肝移植术前心脏功能评估

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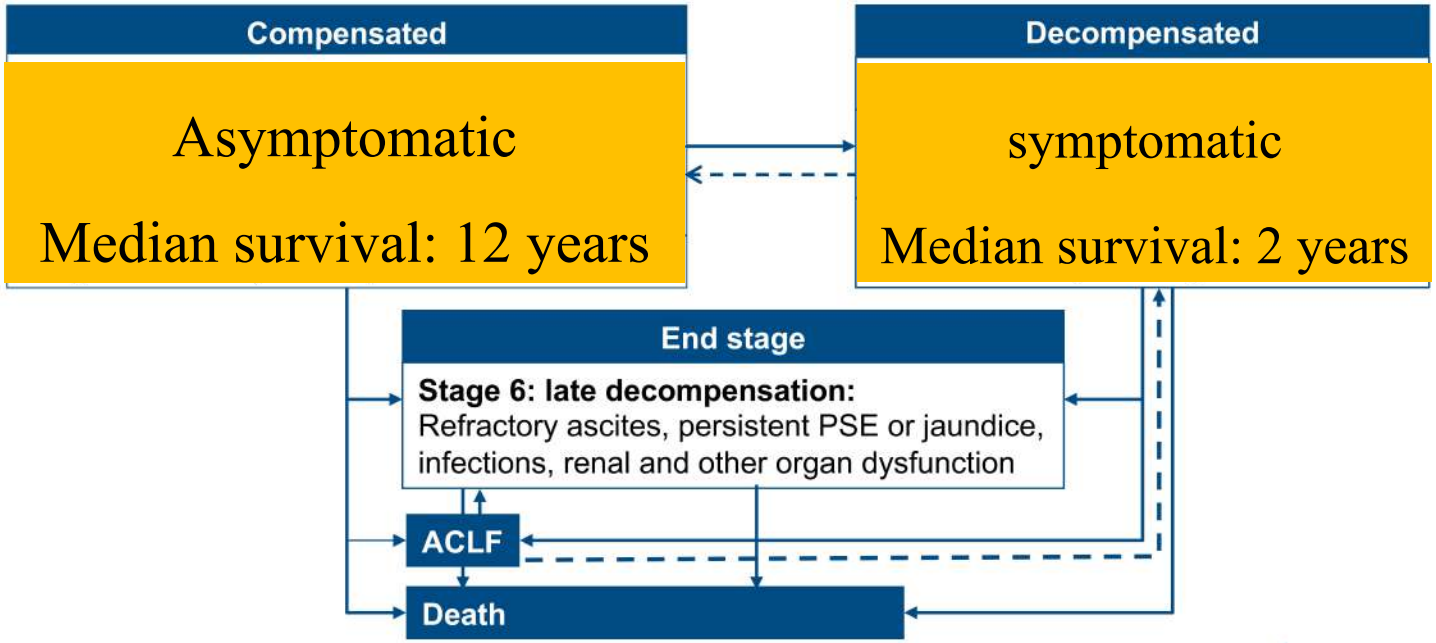
为什么肝移植病人要重视心脏评估

1. 肝硬化病人心血管和呼吸系统问题增加
2. 肝移植手术的特点
   - ➔ 创伤大，应激反应严重
   - ➔ 大量出血的可能和术中液体转移量大
   - ➔ 术中肝血流阻断和开放对心血管功能的挑战
   - ➔ 腔静脉阻断/开放后：缺血/再灌注损伤
3. 术后并发症多，需要强大的心脏功能

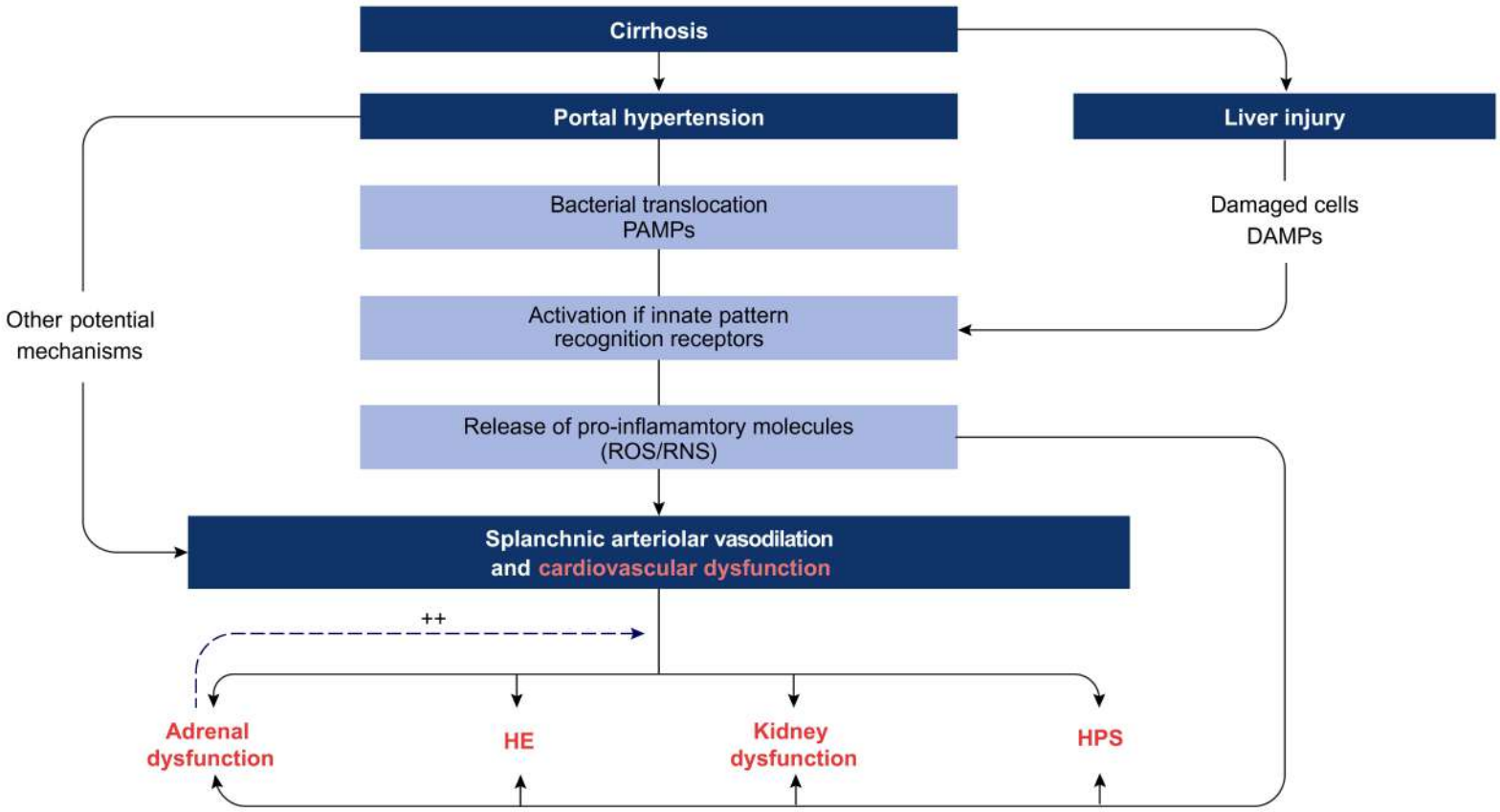
肝硬化的进展：从代偿 → 失代偿

- Transition from compensated cirrhosis to DC occurs at a rate of 5 – 7% per year
- DC is a systemic disease, with multi-organ/system dysfunction



ACLF, acute-on-chronic liver failure; CSPH, clinically significant portal hypertension; DC, decompensated cirrhosis; HVPG, hepatic venous pressure gradient; LSM, liver stiffness measurement; PSE, portosystemic encephalopathy

Pathophysiology of DC



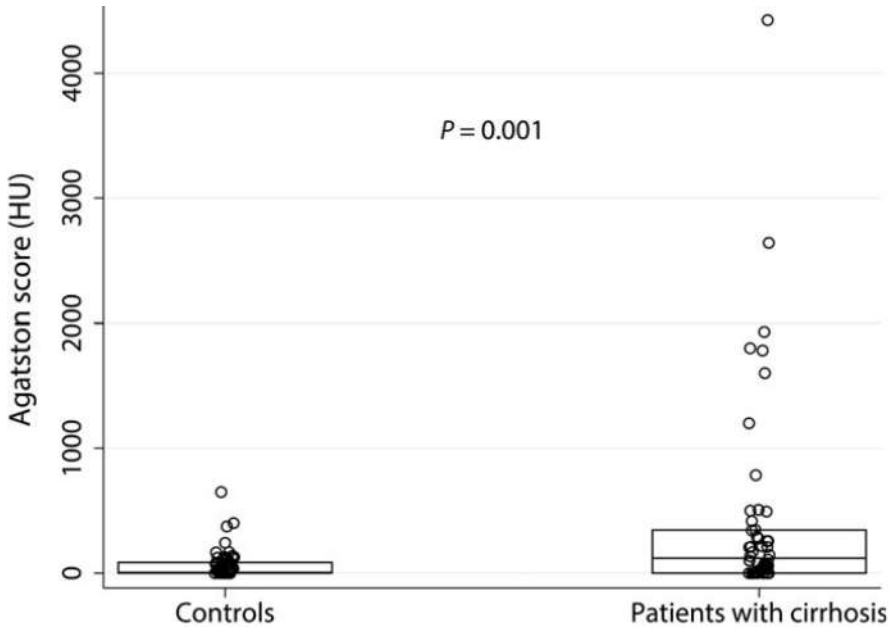
DAMP, damage-associated molecular pattern; DC, decompensated cirrhosis; HE, hepatic encephalopathy; HPS, hepatopulmonary syndrome; PAMP, pathogen-associated molecular pattern; RNS, reactive nitrogen species; ROS, reactive oxygen species

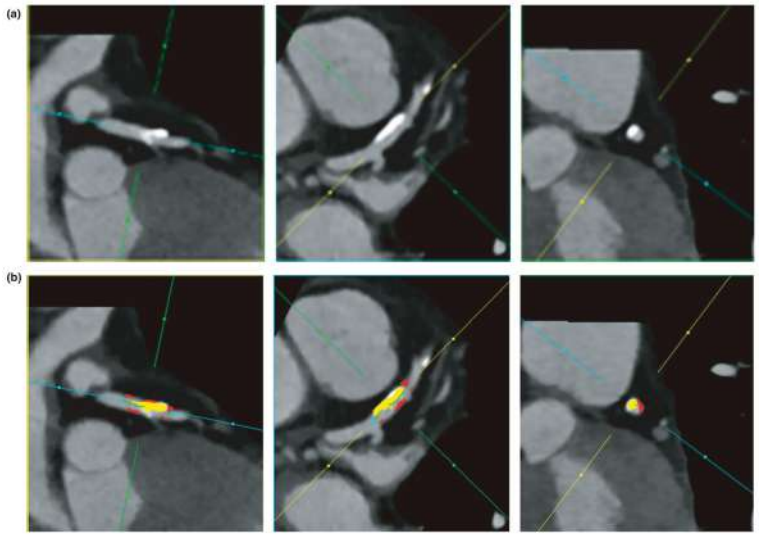
肝移植病人常见的“心肺”问题

1. 合并心肺疾病（内科夹杂症）
   - 冠心病，心瓣膜病变，心肌病，其它心脏疾
   - COPD
2. 失代偿性肝硬化的并发症
   - Cirrhotic Cardiomyopathy
   - Hepato-pulmonary syndrome
   - Portopulmonary hypertension
3. 心衰导致的肝硬化

