文献精读

蒋 虹

厚德 精业 求实 创新

ORIGINAL ARTICLE

Pulmonary Hypertension in Heart Failure

Epidemiology, Right Ventricular Function, and Survival

Mario Gerges[1], Christian Gerges[1], Anna-Maria Pistritto[2], Marie B. Lang[1], Pia Trip[3], Johannes Jakowitsch[1], Thomas Binder[1], and Irene M. Lang[1]

心衰患者肺动脉高压的患病率调查、右心功能及预后的研究

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研究背景

□2015ESC/ERS颁布肺高压诊治指南，指南中对肺动脉高压进行重新的分类

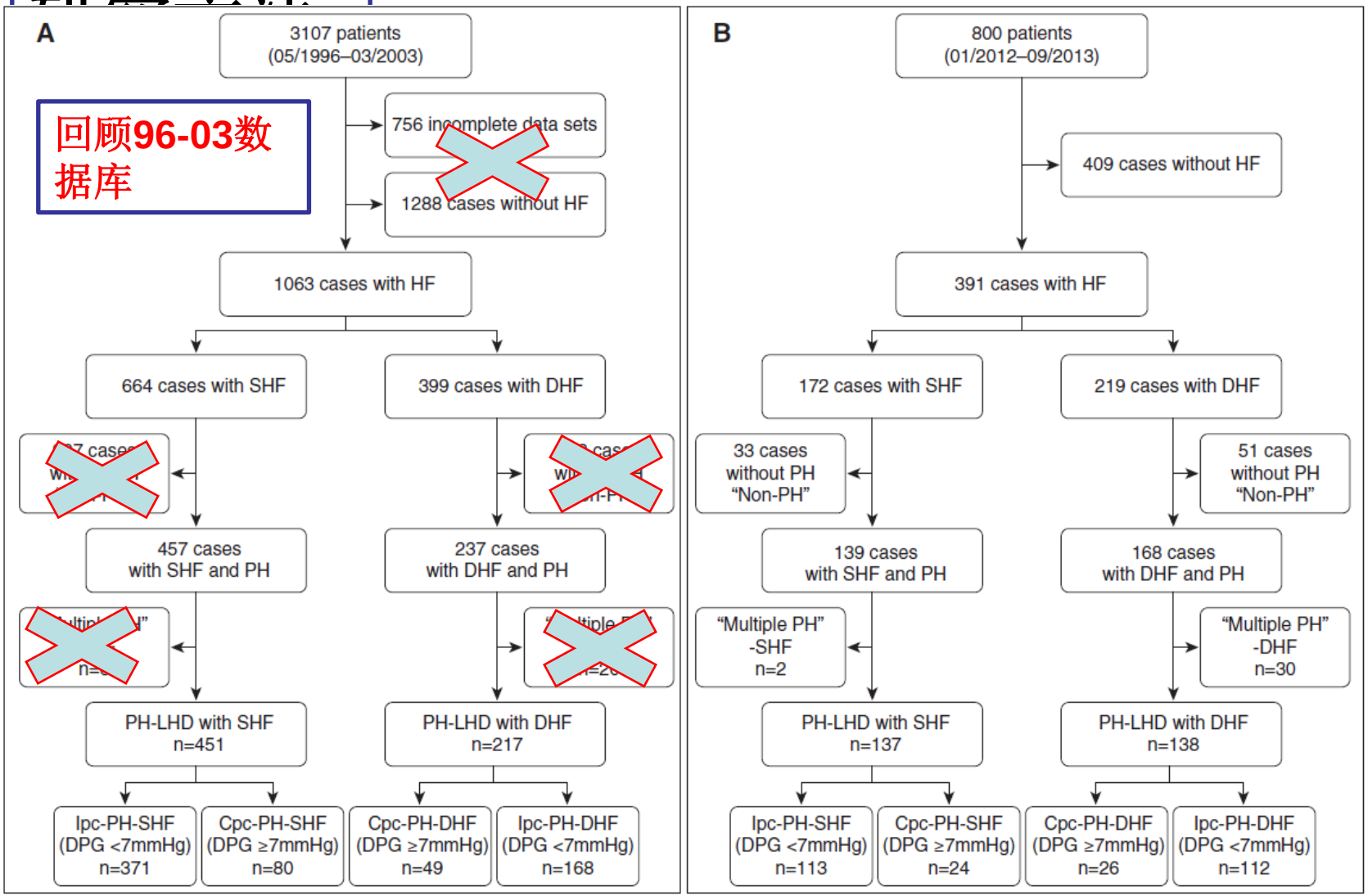
定义	特征	临床分型
肺动脉高压	PAPm≥25 mmHg	所有
毛细血管前肺动脉高压	PAPm≥25 mmHg PAWP≤15 mmHg	1.肺动脉高压 3.源于肺部疾病的肺动脉高压 4.慢性血栓性肺动脉高压 5.未知和（或）多因素机制所致肺动脉高压
毛细血管后肺动脉高压	PAPm≥25 mmHg PAWP>15 mmHg	2.源于左心疾病的肺动脉高压 5.未知和（或）多因素机制所致肺动脉高压
孤立性毛细血管后肺动脉高压（Ipc-PH）	DPG<7 mmHg和（或） PVR≤3 WU	
毛细血管后与毛细血管前肺动脉高压（Cpc-PH）	DPG≥7 mmHg和（或） PVR>3 WU	

