LEE'S PHARM.
李氏大藥廠
Department of medicine and information
医学及信息部

医学信息速递
Medical Information Express

传递最有价值的医学信息

《2022 ESC/ERS指南：肺动脉高压的诊断和管理》解读

产品战略&医学与信息部

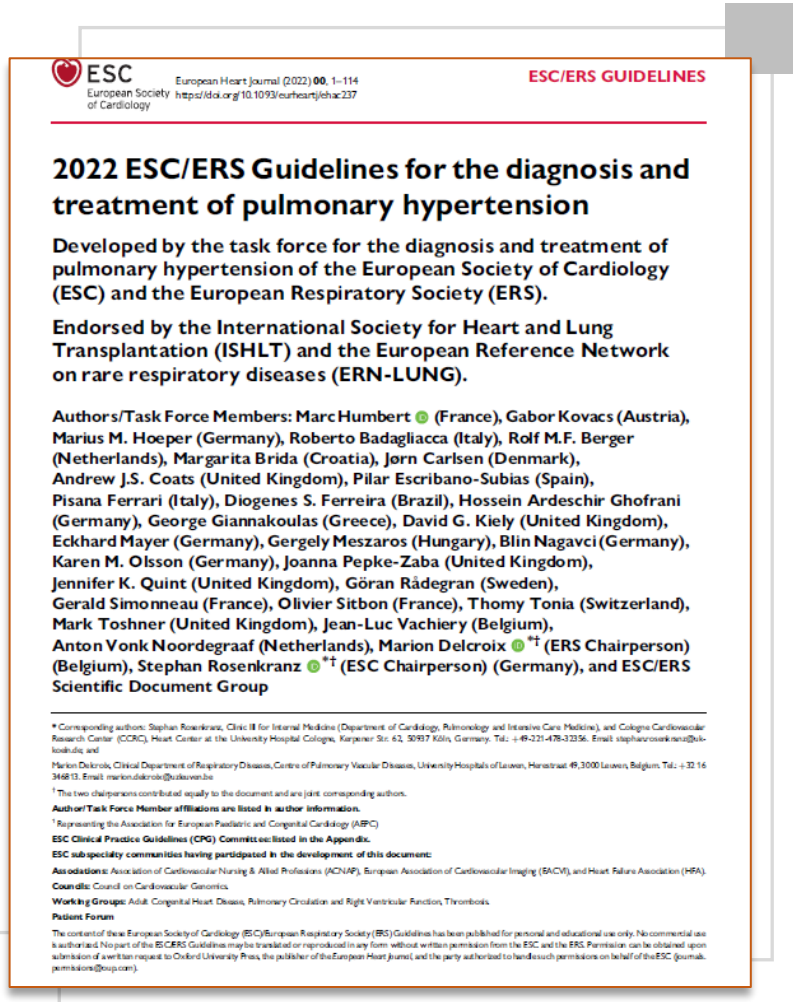
2022-10

目录

01

指南简介

指南简介



ESC European Society of Cardiology

European Heart Journal (2022) 00, 1–114 https://doi.org/10.1093/eurheartj/ehac237

ESC/ERS GUIDELINES

2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

Developed by the task force for the diagnosis and treatment of pulmonary hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS).

Endorsed by the International Society for Heart and Lung Transplantation (ISHLT) and the European Reference Network on rare respiratory diseases (ERN-LUNG).

Authors/Task Force Members: Marc Humbert (France), Gabor Kovacs (Austria), Marius M. Hoeper (Germany), Roberto Badagliacca (Italy), Rolf M.F. Berger (Netherlands), Margarita Brida (Croatia), Jørn Carlsen (Denmark), Andrew J.S. Coats (United Kingdom), Pilar Escribano-Subias (Spain), Pisana Ferrari (Italy), Diogenes S. Ferreira (Brazil), Hossein Ardeschir Ghofrani (Germany), George Giannakoulas (Greece), David G. Kiely (United Kingdom), Eckhard Mayer (Germany), Gergely Meszaros (Hungary), Blin Nagavci (Germany), Karen M. Olsson (Germany), Joanna Pepke-Zaba (United Kingdom), Jennifer K. Quint (United Kingdom), Göran Rådegran (Sweden), Gerald Simonneau (France), Olivier Sitbon (France), Thomy Tonia (Switzerland), Mark Toshner (United Kingdom), Jean-Luc Vachiery (Belgium), Anton Vonk Noordegraaf (Netherlands), Marion Delcroix *† (ERS Chairperson) (Belgium), Stephan Rosenkranz *† (ESC Chairperson) (Germany), and ESC/ERS Scientific Document Group