High burden of coronary atherosclerosis in patients with cirrhosis

- 研究方法
  - ➔ coronary computed tomography angiography
  - ➔ 52 patients from all Child-Pugh classes and aetiologies of cirrhosis without known cardiac disease
  - ➔ 52 persons referred with new-onset chest pain served as controls





图：Agatston coronary artery calcification score

Eur J Clin Invest 2017; 47 (8): 565–573

⚠ **特别提醒：**冠状动脉疾病在肝硬化和新发胸痛患者中同样普遍，但病变更广泛和更严重，且与不良预后相关

Table 2 Qualitative and quantitative characteristics of coronary artery disease in patients with cirrhosis and controls

	Cirrhosis group (n=52)	Control group (n=52)	*P*
Prevalence of coronary artery disease [n (%)]			
Any coronary artery disease	40 (77%)	34 (65%)	0·19
Nonobstructive disease	30 (58%)	28 (54%)	0·69
Obstructive disease	10 (19%)	6 (11%)	0·28
Number of segments involved [n (%)]†			
1–4	22 (55%)	28 (82%)	0·01
≥5	18 (45%)	6 (18%)	
Number of vessels involved [n (%)]†			
1	10 (25%)	16 (47%)	0·02
2	13 (32%)	13 (38%)	
3	17 (43%)	5 (15%)	
Agatston score = 0 [n (%)]	14 (27%)	21 (40%)	0·11
Agatston score > 400 HU [n (%)]	11 (21%)	2 (4%)	0·007

HU, Hounsfield Units.
†Calculated only for patients with coronary artery disease.

Table 3 Characteristics of coronary artery plaques in patients with cirrhosis and controls

	Cirrhosis group (n=52)	Control group (n=52)	*P*
Positive remodelling [n (%)]	37 (71%)	28 (54%)	0·07
Plaque length (mm)	26 (0–58)	5 (0–22)	0·007
CP volume (mm^3)	28 (0–107)	2 (0–20)	0·001
NCP volume (mm^3)	69 (0–200)	34 (0–119)	0·09
LD-NCP volume (mm^3)	9 (0–32)	2 (0–14)	0·10
Total plaque volume (mm^3)	117 (0–310)	36 (0–148)	0·02
CP proportion (%)	34 (22–57)	4 (0–10)	<0·001
NCP proportion (%)	66 (43–78)	91 (78–96)	<0·001
LD-NCP proportion (%)	8 (5–12)	7 (5–16)	0·76

CP, calcified plaque; NCP, noncalcified plaque; LD-NCP, low-density noncalcified plaque.
Parameters are presented as medians (interquartile range) for continuous and n (%) for categorical variables. Units are in parenthesis.

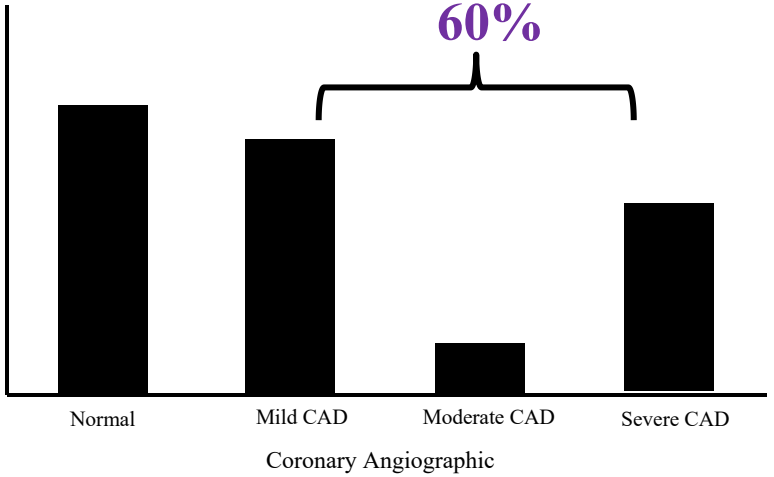
Eur J Clin Invest 2017; 47 (8): 565–573

Cardiac Hemodynamic and Coronary Angiographic Characteristics of Patients Being Evaluated for Liver Transplantation

⚠ **特别提醒：**需要LT的ESLD患者中，术前经过冠脉CTA评估，约26%伴有中、重度冠状动脉狭窄。老年，男性，高血压和糖尿病是主要的危险因素

Patient characteristics

Characteristic	No. (%)
Age (yrs)	57 ± 7
Men	106 (66%)
White	88 (55%)
Black	11 (7%)
Hispanic	13 (8%)
Other	49 (30%)
Etiology of ESLD	
Viral hepatitis	82 (51%)
Alcoholic	25 (16%)
NASH	15 (9%)
Cryptogenic	13 (8%)
Other	26 (16%)
Coronary risk factors	
Hypertension*	49 (30%)
Diabetes mellitus	58 (36%)
Current or previous smoker	51 (32%)
Hyperlipidemia†	10 (6%)
Family history of early coronary heart disease	7 (4%)



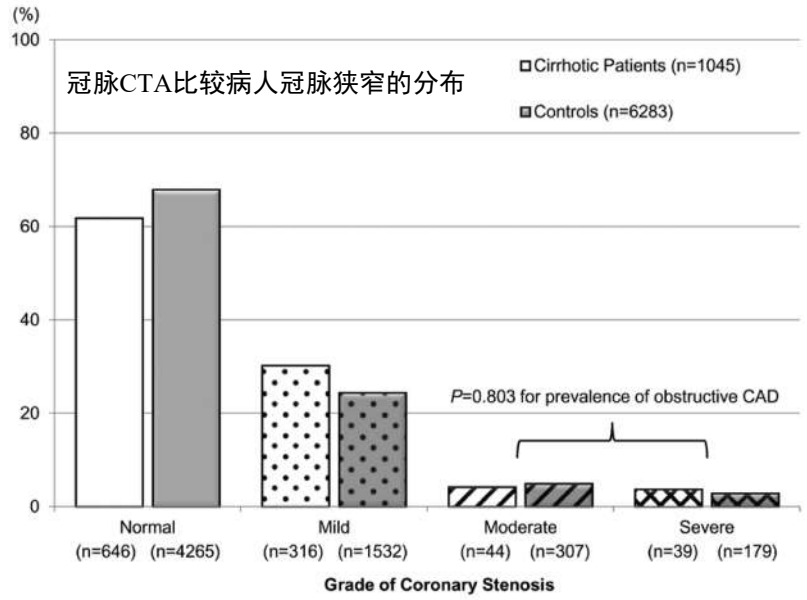
Variable	Coronary Artery Narrowing			p Value
	None (n = 64)	Mild (n = 58)	Moderate to Severe (n = 39)	
Age (yrs)	54 ± 7	59 ± 8	59 ± 7	0.002
Men	33 (52%)	42 (72%)	29 (74%)	0.019
Hypertension	10 (16%)	17 (29%)	23 (59%)	<0.001
Diabetes mellitus	16 (25%)	21 (36%)	22 (56%)	<0.001
Smoker	21 (33%)	15 (26%)	17 (44%)	NS

Am J Cardiol 2006; 98: 178 – 181

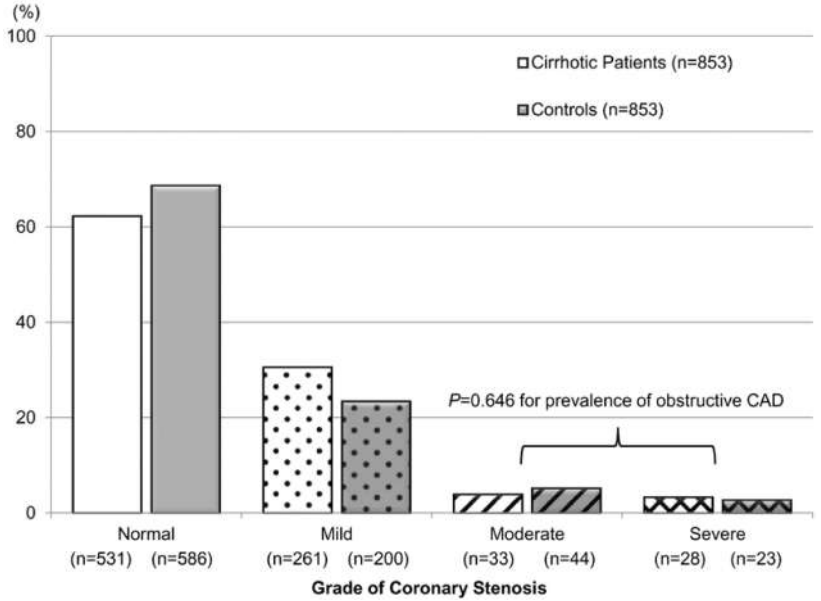
Prevalence and Prediction of Coronary Artery Disease in Patients With Liver Cirrhosis

A Registry-Based Matched Case–Control Study

Jihyun An, MD; Ju Hyun Shim, MD, PhD; Seon-Ok Kim, MS; Danbi Lee, MD, PhD; Kang Mo Kim, MD, PhD; Young-Suk Lim, MD, PhD; Han Chu Lee, MD, PhD; Young-Hwa Chung, MD, PhD; Yung Sang Lee, MD, PhD