PAWP：肺动脉楔压，
DPG：舒张期跨瓣压差（diastolic PAP － mean PAWP），
WU：Wood units

研究背景

- 基于左心功能不全引起的PH患者预后较差。
- 既往研究较多关注PH引起的右心问题。
- 治疗方面：减少左心重塑及扩张肺血管的药物。

回顾96-03数据库


A
3107 patients
(05/1996–03/2003)
756 incomplete data sets
1288 cases without HF
1063 cases with HF
664 cases with SHF
399 cases with DHF
457 cases
with SHF and PH
237 cases
with DHF and PH
PH-LHD with SHF
n=451
PH-LHD with DHF
n=217
Ipc-PH-SHF
(DPG <7mmHg)
n=371
Cpc-PH-SHF
(DPG ≥7mmHg)
n=80
Cpc-PH-DHF
(DPG ≥7mmHg)
n=49
Ipc-PH-DHF
(DPG <7mmHg)
n=168
B
800 patients
(01/2012–09/2013)
409 cases without HF
391 cases with HF
172 cases with SHF
219 cases with DHF
33 cases
without PH
"Non-PH"
51 cases
without PH
"Non-PH"
139 cases
with SHF and PH
168 cases
with DHF and PH
"Multiple PH"
-SHF
n=2
"Multiple PH"
-DHF
n=30
PH-LHD with SHF
n=137
PH-LHD with DHF
n=138
Ipc-PH-SHF
(DPG <7mmHg)
n=113
Cpc-PH-SHF
(DPG ≥7mmHg)
n=24
Cpc-PH-DHF
(DPG ≥7mmHg)
n=26
Ipc-PH-DHF
(DPG <7mmHg)
n=112

患者分组

✓纳入标准：心衰and肺动脉高压患者并行右心导管检查

✓排除标准：缩窄性心包炎，心肌病。先心病，CTEPH,COPD(3-4分，GOLD),肺间质疾病，门脉高压，OSAS

✓分组：EF>45%区分SHF和DHF

——回顾性研究n（SHF)=451，n(DHF)=217

——前瞻性研究n（SHF)=137，n(DHF)=138

DPG》7mmHg区分Ipc-PH和Cpc-PH

——回顾性研究n（Cpc-PH)=129，n （Ipc-PH)=539

——前瞻性研究n（Cpc-PH)=50，n （Ipc-PH)=225

技术方法

- ✓Swan-Ganz导管:PAP,PAWP
- ✓热稀释法：CO，SV
- ✓心脏超声:评价右心功能。
- ✓肺功能检查
- ✓肌酐清除率

技术方法

✓跨肺压(TPG) = mPAP -mPAWP;

✓肺血管阻力（PVR）=TPG/CO 反应右心后负荷

✓肺血管顺应性（C_{PA}）=SV/(sPAP- dPAP）

✓舒张压梯度（DPG） = dPAP- mPAWP

□右心功能评估——理想的右心功能评估应独立于心脏的负荷并且需把右心及肺动脉是一个单元（RV-PV coupling）：

!Endsystolic elastance 收缩末期弹性(Ees， mmHg/ml) = (Piso-mPAP)/SV

!Effective arterial elastance 动脉有效弹性(Ea， mmHg/ml)

