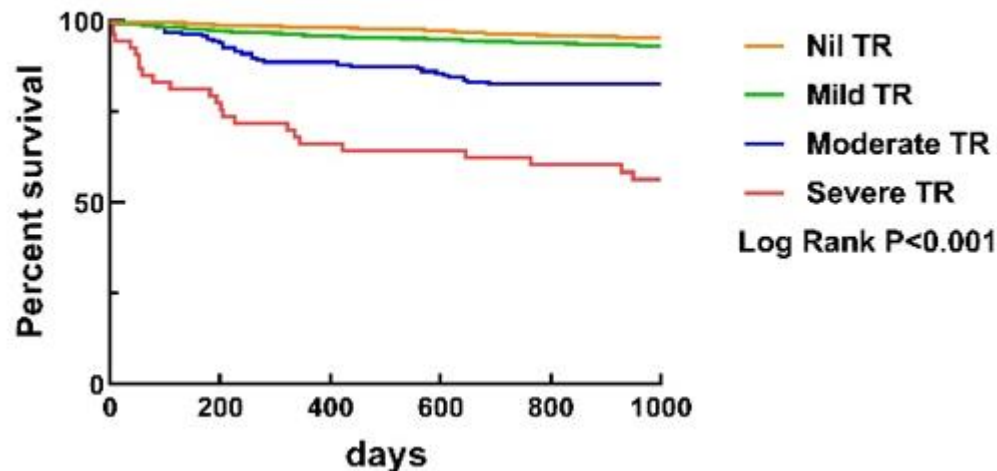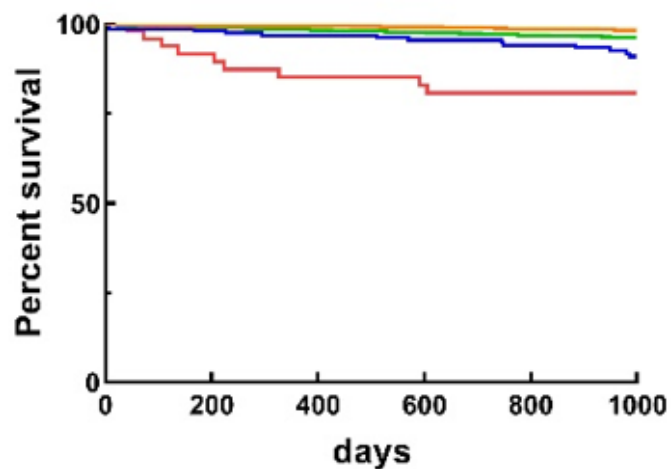
Kaplan-Meier curve for the impact of TR grades on ：
- all-cause mortality.
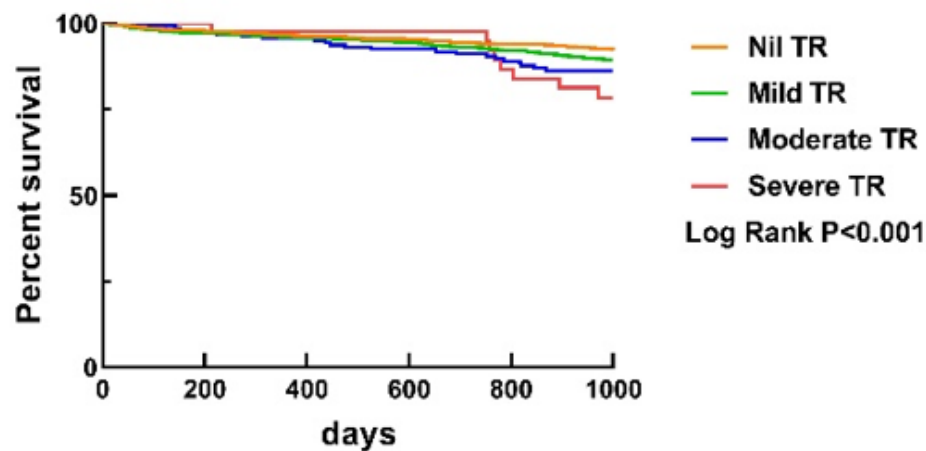- HF hospitalization.
- cardiovascular death (CV-death)
- Non-cardiovascular death (non-CV death).

In all subgroups, except for non-CV death, increasing TR grade is significantly associated with long-term outcomes.

➡️ **The presence of significant (moderate or severe) TR is common in patients with stage A and B HF and stage C HFpEF.**

➡️ **Importantly, the severity of TR is independently associated with mortality and HF requiring hospitalization.**

➡ **The presence of TR may play an integral part and represent a potential therapeutic target for patients at risk of HF and those with HFpEF.**

➡ **Clinical physicians should consider grades of tricuspid regurgitation when performing echocardiography.**

➡ **With the advancement of transcatheter procedure, should we take a more active approach to treat tricuspid regurgitation.**

Acknowledgments

➡️ **Thanks to the medical and nursing staff of the Division of Cardiology, Queen Mary Hospital, for help and support during this study.**

➡️ **Thanks to my supervisor Dr. Yiu Kai-Hang for contributing to study concept and design, analysis and interpretation of data, drafting of manuscript and approval of the final version.**