所有病人（1045 *vs* 6283）的比较



配对病人（853 *vs* 853）的比较

Circulation. 2014; 130: 1353 - 1362

⚠ **特别提醒：**在肝硬化需要做肝移植的病人中，对于具有传统冠心病高危因素的病人应仔细排查

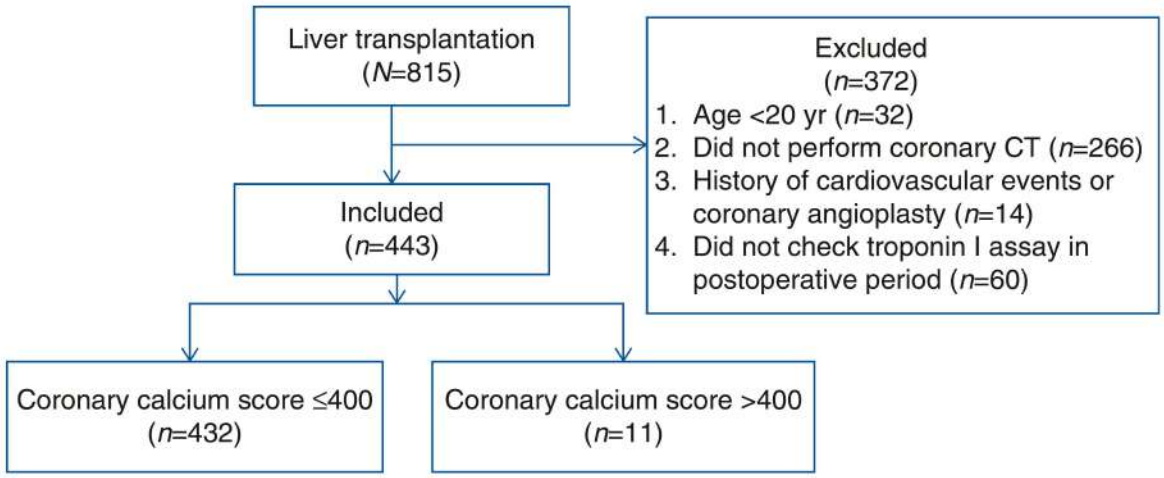
1. 无论冠脉CTA显示其冠心病严重程度如何，均未放弃LT
2. 83例LC合并阻塞性CAD病人中，24例在LT手术前接受冠状动脉造影，其中5例行PCI，1例接受CABG手术。其余患者均接受药物治疗
3. 83例病人中有53例接受了LT手术。多支血管动脉粥样硬化患者LT术后住院期间发生非ST段抬高型心肌梗死，心房颤动和室性心动过速各1例。这3名患者均未在LT前进行血运重建
4. LT术后有2例病人接受了晚期冠脉血运重建
5. 在观察期间，任何有或没有阻塞性CAD的患者在最终接受LT手术期间均未发生其它心脏事件或死亡

analysis using a logistic regression model.
†Family history of cardiovascular disease.

Circulation. 2014; 130: 1353 - 1362

Preoperative coronary calcium score is predictive of early postoperative cardiovascular complications in liver transplant recipients

Y.-G. Kong[1†], J.-W. Kang[2†], Y.-K. Kim[1*], H. Seo[1], T.-H. Lim[2], S. Hwang[3], G.-S. Hwang[1] and S.-G. Lee[3]



Coronary CT Total coronary artery calcification was classified as none (0), minimal (1 – 10), mild (11 – 100), moderate (101 – 400) or severe (> 400) according to the total coronary calcium score

British Journal of Anaesthesia 2015, 114 (3): 437 – 43

⚠ 特别关注

1. 冠状动脉CTA“钙化积分 > 400”和“女性”是LT术后1个月内发生心血管并发症的可靠预测因素
2. 冠状动脉CTA可能是LT候选者术前心血管评估的另一种潜在良好的筛查工具

Age	1.00 (0.96–1.04)	0.867		
Gender				
Male	1.00		1.0	
Female	2.69 (1.34–5.39)	0.005	2.76 (1.37–5.57)	0.005
Body mass index	0.96 (0.88–1.06)	0.432		
Diabetes mellitus	1.75 (0.86–3.55)	0.124		
Smoking history	0.53 (0.24–1.18)	0.120		
Statins therapy	5.57 (0.99–31.46)	0.052	4.20 (0.69–25.63)	0.120

Conclusions. A preoperative coronary calcium score of >400 predicted cardiovascular complications occurring 1 month after LT, suggesting that preoperative evaluation of coronary calcium scores could help predict early postoperative cardiovascular complications in LT recipients.

Safety and Efficacy of Combined Orthotopic Liver Transplantation and Coronary Artery Bypass Grafting

David Axelrod,[1] Alan Koffron,[1] Andre DeWolf,[2] Alfred Baker,[3] John Fryer,[1] Talia Baker,[1] James Frederiksen,[4] Keith Horvath,[4] and Micheal Abecassis[1]

Table 1. Patient Demographic Information

Patient Number	Age (yr)	Gender	UNOS/MELD Status	Diagnosis	Indication for Transplant
1	48	M	2A (19)	Hepatitis C, EtOH abuse	Ascites, variceal bleeding, SBP
2	66	F	2B (9)	Hepatitic C	Hepatocellular carcinoma
3	63	M	29	Nonalcoholic steatohepatitis	Hepatocellular carcinoma, ascites
4	54	M	31	Hepatitis C, EtOH abuse	Hepatocellular carcinoma
5	58	M	26	Polycystic liver disease	Abdominal pain

Table 2. Cardiac Evaluation

		% Occlusion of Coronary Artery			
Patient Number	Ejection Fraction	Left Main	Left Anterior Descending	Right Circumflex Artery	Circumflex
1	60%		70%	50%	30%
2	60%		80%	60%	30%
3	60%		70%	70%	50%
4	55%		70%	95%	50%
5	60%	50%	90%	50%	

Liver Transpl 2004; 10: 1386 – 1390

Table 4. Postoperative Course

Patient Number	Length of Follow-up	Status	ICU LOS (Days)	Hospital LOS (Days)	Complications
1	43 months	Alive	2	9	Pericardial effusion
2	2.5 months	Dead	2	16	Cardiac arrest 2.5 months post operatively
3	24 months	Alive	40	59	Postoperative cardiac arrest, pneumonia
4	10 months	Alive	4	14	Acute rejection
5	10 months	Alive	2	7	None

Abbreviations: ICU, intensive care unit; LOS, length of stay.

Table 3. Operation Performed

Patient Number	Bypass	OLT
1	3 vessels: LAD, RCA, CIRC	Standard bicaval anastomosis
2	3 vessels: LAD, RCA, CIRC	Standard bicaval anastomosis
3	3 vessels: LAD, RCA, CIRC	Standard bicaval anastomosis
4	2 vessels: LAD, RCA	Side to side venacavaplasty
5	2 vessels: LAD, RCA	Side to side venacavaplasty

Abbreviations: LAD, left anterior descending; RCA, right circumflex artery; CIRC, circumflex.

Table 5. Cardiac Results

Patient Number	Post CABG-EF	ECG Changes	Peak Troponin I
1	>55%	None	NA
2	>55%	None	12.5
3	35% with diffuse hypokinesis	Anteroseptal ischemia	97.2
4	>55%	None	NA
5	>55%	None	NA

Abbreviations: ECG, echocardiogram; CABG-EF, coronary artery bypass grafting-ejection fraction.

Liver Transpl 2004; 10: 1386 – 1390

⚠ 特别提醒

无论ESLC病人是存在阻塞性CAD，只要移植前采用现有的CAD治疗策略，LT术后生存率之间没有显着差异

	Unadjusted		Adjusted	
	HR (95% CI)	p-Value	HR (95% CI)	p-Value
CAD-negative	Ref	–	ref	–
CAD-positive	1.05 (0.74, 1.49)	0.780	1.13 (0.79, 1.62)	0.493
CAD-negative	Ref	–	ref	–
CAD-moderate	0.85 (0.48, 1.51)	0.576	0.93 (0.52, 1.66)	0.797
CAD-severe	1.17 (0.78, 1.74)	0.444	1.26 (0.83, 1.91)	0.277
CAD-negative	Ref	–	ref	–
CAD-no intervention	0.67 (0.39, 1.17)	0.164	0.79 (0.45, 1.39)	0.409
CAD-intervention	1.42 (0.95, 2.12)	0.087	1.45 (0.95, 2.21)	0.086

CAD = coronary artery disease; HR = hazards ratio; CI = confidence interval; ref = reference group.

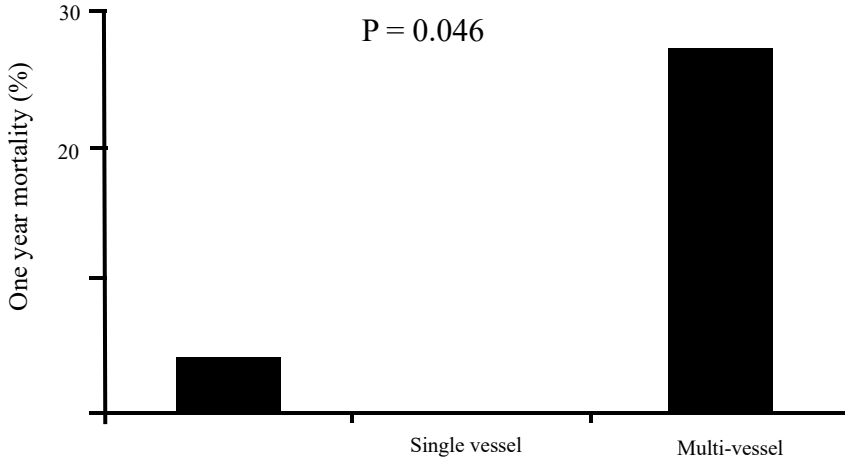
基本资料

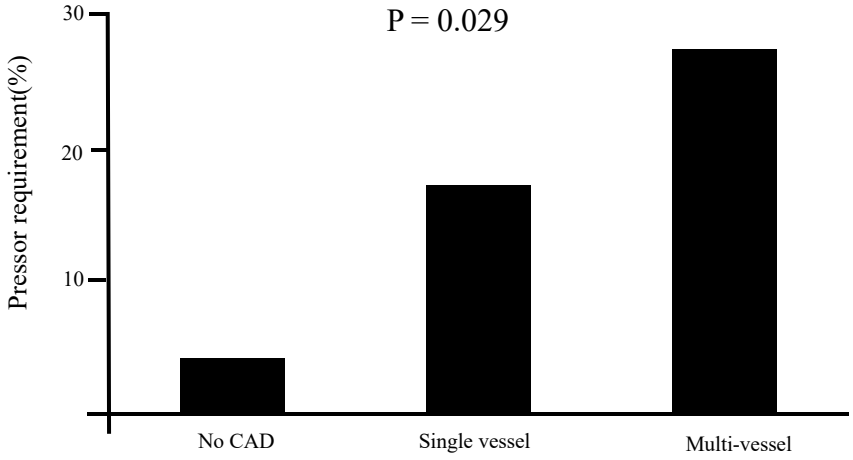
- UCLA等7家顶级肝移植中心的630例肝移植病人，术前均做过冠脉造影
- CAD-negative < 50%，CAD-moderate 50 – 70%，CAD-severe > 70%
- CAD(-) 479例，CAD-mod 55例，CAD-sev 96例
- Intervention包括：PTCA（BMS or DES）和CABG

American Journal of Transplantation 2013; 13: 184 – 191

Multivessel Coronary Artery Disease Predicts Mortality, Length of Stay, and Pressor Requirements After Liver Transplantation

University of California San Francisco, San Francisco, CA





In conclusion, multivessel CAD is associated with higher mortality after liver transplantation when it is documented angiographically before transplantation, even in the absence of severe coronary artery stenosis. This study provides preliminary evidence showing that there may be significant prognostic value in coronary angiography as a part of the pretransplant workup