=mPAP/SV

!TAPSE/sPAP（三尖瓣收缩期位移/收缩期肺动脉压力）

统计学方法

- ✓ANOVA
- ✓Logistic回归危险因素分析
- ✓COX回归模型生存曲线分析

结果

□患病率调查：

	PH-LHD		Cpc-PH
	SHF	DHF	
回顾性研究	67.9%	54.4%	12%
前瞻性研究	79.7%	63%	14-12%

Table 1. Clinical Characteristics of Patients with Heart Failure

	Retrospective HF Cohort (*n* = 1,063)		Prospective HF Cohort (*n* = 391)	
	SHF (*n* = 664)	DHF (*n* = 399)	SHF (*n* = 172)	DHF (*n* = 219)
Age, yr	60.9 ± 11.9	66.5 ± 11.3	66.1 ± 15.1	72.2 ± 12.4
Sex, no. (%)				
Male	511 (77.0)	199 (49.9)	128 (74.4)	105 (61.0)
Female	153 (23.0)	200 (50.1)	44 (25.6)	114 (52.1)
Body mass index, kg/m^2	26.4 ± 4.3	26.9 ± 4.7	27.2 ± 4.8	28.2 ± 5.8
NYHA functional class, no. (%)				
I	32 (4.8)	12 (3.0)	2 (1.2)	14 (6.4)
II	284 (42.8)	225 (56.4)	8 (4.7)	44 (20.1)
III	213 (32.1)	130 (32.6)	85 (49.4)	115 (52.5)
IV	135 (20.3)	32 (8.0)	77 (44.8)	46 (21.0)
Arterial hypertension, no. (%)	246 (37.0)	204 (51.1)	122 (70.9)	171 (78.1)
Stable ischemic heart disease, no. (%)	337 (50.8)	168 (42.1)	85 (49.4)	76 (34.7)
Atrial fibrillation, no. (%)	205 (30.9)	133 (33.3)	67 (39.0)	90 (41.1)
Valvular heart disease, no. (%)	313 (47.1)	209 (52.4)	108 (62.8)	116 (53.0)
Creatinine clearance <60 ml/min, no. (%)	249 (37.5)	202 (50.6)	74 (43.0)	119 (54.3)

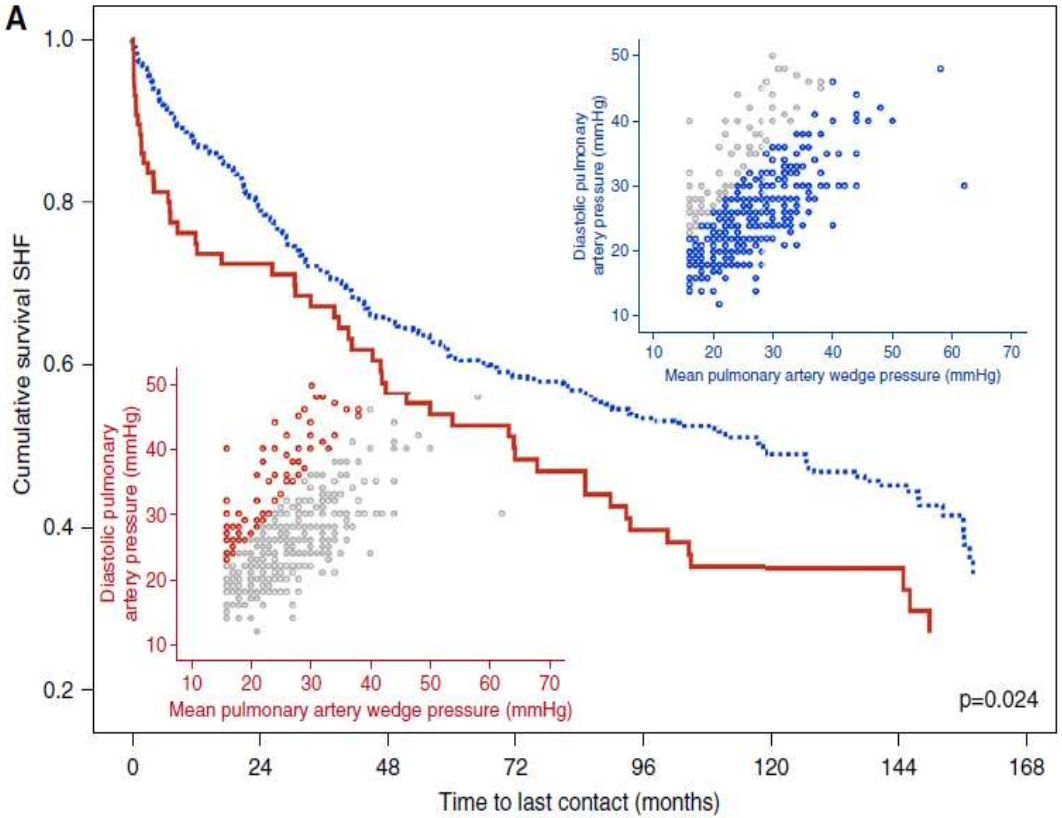
Definition of abbreviations: DHF = diastolic heart failure; HF = heart failure; NYHA = New York Heart Association; SHF = systolic heart failure.