* Corresponding authors: Stephan Rosenkranz, Clinic III for Internal Medicine (Department of Cardiology, Pulmonology and Intensive Care Medicine), and Cologne Cardiovascular Research Center (CCRC), Heart Center at the University Hospital Cologne, Kerpener Str. 62, 50937 Köln, Germany. Tel.: +49-221-478-33356. Email: stephan.rosenkranz@uk-koeln.de; and

Marion Delcroix, Clinical Department of Respiratory Diseases, Centre of Pulmonary Vascular Diseases, University Hospitals of Leuven, Herestraat 49, 3000 Leuven, Belgium. Tel.: +32 16 346813. Email: marion.delcroix@uzleuven.be

† The two chairpersons contributed equally to the document and are joint corresponding authors.

Author/Task Force Member affiliations are listed in author information.

‡ Representing the Association for European Paediatric and Congenital Cardiology (AEPC)

ESC Clinical Practice Guidelines (CPG) Committee: listed in the Appendix.

ESC subspecialty communities having participated in the development of this document:

Associations: Association of Cardiovascular Nursing & Allied Professions (ACNAP), European Association of Cardiovascular Imaging (EACVI), and Heart Failure Association (HFA).

Councils: Council on Cardiovascular Genomics.

Working Groups: Adult Congenital Heart Disease, Pulmonary Circulation and Right Ventricular Function, Thrombosis.

Patient Forum

2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

【制定者】

- 欧洲心脏病学会(ESC,European Society of Cardiology)
- 欧洲呼吸学会(ERS,European Respiratory Society)

【发布日期】2022年8月26日

【杂志】EUROPEAN HEART JOURNAL

内容介绍

内容简介

- 2022年8月，欧洲心脏病学会(ESC)联合欧洲呼吸学会(ERS)共同发布了肺动脉高压的诊断和管理指南；
- 近年来，在肺动脉高压的诊断和管理方面已经取得了实质性的进展，新的证据已被及时纳入本指南中；
- 本指南涵盖了整个PH的范围，重点是诊断和治疗动脉性肺动脉高压（PAH）和慢性血栓栓塞性肺动脉高压（CTEPH）。

02

指南重点更新内容摘录与解读

亮点一

PH定义更新

亮点一

定义更新，肺动脉高压（肺高血压）定义为mPAP＞20mmHg

Table 5 Haemodynamic definitions of pulmonary hypertension

Definition	Haemodynamic characteristics
PH	mPAP >20 mmHg
Pre-capillary PH	mPAP >20 mmHg PAWP ≤15 mmHg PVR >2 WU
IpcPH	mPAP >20 mmHg PAWP >15 mmHg PVR ≤2 WU
CpcPH	mPAP >20 mmHg PAWP >15 mmHg PVR >2 WU
Exercise PH	mPAP/CO slope between rest and exercise >3 mmHg/L/min

CO, cardiac output; CpcPH, combined post- and pre-capillary pulmonary hypertension; IpcPH, isolated post-capillary pulmonary hypertension; mPAP, mean pulmonary arterial pressure; PAWP, pulmonary arterial wedge pressure; PH, pulmonary hypertension; PVR, pulmonary vascular resistance; WU, Wood units.
Some patients present with elevated mPAP (>20 mmHg) but low PVR (≤2 WU) and low PAWP (≤15 mmHg); this haemodynamic condition may be described by the term 'unclassified PH' (see text for further details).