Liver Transpl 2010, 16: 1242 - 1248

Clinical Investigation

Coronary Interventions before Liver Transplantation

Might Not Avert Postoperative Cardiovascular Events

Primary Liver Disease*	Coronary Artery Disease		
	Mild (n=28)	**Moderate** (n=10)	**Severe** (n=13)
Alcohol-induced	3 (10.7)	4 (40)	4 (30.8)
Hepatitis B	2 (7.1)	1 (10)	0
Hepatitis C	5 (17.9)	2 (20)	4 (30.8)
Nonalcoholic steatohepatitis	5 (17.9)	0	2 (15.4)
Primary biliary cirrhosis	4 (14.3)	0	0
Unknown	5 (17.9)	1 (10)	2 (15.4)
Autoimmune	1 (3.6)	0	1 (7.7)
α_1-antitrypsin deficiency	1 (3.6)	1 (10)	0
Primary sclerosing cholangitis	1 (3.6)	0	0
Schistosomiasis	1 (3.6)	0	0
Drug-induced	0	1 (10)	0

*Difference in cause between groups, P=0.188

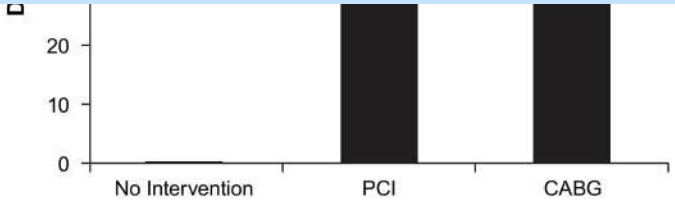
Data are presented as number and percentage. P <0.05 was considered statistically significant.

＝51例

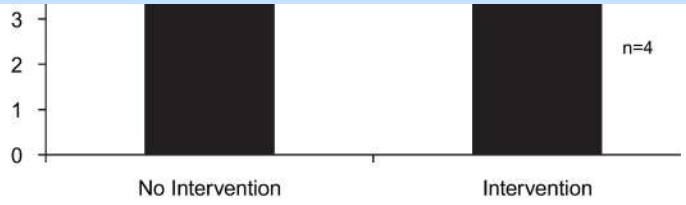
Tex Heart Inst J, 2015; 42(5): 438 - 42)

⚠ 重要信息

- 无论是否在术前进行冠状血管再通手术，患有严重冠心病的病人在肝移植（LT）手术后死亡率很高



上图：Graph compares mortality rate on the basis of coronary intervention. P < 0.05 was considered statistically significant



上图：Graph compares the outcome of patients with severe coronary artery disease based on coronary intervention

Outcome	No Intervention (n=41)	Intervention (n=10)	*P* Value
Alive	29 (70.7)	5 (50)	0.172
Dead	12 (29.3)	5 (50)	—
Cardiac cause	0	4 (80)	<0.0001
Noncardiac cause	12 (100)	1 (20)	0.172

上表：Data are presented as number and percentage. P < 0.05 was considered statistically significant
在Intervention组，9例严重CAD病人，1例中度CAD病人

Variable	All Patients (N=51)	Coronary Artery Disease			*P* Value
		Mild (n=28)	Moderate (n=10)	Severe (n=13)	
Outcome	—	—	—	—	0.624
Alive	34 (66.7)	18 (64.3)	8 (80)	8 (61.5)	—
Dead	17 (33.3)	10 (35.7)	2 (20)	5 (38.5)	—
Cardiac cause	4 (23.5)	0	0	4 (80)	0.001
Noncardiac cause	13 (76.5)	10 (100)	2 (100)	1 (20)	—
Liver	2 (15.4)	1 (10)	1 (50)	0	—
Sepsis	5 (38.5)	4 (40)	1 (50)	1 (100)	—
Other	6 (46.2)	5 (50)	0	0	—

Data are presented as number and percentage. *P* <0.05 was considered statistically significant.

Tex Heart Inst J, 2015; 42(5): 438 - 42)

冠心病和“肝移植”

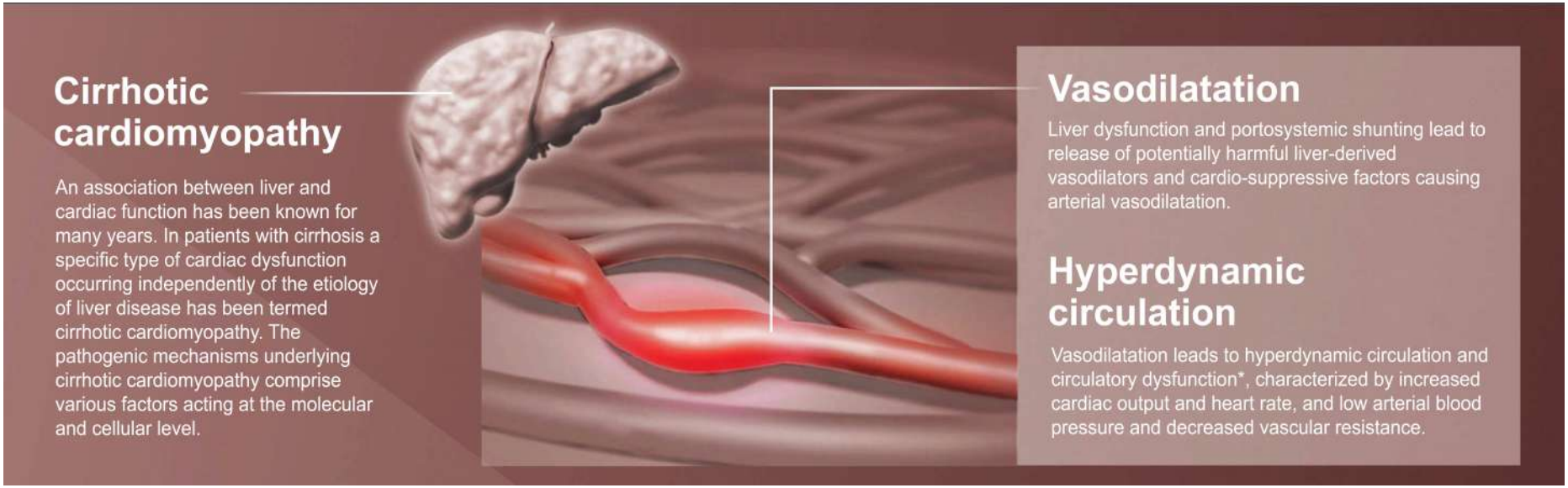
- 在等待肝移植病人中， 25%的具有冠心病危险因素者其冠脉狭窄已经 > 50%
- 患有糖尿病或 > 2个心脏危险因素的LT候选病人最有可能同时患有CAD
- 多支冠脉病变LT术后死亡率↑，术中和术后循环不稳定的几率↑
- 肝移植前药物应激试验（DSE，放射性核素应激试验和单光子发射计算机断层扫描）的阴性诊断价值较高
- 药物应激试验阳性的病人应继续进行冠脉造影或冠脉CTA检查

接上一张

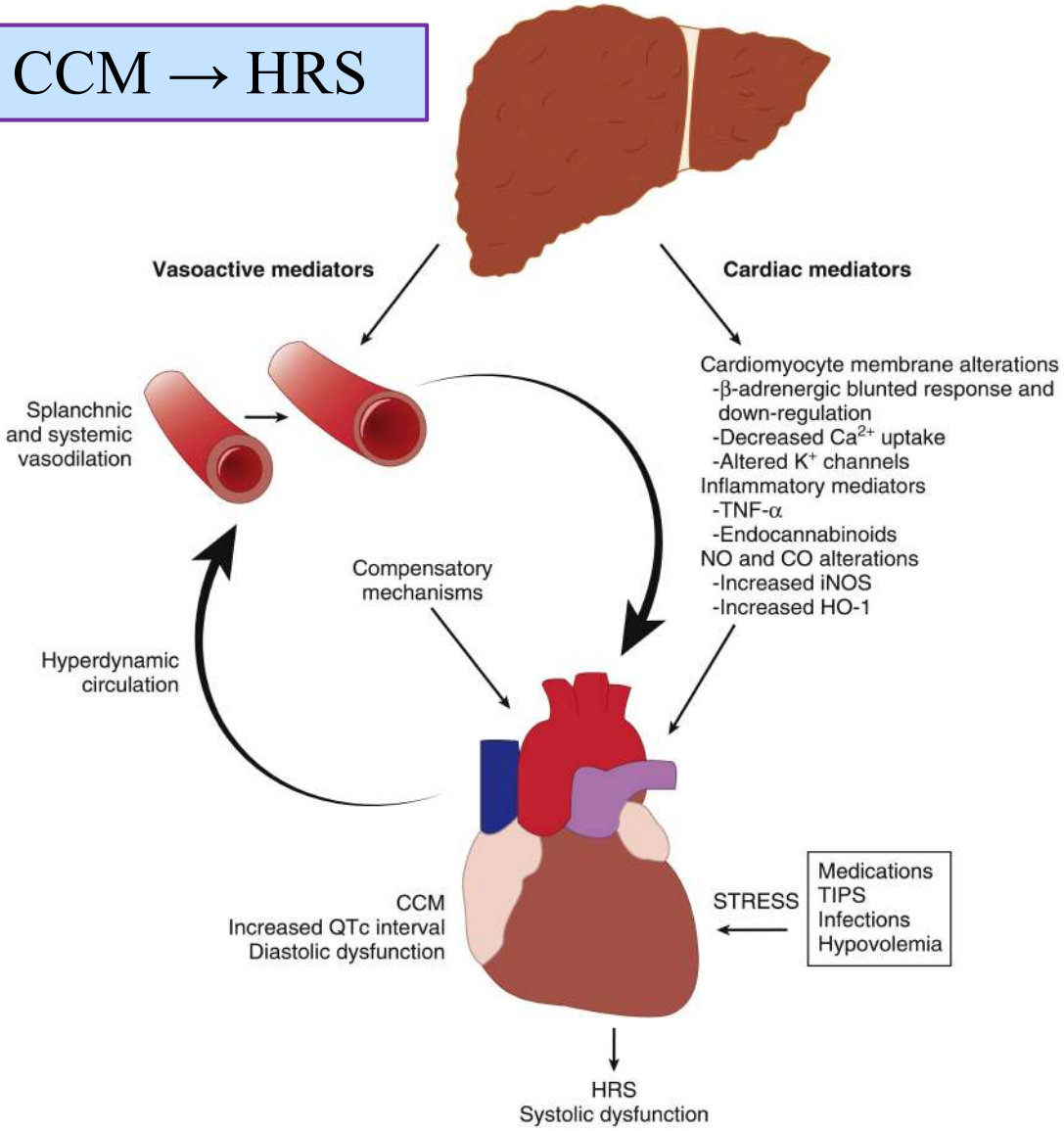
- 心肺联合运动试验（CPET）测定病人的最大氧消耗（VO_{2max}）、峰值氧消耗（VO_{2peak}）和无氧阈氧消耗（VO_{2AT}），可提供“额外的”评估预后的参考信息。6分钟步行或登楼试验是简易的心肺联合运动试验
- 运动（应激）试验阳性的病人应考虑冠脉CTA或冠脉造影
- 严重冠脉狭窄且有症状的LT候选病人有做冠脉血管再通的指征