Cpc-PH组与Ipc-PH 组的比较

Hemodynamic and Echocardiographic Variable	PH in SHF (*n* = 137)		PH in DHF (*n* = 138)		iPAH (*n* = 12)
	Ipc-PH in SHF (*n* = 113)	Cpc-PH in SHF (*n* = 24)	Ipc-PH in DHF (*n* = 112)	Cpc-PH in DHF (*n* = 26)	
Hemodynamic data					
Heart rate, beats/min	75.6 ± 15.1	81.7 ± 13.4	70.2 ± 14.6	73.1 ± 12.8	75.7 ± 16.7
Cardiac output, L/min	4.7 ± 1.4	4.7 ± 1.7	5.5 ± 1.6	5.5 ± 2.0	4.3 ± 0.8
Cardiac index, L/min/m^2	2.5 ± 0.7	2.3 ± 0.7	2.9 ± 0.8	2.9 ± 0.9	2.4 ± 0.4
Mixed venous oxygen saturation, %	62.9 ± 10.0	60.9 ± 11.2	62.9 ± 9.9	60.9 ± 12.0	60.9 ± 12.8
Systemic vascular resistance, Wood units	18.9 ± 7.3	20.3 ± 13.3	17.1 ± 6.6	17.1 ± 7.6	19.9 ± 5.0
Pulmonary vascular resistance, Wood units	2.7 ± 1.5	5.7 ± 3.0*	2.4 ± 1.2	5.4 ± 3.9†	11.1 ± 6.4
Pulmonary arterial compliance, ml/mm Hg	2.3 ± 1.3	2 ± 1.1	2.7 ± 1.2	2.5 ± 2.8	1.3 ± 0.8
Systemic vascular resistance–compliance time, s	1.54 ± 1.36	1.38 ± 0.83	1.04 ± 0.36	0.87 ± 0.48	1.04 ± 0.30
Pulmonary vascular resistance–compliance time, s	0.30 ± 0.13	0.62 ± 0.49*	0.34 ± 0.13	0.49 ± 0.18†	0.69 ± 0.26
Mean right atrial pressure, mm Hg	13.6 ± 7	15.3 ± 5.9	11.9 ± 5.8	14.5 ± 6.1†	9.9 ± 5.7
Mean pulmonary arterial pressure, mm Hg	38.2 ± 8.4	47.2 ± 9.2*	34.3 ± 7.0	44.2 ± 13.2†	52.3 ± 17.4
Mean pulmonary arterial wedge pressure, mm Hg	26.4 ± 7.1	22.8 ± 5.5	21.9 ± 5.7	20.4 ± 7.6	8.6 ± 3.1
Transpulmonary gradient, mm Hg	11.9 ± 5.6	23.6 ± 6.1*	12.4 ± 5.6	24.1 ± 10.4†	43.1 ± 16.7
Diastolic pulmonary vascular pressure gradient, mm Hg	−0.9 ± 6.1	11.5 ± 4.6*	−0.4 ± 5.1	12.2 ± 6.4†	23.6 ± 17.6
P_{iso}, mm Hg	89.6 ± 18.7	89.7 ± 23.0	87.2 ± 16.3	101.2 ± 28.5	124.3 ± 26.9
Ees, mm Hg/ml	0.84 ± 0.45	1.00 ± 0.66	0.62 ± 0.19	1.14 ± 1.0	1.47 ± 0.79
Ea, mm Hg/ml	0.72 ± 0.40	1.01 ± 0.59*	0.48 ± 0.20	0.81 ± 0.68†	1.08 ± 0.70
Ees/Ea	1.52 ± 0.51	1.05 ± 0.25*	1.45 ± 0.29	1.17 ± 0.27†	1.40 ± 0.44
Echocardiographic data					
Ejection fraction, %	33.9 ± 14.0	29.8 ± 11.0	60.1 ± 11.0	56.9 ± 9.7	65.8 ± 11.0
RV/LV ratio	0.7 ± 0.2	0.7 ± 0.1	0.8 ± 0.2	1.0 ± 0.2†	1.6 ± 0.8
E/A ratio	2.0 ± 1.1	2.4 ± 0.8	1.4 ± 0.9	1.1 ± 0.9	0.8 ± 0.2
E/e′ ratio	18.3 ± 7.0	22.2 ± 7.3	20.6 ± 7.2	20.5 ± 7.3	10.5 ± 5.8
Left atrial volume index, ml/m^2, mm Hg	51.5 ± 19.2	56.4 ± 24.1	47.3 ± 20.3	42.8 ± 22.6	22.5 ± 14.6
Tricuspid regurgitation jet velocity, m/s	3.3 ± 0.6	3.4 ± 0.6	3.4 ± 0.6	3.8 ± 0.6	4.5 ± 0.7
TAPSE, mm	16.0 ± 4.5	13.3 ± 4.5*	18.7 ± 5.0	14.3 ± 3.0†	13.3 ± 4.4
TAPSE/sPAP ratio, mm/mm Hg	0.30 ± 0.12	0.22 ± 0.11*	0.32 ± 0.11	0.22 ± 0.08†	0.14 ± 0.11