01 2018年世界肺动脉高压大会，首次提出拟将肺动脉高压（肺高血压）诊断标准定为mPAP＞20mmHg，在今年的指南中，最终确定为此；

02 同时，对毛细血管前性肺动脉高压的定义相应更改为：mPAP＞20mmHg；PAWP≤15mmHg；PVR＞2WU；

03 但近期拜访国内专家时，大多专家认为该改动不一定适合中国诊疗现状，或会因此造成过度诊疗，但均认可肺动脉平均压处于20到25mmHg的患者应该密切随访。

亮点二

新增随访患者危险分层

亮点二

新增随访患者危险分层，将“中高危”进行强调。

Table 18 Variables used to calculate the simplified four-strata risk-assessment tool

Determinants of prognosis	Low risk	Intermediate–low risk	Intermediate–high risk	High risk
Points assigned	1	2	3	4
WHO-FC	I or II[a]	-	III	IV
6MWD, m	>440	320–440	165–319	<165
BNP or NT-proBNP,[a] ng/L	<50 <300	50–199 300–649	200–800 650–1100	>800 >1100

© ESC/ERS 2022

6MWD, 6-minute walking distance; BNP, brain natriuretic peptide; NT-proBNP, N-terminal pro-brain natriuretic peptide; WHO-FC, World Health Organization functional class.
Risk is calculated by dividing the sum of all grades by the number of variables and rounding to the next integer.
[a]WHO-FC I and II are assigned 1 point as both are associated with good long-term survival.

Table 16 Comprehensive risk assessment in pulmonary arterial hypertension (three-strata model)

Determinants of prognosis (estimated 1-year mortality)	Low risk (<5%)	Intermediate risk (5–20%)	High risk (>20%)
Clinical observations and modifiable variables			
Signs of right HF	Absent	Absent	Present
Progression of symptoms and clinical manifestations	No	Slow	Rapid
Syncope	No	Occasional syncope[a]	Repeated syncope[b]
WHO-FC	I, II	III	IV
6MWD[c]	>440 m	165–440 m	<165 m
CPET	Peak VO_2 >15 mL/min/kg (>65% pred.) VE/VCO_2 slope <36	Peak VO_2 11–15 mL/min/kg (35–65% pred.) VE/VCO_2 slope 36–44	Peak VO_2 <11 mL/min/kg (<35% pred.) VE/VCO_2 slope >44
Biomarkers: BNP or NT-proBNP[d]	BNP <50 ng/L NT-proBNP <300 ng/L	BNP 50–800 ng/L NT-proBNP 300–1100 ng/L	BNP >800 ng/L NT-proBNP >1100 ng/L
Echocardiography	RA area <18 cm^2 TAPSE/sPAP >0.32 mm/mmHg No pericardial effusion	RA area 18–26 cm^2 TAPSE/sPAP 0.19–0.32 mm/mmHg Minimal pericardial effusion	RA area >26 cm^2 TAPSE/sPAP <0.19 mm/mmHg Moderate or large pericardial effusion
cMRI[e]	RVEF >54% SVI >40 mL/m^2 RVESVI <42 mL/m^2	RVEF 37–54% SVI 26–40 mL/m^2 RVESVI 42–54 mL/m^2	RVEF <37% SVI <26 mL/m^2 RVESVI >54 mL/m^2
Haemodynamics	RAP <8 mmHg CI ≥2.5 L/min/m^2 SVI >38 mL/m^2 SvO_2 >65%	RAP 8–14 mmHg CI 2.0–2.4 L/min/m^2 SVI 31–38 mL/m^2 SvO_2 60–65%	RAP >14 mmHg CI <2.0 L/min/m^2 SVI <31 mL/m^2 SvO_2 <60%