肝硬化病人的心功能状态

- 高循环动力状态
  - → CO增加；心率增快
  - → 低血压；低外周阻力
- 液体分布异常
  - → 内脏血流增加；内脏水肿
  - → 低血容量



From LC → CCM → HRS

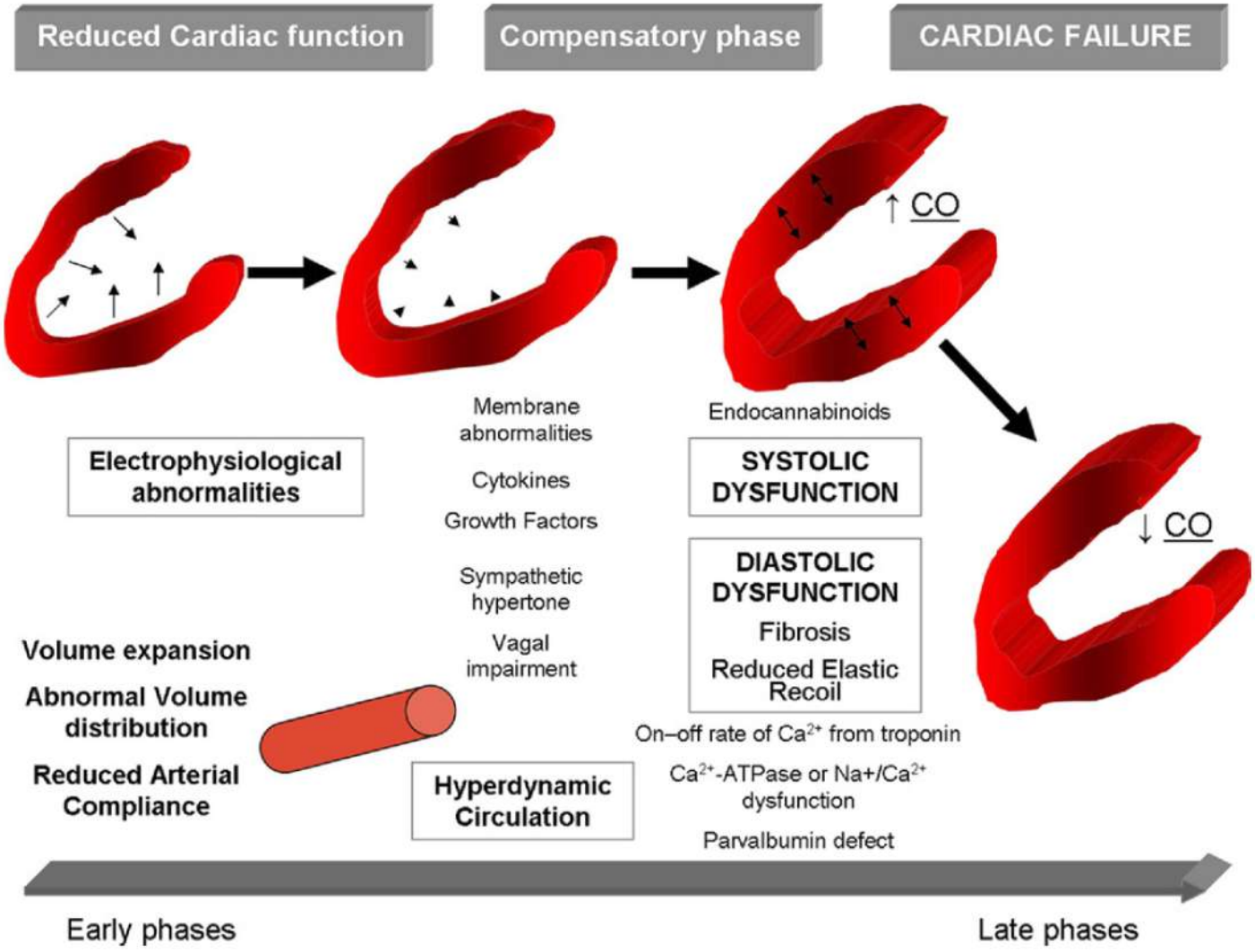


CCM, Cirrhotic cardiomyopathy; HO-1, heme oxygenase 1; HRS, hepatorenal syndrome; iNOS, inducible nitric oxide synthase; LC, Liver cirrhosis; QTc, cor-rected QT; TIPS, transjugular intrahepatic portosystemic shunt; TNF-α, tumor necrosis factor α

Cirrhotic Cardiomyopathy

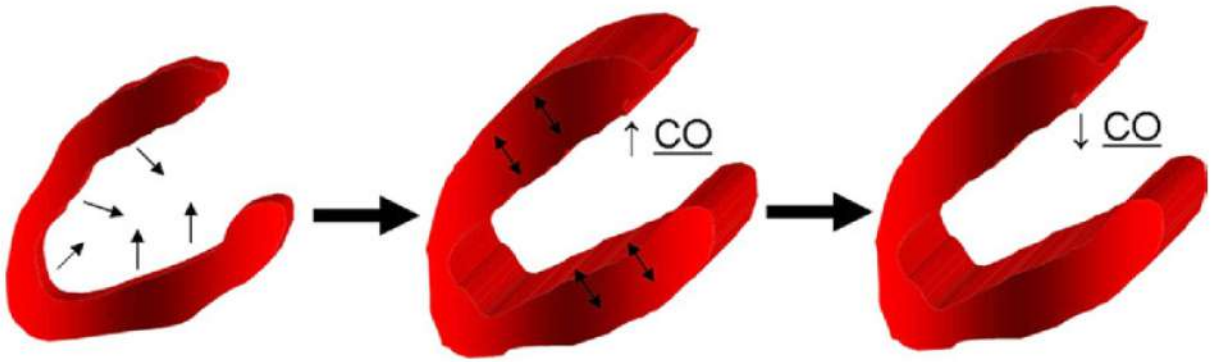
- 血管功能障碍：来自于门脉高压
  - → 内脏动脉扩张；门-体分流（短路）
  - → 内皮素，前列腺素，NO，CO和内源性大麻素
  - → 静息高动力状态是对内脏动脉舒张的反应
- 心肌细胞膜改变
- 容量增加
  - → 随着肝硬化进展，容量重新分布，内脏液体过量，而血容量减少

Cirrhotic Cardiomyopathy

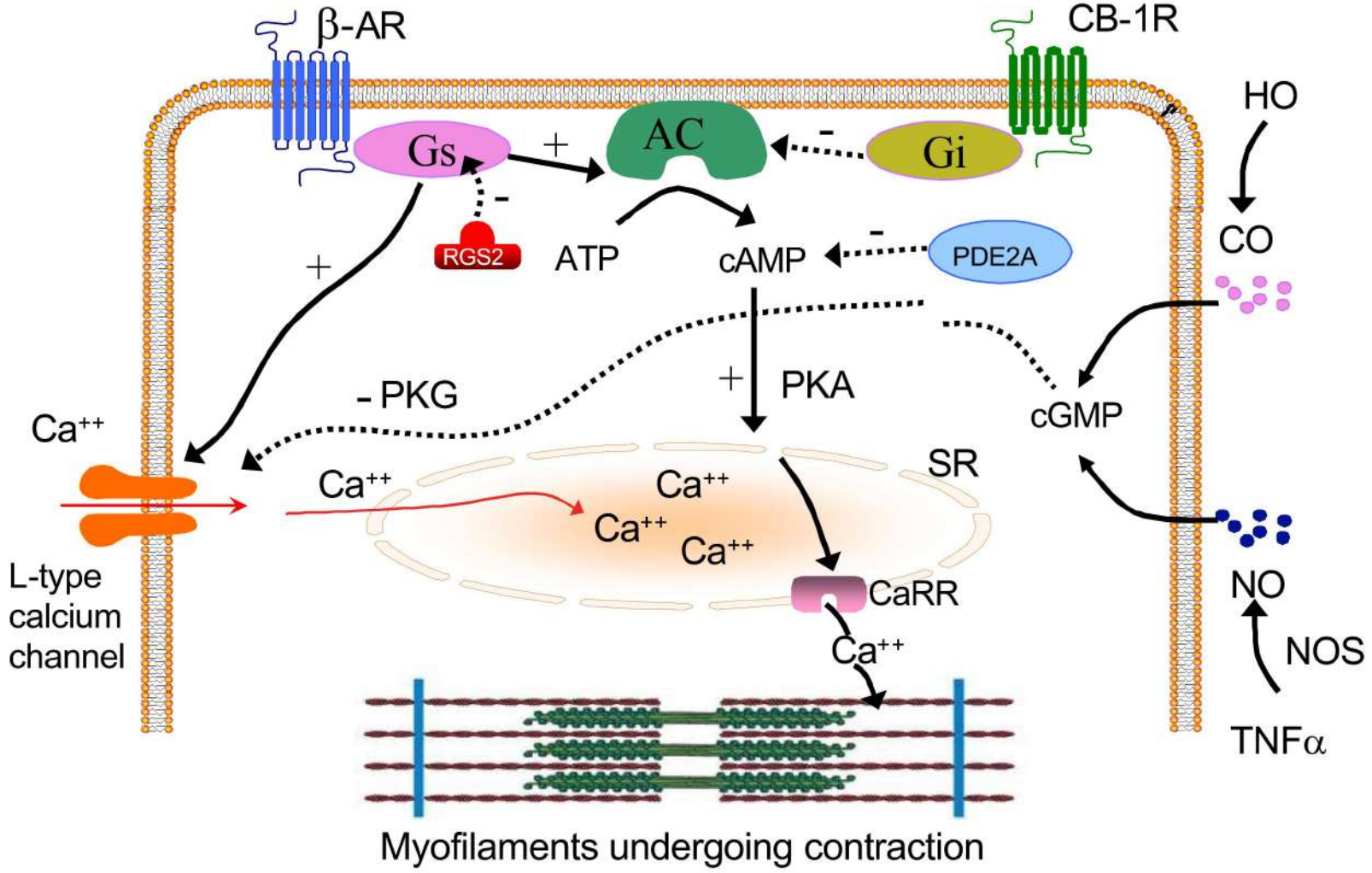


CCM 的临床表现

Reduced Cardiac Function	Compensatory Phase	Cardiac Failure



Clinical Findings	Hyperdynamic State	Hyperdynamic state ↑↑↑ Palpitation Tachycardia	Hypotension Cardiac failure sign and symptoms Pulmonary edema
ECG Abnormalities	QT prolongation	Multiple extrasystoles QT prolongation ↑↑↑	Bundle branch block ST – segment depression Electrical and mechanical dyssynergy
Echocardiographic Findings	Prolonged isovolumetric relaxation time	Prolonged isovolumetric relaxation time (>80ms) Decreased pattern of contractility Diastolic Dysfunction	Enlarged left atrium Decreased wall motion Increased wall thickness Systolic Dysfunction