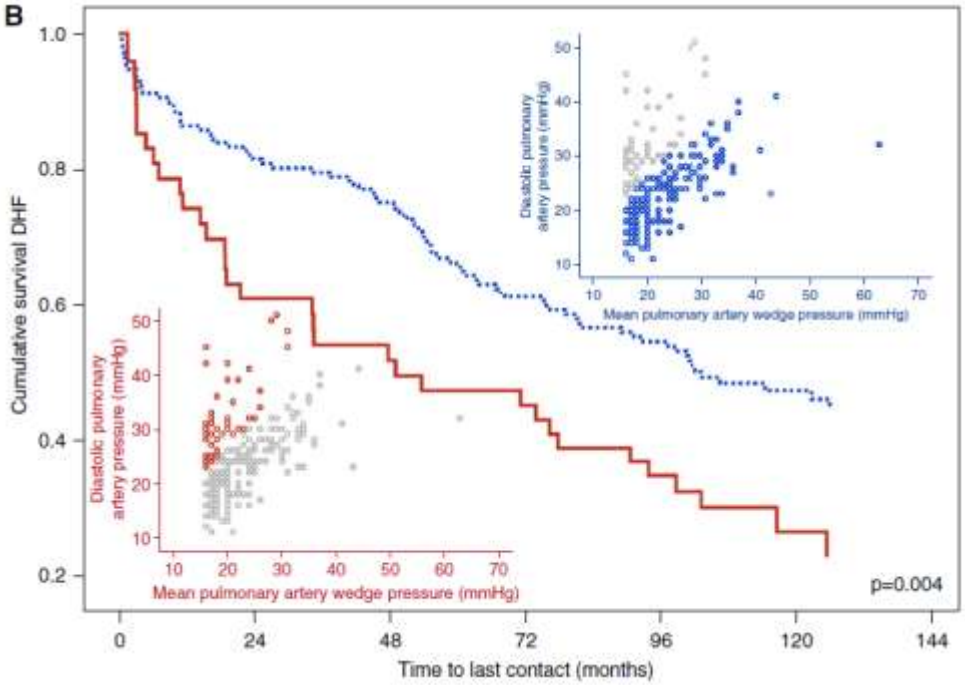
- SHF组与DHF组的血流动力学指标基本相同（RV-PV coupling和RV收缩性）， mPAWP也相同（不同病因）；
- Cpc-PH组较Ipc-PH 组的PVR,TPG,PAP、mPAWP高；
- 回顾性研究与前瞻性研究相比Cpc-PH患病率相同，虽然心脏超声广泛应用，但无法区分Cpc-PH和Ipc-PH 。