© ESC/ERS 2022

6MWD, 6-minute walking distance; BNP, brain natriuretic peptide; CI, cardiac index; cMRI, cardiac magnetic resonance imaging; CPET, cardiopulmonary exercise testing; HF, heart failure; NT-proBNP, N-terminal pro-brain natriuretic peptide; PAH, pulmonary arterial hypertension; pred., predicted; RA, right atrium; RAP, right atrial pressure; sPAP, systolic pulmonary arterial pressure; SvO_2, mixed venous oxygen saturation; RVESVI, right ventricular end-systolic volume index; RVEF, right ventricular ejection fraction; SVI, stroke volume index; TAPSE, tricuspid annular plane systolic excursion; VE/VCO_2, ventilatory equivalents for carbon dioxide; VO_2, oxygen uptake; WHO-FC, World Health Organization functional class.
[a]Occasional syncope during heavy exercise or occasional orthostatic syncope in a stable patient.
[b]Repeated episodes of syncope even with little or regular physical activity.
[c]Observe that 6MWD is dependent upon age, height, and burden of comorbidities.

补充说明

- 在过去的临床实践中，多位教授均提出过“中高危”患者的强化治疗概念，在本次指南更新中，正式将这一说法标准化；
- 指南中强调，治疗过程中“中高危”患者应该使用以静脉/皮下前列环素类似物为基础的靶向药治疗，正式将治疗的最低要求前移；
- 这将大大规范随访患者的充分治疗。同时，该”四分法“危险分层无需右心导管指标，使得患者随访更易进行。

三分法

◆ 本指南中三分法相较于2018、2021中国指南来说，项目增加较多，但并未具体描述如何使用该表对患者进行危险分层。现结合2018尼斯会议中该部分内容推测：

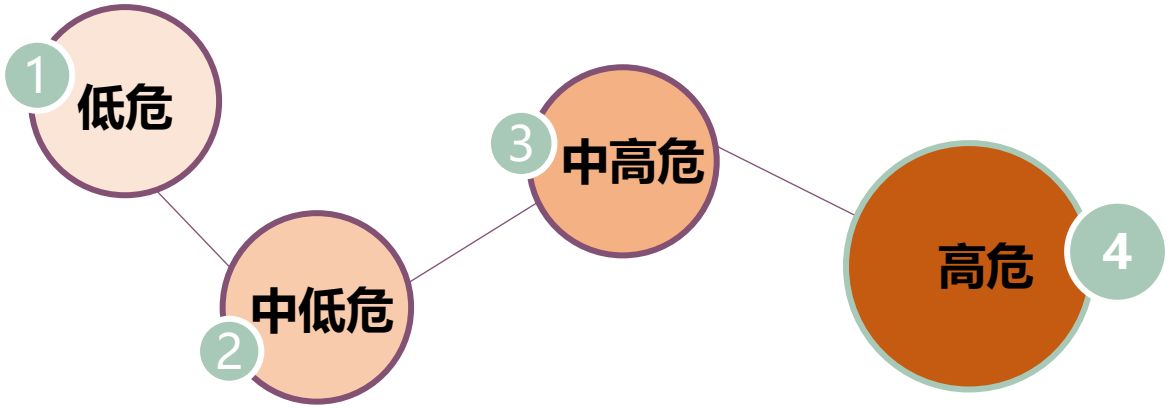
低危：至少三个低风险指标，且无高风险指标；
高危：至少2个高风险指标，其中必须包括“血流动力学”；
中危：不符合低危和高危定义的则为中危。