Gs = stimulatory G proteins, AC = adenylate cyclase, PDE2A = Cyclic nucleotide phosphodiesterase, CaRR= Calcium release receptor, PKA = protein kinase A; PKG = protein kinase G; RGS2 = regulator of G-protein signaling 2

Systolic Dysfunction: Pathophysiology

- The adrenergic pathway
  - β受体密度下降，功能减弱
  - 受体后机制
    - Gs蛋白↓→cAMP↓
    - 抑制性信号↑
    - AC基因表达↓
- The Endocanabinoids（内源性大麻素）
  - EC系统CB-1 → Gi → AC↓ → 负性肌力作用
- Other pathways
  - NO合成酶（NOS） → NO
  - 亚铁血红素氧合酶（HO） → CO

肝硬化性心肌病的循证证据

- Cardiac evaluation in patients with cirrhosis is important since CCM can influence prognosis

Recommendation	Grade of evidence	Grade of recommendation
肝硬化患者的超声心动图应进行“动态应激试验†”（高循环动力和后负荷下降可以掩盖收缩功能障碍） • 运动/药理学应激†后没有CO增加说明有收缩功能障碍	II-1	1
心肌应变成像和左心室整体纵向收缩应变可能对评价失代偿性肝硬化患者左心室收缩功能有用	II-2	2
心脏MRI可识别结构变化	III	2
在收缩功能正常时，舒张功能障碍可作为CCM的早期症状出现，应使用ASE标准进行诊断 • Average E/e'>14 • Tricuspid velocity >2.8 m/s • LAVI >34 ml/m^2	II-1	1

ASE, American Society of Echocardiography; CCM, cirrhotic cardiomyopathy; CO, cardiac output; DC, decompensated cirrhosis; ECG, electrocardiogram; GLS, global longitudinal systolic strain; LAVI, left atrial volume index; MRI, magnetic resonance imaging

肝硬化性心肌病循证证据

Recommendation	Grade of evidence	Grade of recommendation
In patients with AD, reduced CO (as a manifestation of CCM) is associated with the development of AKI (specifically hepatorenal dysfunction) after infections such as SBP	II-1	1
QTc interval prolongation is common in cirrhosis and may indicate a poor outcome • Agents that can prolong the QT interval should be used cautiously	II-2	2
Detailed functional cardiac characterization should be part of the assessment for • TIPS insertion • LT	 II-2 II-1	 2 1
Standardized criteria and protocols for the assessment of systolic and diastolic function in cirrhosis are needed	II-2	2

AD, acute decompensation; AKI, acute kidney injury; CCM, cirrhotic cardiomyopathy; CO, cardiac output; LT, liver transplantation; SBP, spontaneous bacterial peritonitis; TIPS, transjugular intrahepatic portosystemic shunt

Cirrhotic Cardiomyopathy 诊断标准

Systolic dysfunction	• Blunted increase in cardiac output on exercise, volume challenge, or pharmacological stimuli • Resting ejection fraction <55%
Diastolic dysfunction	• E/A ratio <1.0 (age corrected) • Prolonged deceleration time (> 200 msec) • Prolonged isovolumic relaxation time (> 80 msec)
Supportive criteria	• Electrophysiological abnormalities • Abnormal chronotropic response • Electromechanical uncoupling/dys-synchrony • Prolonged Q-Tc interval • Enlarged left atrium • Increased myocardial mass • Increased brain natriuretic peptide (BNP) & proBNP levels • Increased troponin I levels

CCM的相关总结

- 40% - 50%的终末期肝硬化病人伴有CCM。最常见的类型是舒张性心衰。30% - 60%的病人伴有QT间期延长
- 肝移植是CCM病人唯一确切可靠的治疗。肝移植可以逆转心功能障碍并改善电生理异常。但是，肝移植手术本身对CCM病人具有高度的挑战性
- 超声心动图是CCM可疑病人的常规检查
  - ➔ 静息 → 舒张性心衰；DSE → 诱发收缩性心衰

接上一张幻灯

- 并不存在肝移植手术LVEF的cut-off。部分肝移植中心只做LVEF > 40%的病人
- 在终末期肝硬化的病人中，约有40%的病人伴有左心室流出道狭窄。这些病人并非LT的禁忌证，但临床上出现低血压和低心排时应及时和其它类型的心衰鉴别诊断

Hepatopulmonary syndrome

- 定义
  - HPS is defined as a disorder in pulmonary oxygenation, caused by intrapulmonary vasodilatation and, less commonly, by pleural and pulmonary arteriovenous communications occurring in the clinical setting of portal hypertension
- 临床症状
  - 呼吸困难和平卧位呼吸
  - dyspnoea and platypnoea

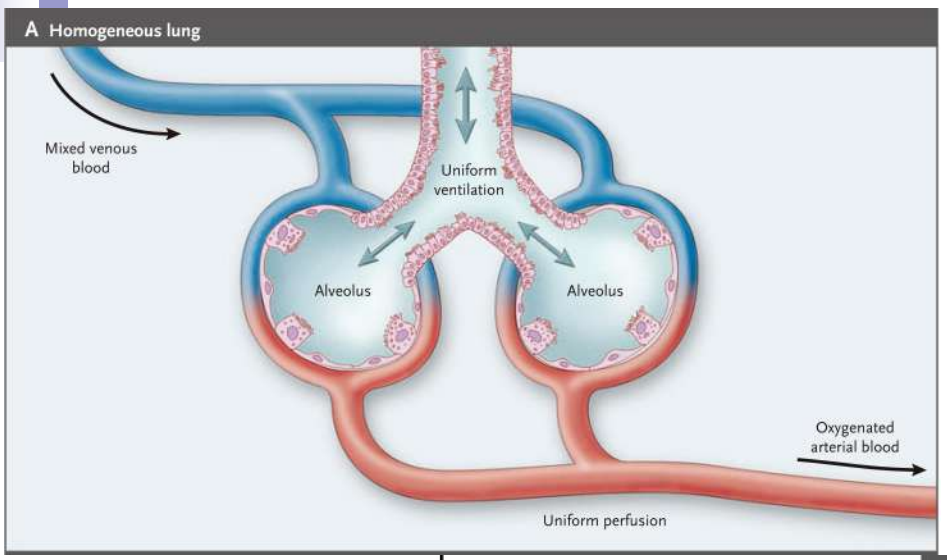
Pathogenesis of HPS & PPH

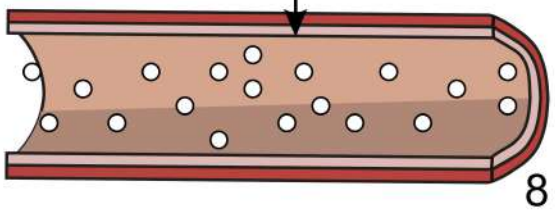
Pathogenesis of HPS

CO, carbon monoxide; CX3CL1, fractalkine; eNOS, endothelial nitric oxide synthase; ET, endothelin; HO, haem oxygenase-1; HPS, hepatopulmonary syndrome; iNOS, inducible nitric oxide synthase; NO, nitric oxide; VGF-A, vascular endothelial growth factor A

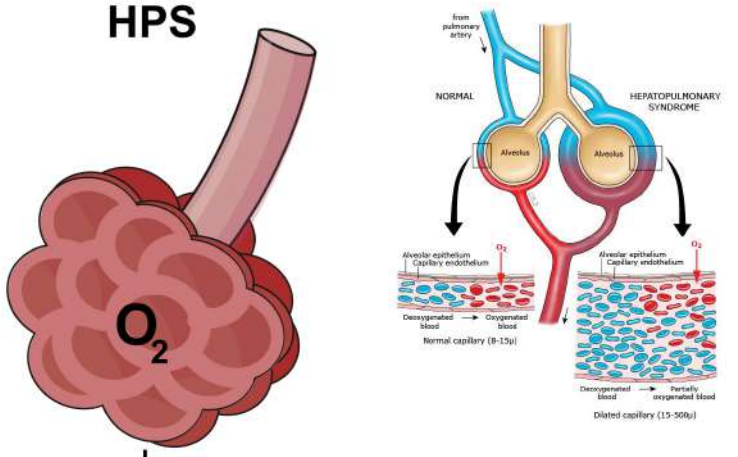
EASL CPG decompensated cirrhosis. J Hepatol, 2018, 69: 406 - 460

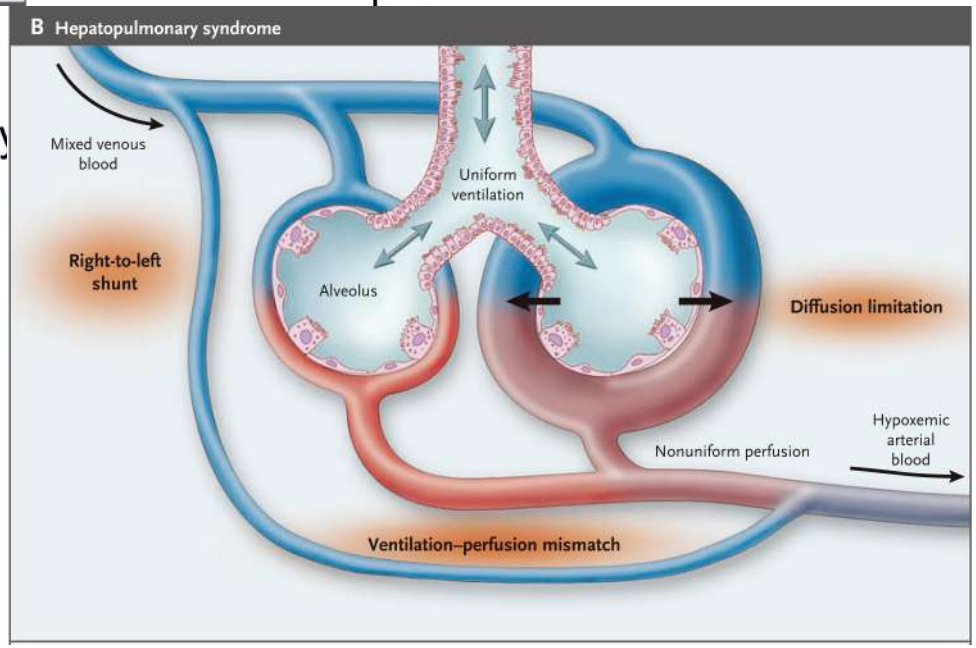
Pathophysiology of HPS





Capillary





Diagnosis of HPS

- Hypoxia with partial pressure of oxygen < 80 mmHg or alveolar–arterial oxygen gradient ≥15 mmHg in ambient air (≥20 mmHg in patients older than 65 years)
- Pulmonary vascular defect with positive findings on contrast-enhanced echocardiography or abnormal uptake in the brain (> 6%) with radioactive lung-perfusion scanning
- Commonly in presence of portal hypertension, and in particular
  - ➔ Hepatic portal hypertension with underlying cirrhosis
  - ➔ Pre-hepatic or hepatic portal hypertension in patients without underlying cirrhosis
- Less commonly in presence of
  - ➔ Acute liver failure, chronic hepatitis