□生存率分析：



Cpc-PH患者生存率较低

□生存率分析：



Cpc-PH患者生存率较低

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RV/LV ratio	0.7 ± 0.2	0.7 ± 0.1	0.8 ± 0.2	1.0 ± 0.2†	1.6 ± 0.8
E/A ratio	2.0 ± 1.1	2.4 ± 0.8	1.4 ± 0.9	1.1 ± 0.9	0.8 ± 0.2
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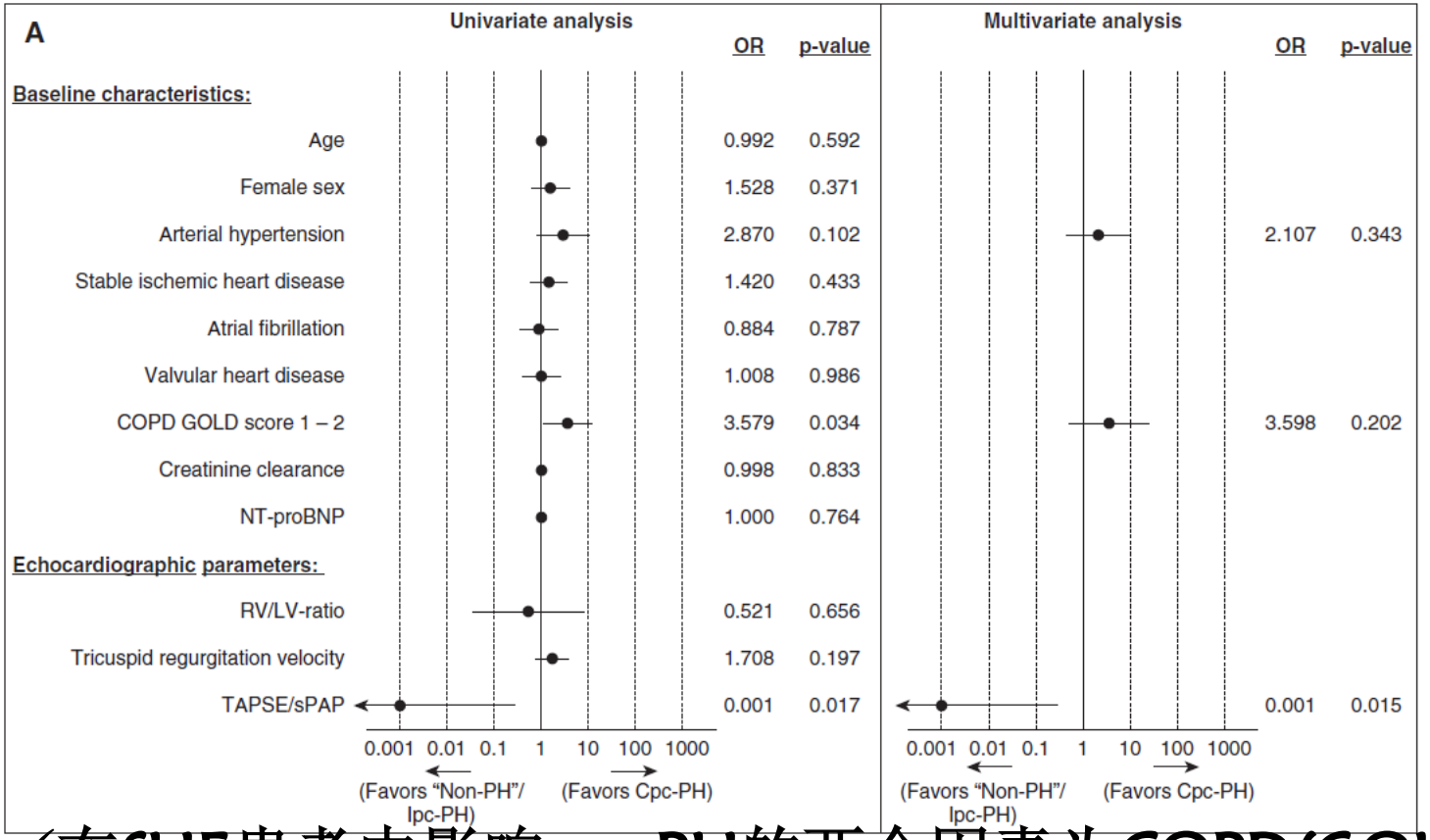
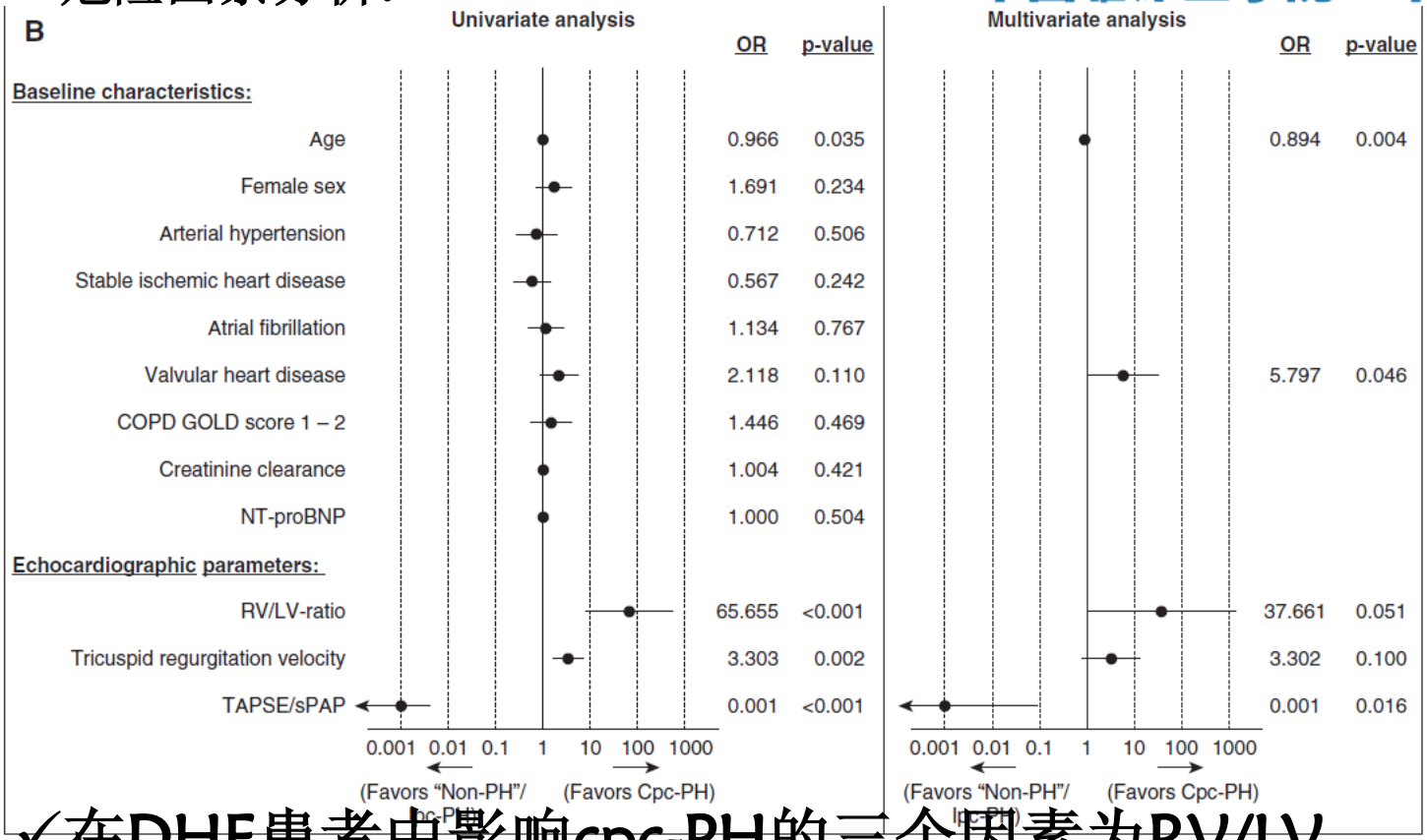
□危险因素分析：