预后的决定因素（估计的1年死亡率）	低风险（＜5%）	中风险（5%-20%）	高风险（＞20%）
临床判定的标准			
右心衰的症状体征	不存在	不存在	出现
肺高压的症状进展	没有	轻微	突出
晕厥	没有	偶尔出现	反复出现
WHO心功能分级	I,II	III	IV
6分钟步行距离	＞440m	165-440m	＜165m
CPET心肺运动试验	峰值 VO_2＞15 mL/min/kg (＞65% 预计值) VE/VCO_2 斜率＜36	峰值 $VO_2$11-15 mL/min/kg (35%-65% 预计值) VE/VCO_2 斜率 36-44	峰值 VO_2＜11 mL/min/kg (＜35% 预计值) VE/VCO_2 斜率＞44
BNP或NT-proBNP	BNP＜50 ng/L NT-proBNP＜300 ng/L	BNP 50–800 ng/L NT-proBNP 300–1100 ng/L	BNP ＞800 ng/L NT-proBNP ＞1100 ng/L
超声心动图	右房面积＜18 cm^2 TAPSE/sPAP＞0.32 mm/mmHg 无心包积液	右房面积18–26 cm^2 TAPSE/sPAP 0.19–0.32 mm/mmHg 少量心包积液	右房面积＞26 cm^2 TAPSE/sPAP＜0.19 mm/mmHg 中到大量心包积液
心脏核磁共振	右室收缩功能＞54% 每博指数＞40 mL/m^2 右室收缩末期容积指数＜42 mL/m^2	右室收缩功能 37–54% 每博指数 26–40 mL/m^2 右室收缩末期容积指数42–54 mL/m^2	右室收缩功能＜37% 每博指数＜26 mL/m^2 右室收缩末期容积指数＞54 mL/m^2
血流动力学	右房压＜8 mmHg 心指数≥2.5 L/min/m^2 每博指数＞38 mL/m^2 SvO_2 ＞65%	右房压 8–14 mmHg 心指数 2.0–2.4 L/min/m^2 每博指数 31–38 mL/m2 SvO_2 60–65%	右房压＞14 mmHg 心指数＜2.0 L/min/m^2 每博指数＜31 mL/m^2 SvO_2 ＜60%

四分法

◆ 该分类方法建议在患者治疗后随访时使用。具体使用方法为根据患者的三个指标：心功能、6分钟步行距离、BNP（或NT-proBNP），每一个指标进行1~4分的打分，总分再除以3，最后将得到的数字四舍五入取整，根据取整后数字进行危险分层划分：