Diagnosis of HPS

- In patients with portal hypertension and the clinical suspicion of HPS partial pressure of oxygen (PaO_2) in ABG should be assessed

Recommendation	Grade of evidence	Grade of recommendation
In patients with chronic liver disease, HPS should be suspected and investigated in presence of tachypnoea and polypnoea, digital clubbing and/or cyanosis	II-2	1
Screening in adults: • If pulse oximetry SpO_2 < 96% – ABG analysis should be performed • If ABG PaO_2 <80mmHg and/or P[A-a]O_2 ≥15 mmHg* (in ambient air) – further investigations should be performed	II-2	1
The use of contrast (microbubble) echocardiography to characterize HPS is recommended	II-2	1

ABG, arterial blood gas; HPS, hepatopulmonary syndrome; PaO_2, arterial partial pressure of oxygen; P[A-a]O_2, alveolar-arterial oxygen gradient; SpO_2, pulse oximetric saturation

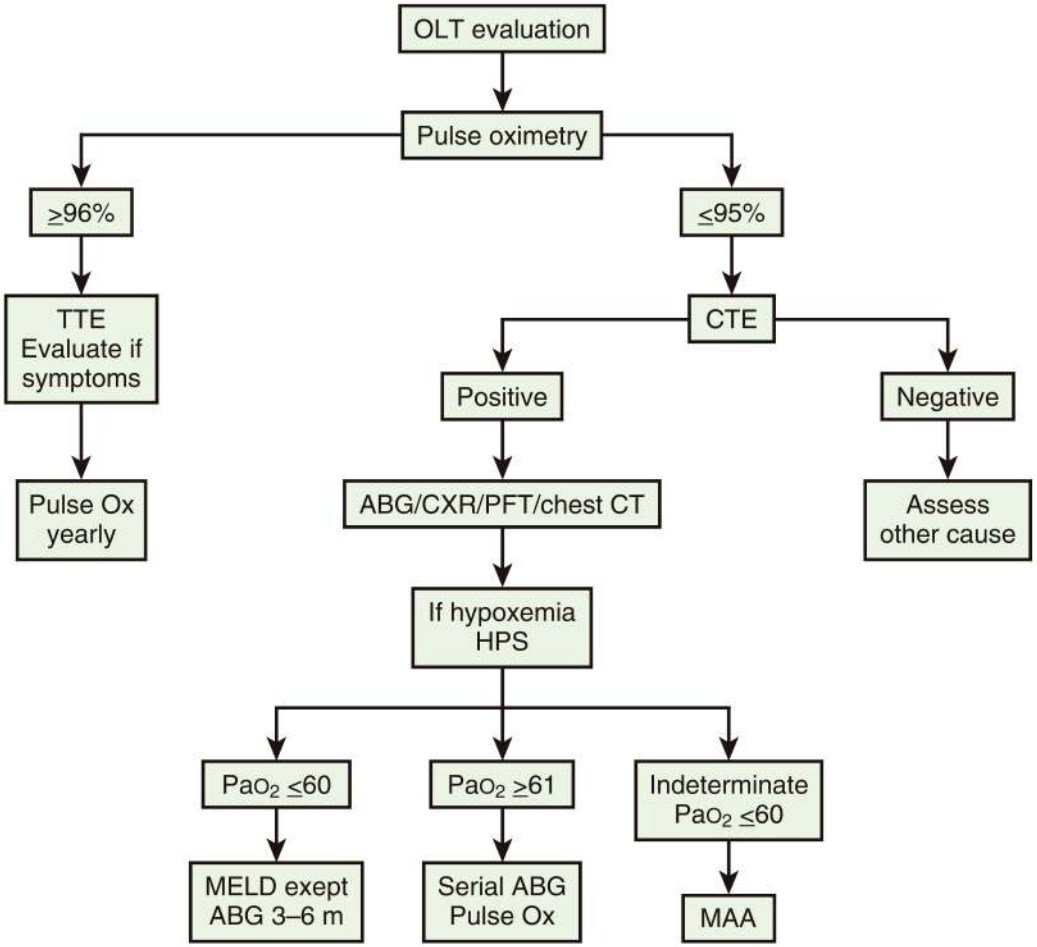
Diagnosis of HPS

- When PaO_2 suggests HPS, further investigations are needed to determine the underlying mechanism

Recommendation	Grade of evidence	Grade of recommendation
MAA scan should be performed to quantify the **degree of shunting** in patients with severe hypoxaemia and coexistent intrinsic lung disease, or to assess the prognosis in patients with HPS and very severe hypoxaemia (PaO_2 < 50 mmHg)	II-2	1
Neither contrast echocardiography nor MAA scan can definitively differentiate discrete arteriovenous communications from diffuse precapillary and capillary dilatations or cardiac shunts • Pulmonary angiography should be performed only in patients with the severe hypoxaemia (PaO_2 < 60 mmHg), poorly responsive to administration of 100% oxygen, and in whom there is a strong suspicion of arteriovenous communications that are amenable to embolization	II-2	1
Trans-oesophageal contrast-enhanced echocardiography (although associated with risks) can definitively exclude intra-cardiac shunts	II-2	2

MAA: technetium-99 m–labelled macro-aggregated albumin，锝-99m (^{99m}Tc)
大颗粒聚合白蛋白扫描

Overview of HPS



ABG, Arterial blood gases; *CT,* computed tomography; *CTE,* contrast transthoracic echocardiogram; *CXR,* chest X-ray; *HPS,* hepatopulmonary syndrome; *MAA,* technetium-99m-labeled macroaggregated albumin scan; *MELD,* Model for End-Stage Liver Disease; *OLT,* orthotopic liver transplant; *Ox,* oximetry; *Pao2,* partial pressure of oxygen in arterial blood; *PFT,* pulmonary function test; *TTE,* transthoracic echocardiogram.

HPS的治疗

- There is no established medical therapy currently available for HPS, the only successful treatment for HPS is LT

Recommendations for medical treatment	Grade of evidence	Grade of recommendation
Long-term oxygen therapy is recommended in patients with HPS and severe hypoxaemia despite the lack of available data concerning effectiveness, tolerance, cost effectiveness, compliance and effects on survival rates of this therapy	II-2	1
No recommendation can be proposed regarding the use of drugs or the placement of TIPS for the treatment of HPS	I	1
Recommendations for liver transplantation		
患有肝肺综合征（HPS）且PaO_2 < 60 mmHg者应进行肝移植（LT）评估，因为LT是目前唯一被证实有效的HPS治疗方法	II-2	1
Severe hypoxaemia (PaO_2 < 45 – 50 mmHg) is associated with increased post-LT mortality • ABG analysis should be carried out every 6 months to facilitate prioritization to LT	II-2	1

ABG, arterial blood gas; HPS, hepatopulmonary syndrome; LT, liver transplantation; PaO_2 arterial partial pressure of oxygen; TIPS, transjugular intrahepatic portosystemic shunt

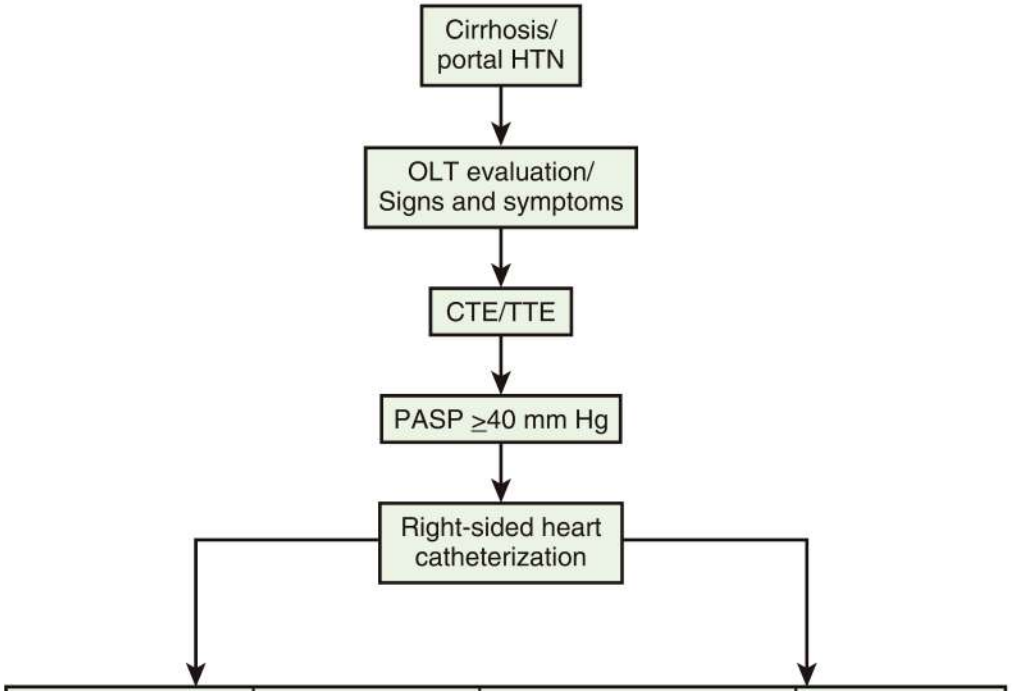
Portopulmonary hypertension

- PPHT occurs in patients with portal hypertension in the absence of other causes of arterial or venous hypertension
- Classification is based on mean pulmonary arterial pressure (mPAP), and assumes high pulmonary vascular resistance (PVR) and normal pulmonary occlusion pressures
  - ➔ Mild: mPAP ≥25 and <35 mmHg
  - ➔ Moderate: mPAP ≥35 and <45 mmHg
  - ➔ Severe: mPAP ≥45 mmHg

Portopulmonary hypertension

- Incidence between 3% – 10% cirrhosis patients based on haemodynamic criteria; women are at 3× greater risk and it is more common in autoimmune liver disease
- There is no clear association between the severity of liver disease or portal hypertension and the development of severe PPHT

Diagnostic approach to PPHT



	mPAP (9–18 mm Hg)	PVR (>250 dyn-sec/cm^{-5})	PCWP (6–12 mm Hg)
PPHTN	↑	↑	NL
Hyperdynamic*	↑	NL	NL/↑
Volume overload*	↑	NL	↑

CTE, Contrast transthoracic echocardiography; HTN, hypertension; mPAP, mean pulmonary artery pressure; NL, normal; OLT, orthotopic liver transplant; PASP, pulmonary artery systolic pressure; PCWP, pulmonary capillary wedge pressure; PPHTN, portopulmonary hypertension; PVR, pulmonary vascular resistance; TTE, trans-thoracic echocardiography.