✓在SHF患者中影响cpc-PH的两个因素为COPD(GOLD1-2分）(OR=3.579)和TAPSE/sPAP (OR=0.001)。

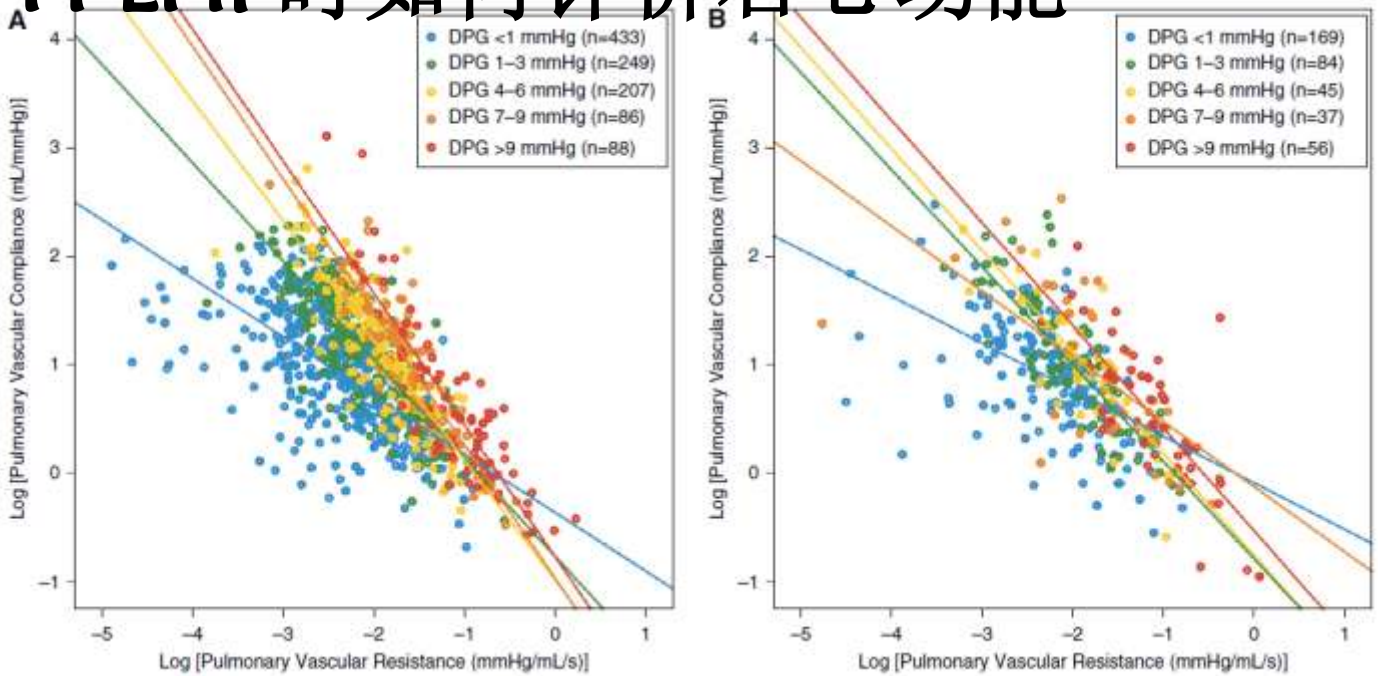
TAPSE/sPAP<0.27mm/mm的特异性61.1%敏感性80%。

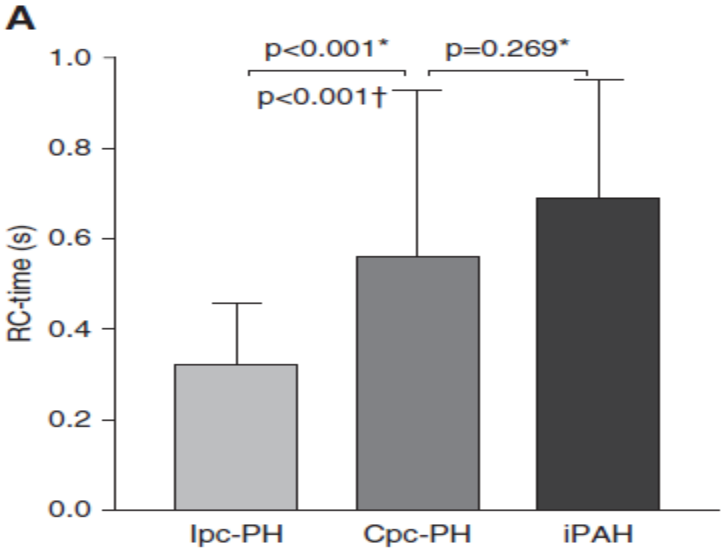
◻危险因素分析：



✓在DHF患者中影响cpc-PH的三个因素为RV/LV (OR=65.655),age (OR=0.966)和TAPSE/sPAP (OR=0.001)，VHD和age<77.47联合TAPSE/sPAP<0.31mm/mm的特异性97.5%敏感性38.5%