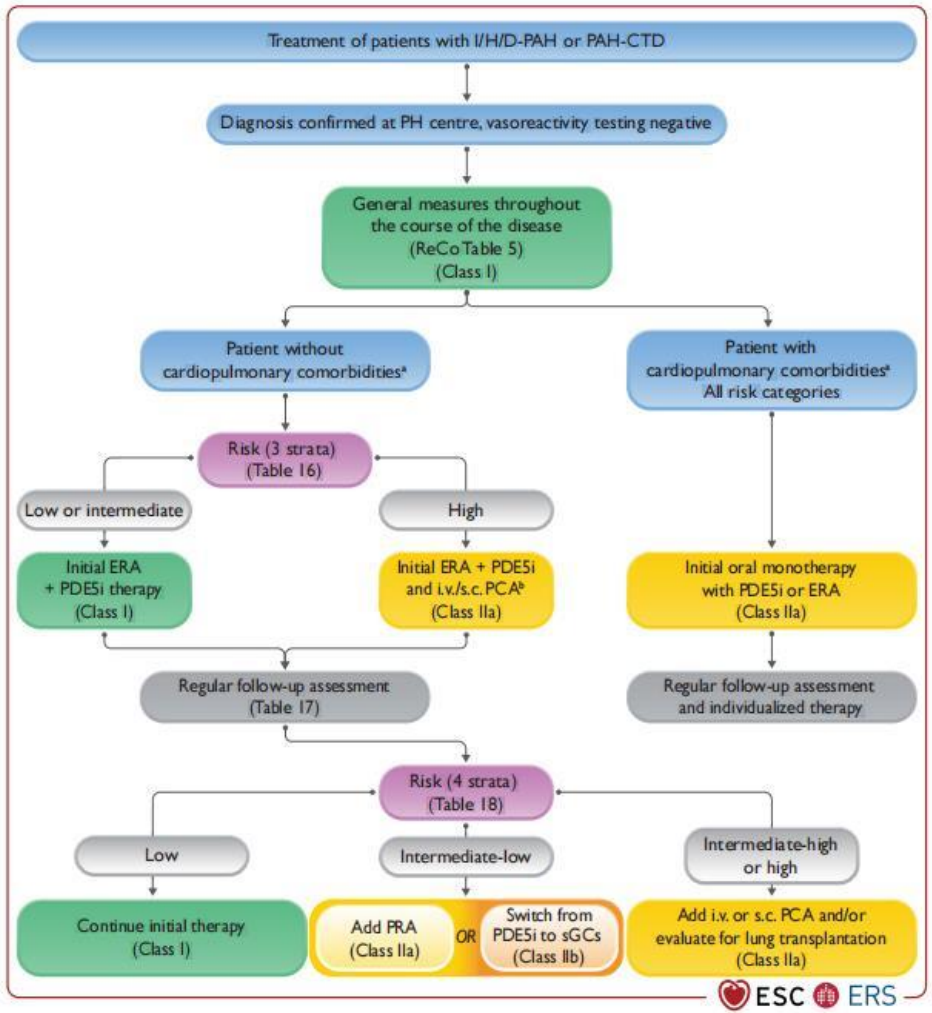
低　危：1分
中低危：2分
中高危：3分
高　危：4分



预后决定因素	低危	中低危	中高危	高危
该项所占分值	1	2	3	4
WHO心功能分级	I或II	-	III	IV
6分钟步行距离，m	> 440	320-440	165-319	< 165
BNP 或 NT-proBNP，ng/L	< 50 < 300	50-199 300-649	200-800 650-1100	> 800 > 1100

☑ 例如：某患者随访中，心功能III级（3分），六分钟步行距离 470m（1分），BNP 811ng/L（4分），总分8分，平均2.67分，四舍五入为3分，故该患者虽然有低危指标，但综合评估仍为中高危。

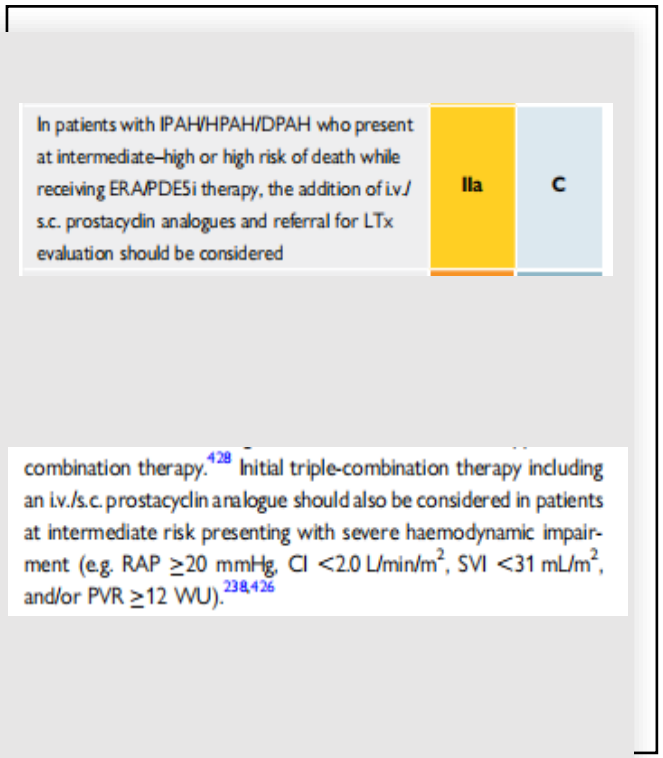
- 一定关注危险分层！四分法危险分层简单、易行，且不需要右心导管评估，值得在随访中推广；
- 随访中，曲前列尼尔的推荐时间前移，中高危就应该强调使用；
- 随访中，司来帕格仅在中低危患者进行推荐，其余治疗环节均未推荐。



指南更新推荐

- 对于没有左心相关因素（左室舒张功能障碍，包括高血压、冠心病、糖尿病等）的第一大类肺动脉高压患者，指南建议初诊时使用**三分法**进行危险分层；
  - ① 对于低、中危患者，采用ERA（内皮素受体拮抗剂：安立生坦、波生坦、马昔滕坦等）+PDE5i（五型磷酸二酯酶抑制剂：西地那非等）的二联口服进行治疗；
  - ② 对于高危患者应该在上述二联基础上，加用静脉/皮下前列环素类似物（曲前列尼尔）联合治疗；
- 治疗评估中，随访时应采用**四分法**进行危险分层。
  - ① 对于低危患者维持治疗；
  - ② 对于中低危患者，指南推荐了两种策略：或可加用PRA（前列环素受体激动剂：司来帕格），或可将二联治疗中的PDE5i换为sGCs（鸟苷酸环化酶激动剂：利奥西呱）；
  - ③ 而对于中危及高危患者，则应该采用以静脉/皮下前列环素为基础的三联治疗（若依然控制不佳，则考虑肺移植）。