PPHT的监测和治疗

- The evidence base for pharmacological therapies in PPHT is limited

Recommendation	Grade of evidence	Grade of recommendation
Screening for PPHT should be via TDE in patients deemed potential recipients for TIPS or LT • In those with a positive screening test, right heart catheterization should be performed	II-1	1
In patients with PPHT who are listed for LT, echocardiography should be repeated on the waitlist (the specific interval is unclear)	III	1
β-blockers should be stopped and varices managed by endoscopic therapy in cases of proven PPHT	II-3	1
Therapies approved for primary pulmonary arterial hypertension may improve exercise tolerance and haemodynamics in PPHT • However, endothelin antagonists should be used with caution because of concerns over hepatic impairment	II-2	1
TIPS should not be used in patients with PPHT	II-3	1

LT, liver transplantation; PPHT, portopulmonary hypertension; TDE, transthoracic doppler echocardiography; TIPS, transjugular intrahepatic portosystemic shunt

PPHT病人的肝移植

- Although severe PPHT has, historically, been a contraindication for LT, the advent of improved haemodynamic control (with agents such as IV prostacyclin) allows LT to be considered

Recommendation	Grade of evidence	Grade of recommendation
If mPAP <35 mmHg and right ventricular function is preserved, LT should be considered	II-2	1
mPAP of ≥ 45 mmHg should be considered an absolute contraindication to LT irrespective of therapy applied	III	1
Therapy to lower mPAP and improve right ventricular function should be commenced in patients with mPAP ≥ 35 mmHg • Right ventricular function should be periodically evaluated	II-2	1
MELD exception can be considered in patients with proven PPHT in whom targeted therapy fails to decrease mPAP < 35 mmHg but does facilitate normalization of PVR to < 240 dyn.s/cm^{-5} and right ventricular function	II-3	2
MELD exception should be advocated in patients with proven PPHT of moderate severity (mPAP ≥ 35 mmHg) in whom targeted treatment lowers mPAP < 35 mmHg and PVR < 400 dyn.s/cm^{-5}	II-2	1

IV, intravenous; LT, liver transplantation; MELD, Model for End-Stage Liver Disease; mPAP, mean pulmonary arterial pressure; PPHT, portopulmonary hypertension; PVR, pulmonary vascular resistance

心肺评估常用检查

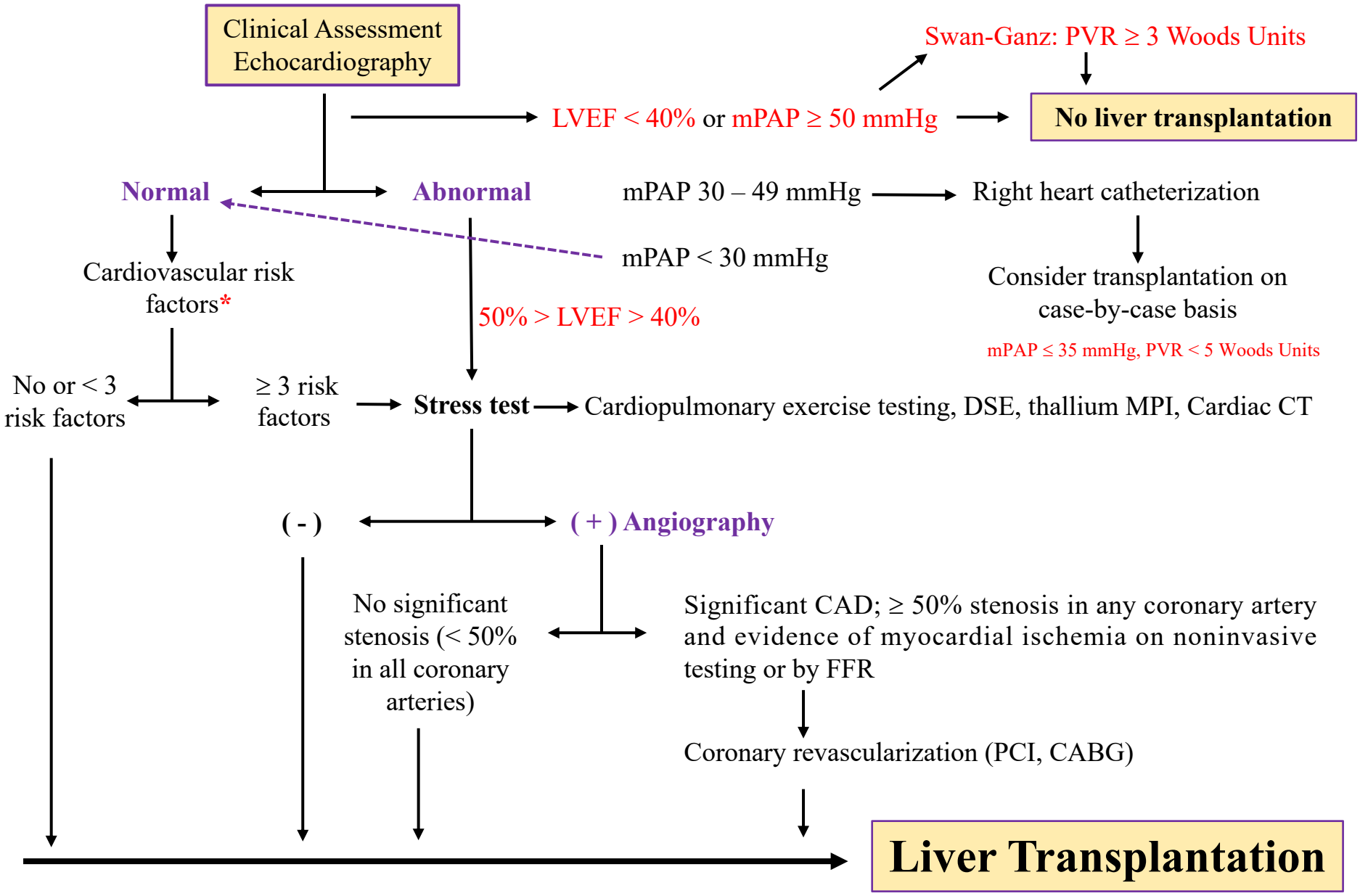
- ECG
- 心脏应激试验（运动应激或药物应激）
- 心导管检查（左心/右心导管）
- 对比增强超声心动图（contrast-enhanced echocardiography）
- 心肌应变成像（Myocardial strain imaging）
- Pulse Oximetry
- ABG (arterial blood gas)
- X线胸片
- 对比增强胸部CT
- 肺功能检查（PFT with DLco）

肝移植的绝对和相对禁忌证

Cardiac or pulmonary vascular condition	Absolute contraindications	Relative contraindications
Coronary artery disease	Nonrevascularized obstructive severe multivessel CAD	Nonrevascularized obstructive moderate CAD not involving left main or proximal LAD coronary arteries
Cardiomyopathy and heart failure	Left ventricular ejection fraction <40% Moderate to severe right heart failure	Left ventricular ejection fraction <50% Hypertrophic cardiomyopathy with resting left ventricular outflow tract obstruction
Portopulmonary hypertension	Severe pulmonary hypertension associated with right heart failure and/or not responsive to medical therapies	Moderate pulmonary hypertension with preserved right ventricular function not responsive to medical therapy
Cardiac arrhythmias	Recurrent ventricular arrhythmias	Recurrent unstable arrhythmias
Valvular heart disease	Severe irreversible valvular disease	Moderate pulmonary hypertension with preserved right ventricular function not responsive to medical therapy
Congenital heart disease	Congenital heart disease plus moderate to severe right heart failure not responsive to medical therapy	Congenital heart disease plus moderate pulmonary hypertension with preserved right ventricular function not responsive to medical therapy

CAD, coronary artery disease; LAD, left anterior descending.

[a]Expert consultation with a cardiologist or pulmonary hypertension specialist familiar with liver transplantation surgery is recommended prior to decision making in all situations.



* Relevant risk factors: diabetes mellitus, prior cardiovascular disease, left ventricular hypertrophy, > 60 year, smoking, hypertension and dyslipidemia

TABLE 2 Summary of recommendations and considerations for the assessment of cardiac and pulmonary vascular disease among liver transplant candidates with end-stage liver disease

Cardiac or pulmonary vascular condition	Diagnostic modality	Test operating characteristics[c] PPV	NPV	Special considerations in ESLD	GRADE recommendations
Coronary artery disease				LT candidates with DM or ≥2 traditional cardiac risk factors[a] are most likely to have obstructive CAD	Consider invasive or noninvasive angiography if known CAD, abnormal noninvasive test or a high pretest probability of CAD (DM or ≥2 traditional risk factors) **(2C)**
	Noninvasive stress testing			LT candidates may not achieve maximal chronotropy on pharmacologic stress testing	The decision to pursue stress testing should be based on individualized evaluation of the candidate's pretest probability for having CAD (see above) **(1C)**
	DSE	0%-33%	75%-100%	Resting microvascular vasodilation limits available coronary flow reserve	
	Vasodilator testing[d]	15%-22%	77%-100%		
	Functional testing				For ambulatory patients, functional testing may be useful to identify those LT candidates who are at increased risk for poor outcomes and who may benefit from prehabilitation **(2C)**
	Cardiopulmonary exercise testing (CPET)	Unknown	Unknown	VO_2 max, a measure of CV fitness, is achieved in <35% of patients with ESLD; VO_2 peak can be used as a surrogate[31] Anaerobic threshold (AT), a measure of cardiopulmonary reserve, can be obtained in >90% of patients with ESLD Reduction in VO_2 peak <15 mL/min per kg places a patient in class III-IV heart failure category and predicts poor prognosis Reduction in aerobic capacity predicts outcomes in waitlist candidates and at 90 and 100 d post-LT -AT <9.0 mL/min per kg is associated with reduced 90-d survival -AT of <9.2 mL/minute per kg is associated with increased length of hospital stay	
	6-minute walk test (6MWT)	Unknown	Unknown	6MWD < 250 meters is associated with increased risk of death For each 100-meter increase in 6MWD survival increases by 42% (HR, 0.58; P = .02)[35]	
	Noninvasive coronary CT angiography (CCTA)	17%[b]	95%[b]	CAC score > 400 HU predicts: -Significant CAD requiring revascularization[36] -1 month post-LT complications (OR, 95% CI: 4.62, 1.1-18.7)[37]	Consider CCTA in patients with normal body habitus who are able to lie still, perform required breath-holding maneuvers, and who have a regular nontachycardic rhythm **(2C)** In candidates with advanced CKD and suspected CAD, consultation with a nephrologist and standard preventive measures for contrast-induced nephropathy are recommended **(1C)**
	Coronary artery calcium (CAC) score				

(Continues)

感谢您的关注