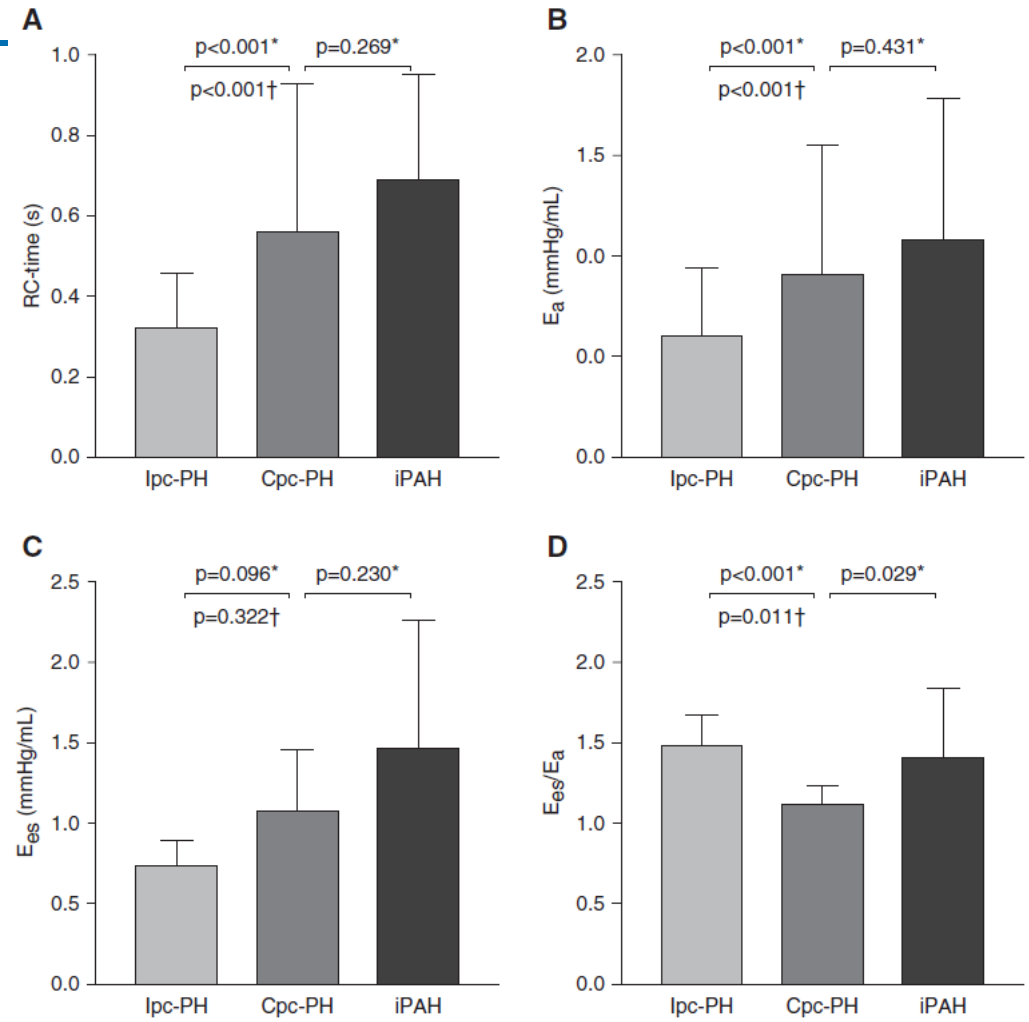
□PH-LHF时如何评价右心功能





✓RC-time和DPG用于评估PH-LHD患者右心负荷

□PH-LHF时如何评价右心功能



✓既往PVR由于mPAWP无法准确评估。

✓RC-time，DPG

✓RV-PV coupling可以用于评估右心功能

✓coupling在SHF和DHF中无差别，说明RV受损与左室收缩功能无关。但从图中也看出RV-PV coupling在Cpc-PH中最差

- Cpc-PH is uncommon in heart failure and may be a cause of clinical worsening because of associated right ventricle(RV) failure
- The prevalence of Cpc-PH did not appear specific to systolic or diastolic heart failure
- Predictors of Cpc-PH were younger age, coexistent chronic obstructive pulmonary disease or valvular heart disease, and, TAPSE/sPAP
- RV afterload may also increase more than estimated from PVR because of a disproportionate decrease in pulmonary arterial compliance

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