在强调**中高风险、高风险**患者应选用静脉/皮下**前列环素类似物**进行治疗的同时，指南小字部分还特别提到：对于有**“严重”血流动力血障碍的中风险**患者，也应该加用静脉/皮下**前列环素类似物**进行治疗。



In patients with IPAH/HPAH/DPAH who present at intermediate–high or high risk of death while receiving ERA/PDE5i therapy, the addition of i.v./s.c. prostacyclin analogues and referral for LTx evaluation should be considered	IIa	C

combination therapy.[428] Initial triple-combination therapy including an i.v./s.c. prostacyclin analogue should also be considered in patients at intermediate risk presenting with severe haemodynamic impairment (e.g. RAP ≥20 mmHg, CI <2.0 L/min/m^2, SVI <31 mL/m^2, and/or PVR ≥12 WU).[238,426]

补充说明

- “严重”血流动力学障碍定义为：RAP右房压≥20mmHg，CL心指数＜2L/min/m^2，SVI每搏量指数＜31ml/m^2，伴或不伴PVR肺血管阻力≥12WU。
- 该项更新有助于在部分其余指标尚可，但右心导管结果较差的患者中进行治疗强化。

亮点三

强调曲前列尼尔在CTEPH患者中的使用必要性

亮点三

强调**曲前列尼尔**在CTEPH患者中的使用必要性，并且对西地那非等PDE5i及马昔滕坦等ERAs类药物在该类型患者中的使用提出质疑。

10.2.2. Medical therapy

To manage the microvascular component of CTEPH (*Figure 15*), medical therapies have been used off-label based on uncontrolled studies and/or regional approvals. Meanwhile, three RCTs have successfully been conducted. The first phase 3 RCT investigated the efficacy of riociguat in patients with inoperable CTEPH or those with persistent/recurrent PH after PEA.[775] Riociguat, after 16 weeks of therapy, improved 6MWD and reduced PVR by 31% compared with placebo, and is approved for this indication. Treprostinil s.c. was investigated in a phase 3 RCT, which showed improved 6MWD at week 24 in patients with inoperable CTEPH or those with persistent/recurrent PH after PEA receiving a high dose compared with a low dose;[776] s.c. treprostinil is approved for this indication. In a phase 2 study including only patients with inoperable CTEPH, macitentan 10 mg improved PVR and 6MWD vs. placebo

Other medical therapies—PDE5is (e.g. sildenafil) and ERAs (e.g. bosentan)—have been used off-label, as their efficacy in inoperable CTEPH has not been proven by RCTs or registry data.[769,778,779] However, oral combination therapy, including PDE5is and ERAs, is common practice in patients with CTEPH with severe haemodynamic compromise.[780]

补充说明

- ✓ 静脉/皮下曲前列尼尔治疗近年来在CTEPH领域积累了充分的询证学证据，也因此在欧洲获批了相应的适应症；
- ✓ 在该版指南中，强调了曲前列尼尔皮下使用能改善CTEPH患者的六分钟步行距离等预后指标；
- ✓ 同时指出，高剂量（指南原文并未说明高剂量的定义，但根据其参考文献得知为30ng·kg^{-1}·min^{-1}）使用的获益会优于低剂量使用。

建议	建议级别	证据等级
CTEPH慢性血栓栓塞性肺动脉高压		
所有CTEPH患者均推荐终身抗凝治疗	I	C
建议对CTEPH患者进行抗磷脂综合征检测	I	C
对于患有抗磷脂综合征的CTEPH患者，推荐使用VKAs（华法林等抗凝药）进行抗凝	I	C
建议所有CTEPH患者都由CTEPH专业中心进行收治，以评估药物-手术结合的多模式治疗管理	I	C
对于CTEPH及肺动脉内纤维化阻塞的患者，建议PEA手术治疗	I	B
对于评估后不能做PEA手术或PEA术后残余PH的患者，建议BPA介入治疗	I	B
对于出现症状的但不能手术、或术后复发的CTEPH患者，建议使用利奥西呱	I	B
建议对PEA术后、BPA术后及药物治疗的CTEPH患者进行长期随访	I	C
对于PEA术后复发或持续PH的患者，或者没有条件行PEA手术的患者，应该考虑多模式治疗（药物+BPA）	IIa	C
曲前列尼尔被推荐用于不能手术或术后复发、持续PH的心功能III-IV级CTEPH患者	IIb	B
对于没有手术条件的患者，可以考虑超适应症使用肺动脉高压靶向药	IIb	B
对于不能手术的CTEPH患者，药物联合方案可以考虑鸟苷酸环化酶激动剂（利奥西呱）或五磷酸二酯酶抑制剂（西地那非）+内皮素受体拮抗剂+肠外前列环素类似物（静脉/皮下曲前列尼尔）	IIb	C
对于血管远端病变占比高或PEA手术风险大的患者，可考虑BPA介入治疗	IIb	C

▶ 在不能手术（包括PEA外科手术及BPA内科介入）、或目前评估不适合做手术的患者中，以及已经做了手术但肺动脉高压复发或持续存在的患者中，该指南建议使用靶向药联合治疗，并且强调对于一些高危患者（这里的高危特指心功能III-IV级）应该使用**曲前列尼尔**进行治疗。

The recommendation on the use of medical therapy before interventional therapy in patients with CTEPH who are considered inoperable but candidates for BPA is based on PICO question IV (Supplementary Data, *Section 10.2*). The included evidence suggests that pre-treatment improves pulmonary haemodynamics and safety of the procedure. This is confirmed by the clinical experience of Task Force members. However, due to the low certainty of the evidence, the recommendation is conditional.

- **对于我们之前提到过的CTEPH患者药物“术前达标”治疗，指南也进行了观点阐述：**指南认为，对于不适合手术或者不适合PEA外科手术但准备做BPA内科球囊扩张的患者，**使用靶向药治疗可以改善患者的血流动力学状态，增加手术安全性以及改善术后效果**；
- 但指南也表示，目前该方案还缺乏经验积累，需要更多询证学证据进行验证。

亮点四

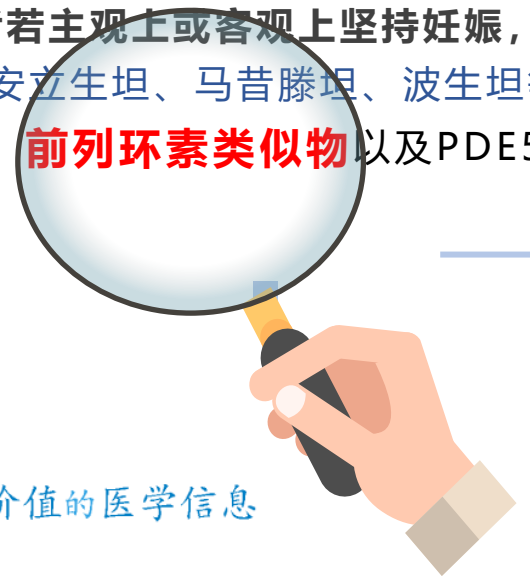
首次在妊娠相关肺动脉高压患者中，提出治疗建议，并强调静脉/皮下曲前列尼尔的安全性

亮点四

首次在妊娠相关肺动脉高压患者中，提出治疗建议，并强调静脉/皮下**曲前列尼尔**的安全性。

Women with PH who become pregnant or present during pregnancy with newly diagnosed PAH should be treated, whenever possible, in centres with a multidisciplinary team experienced in managing PH in pregnancy. If pregnancy is continued, PAH therapy may have to be adjusted. It is recommended to stop endothelin receptor antagonists (ERAs), riociguat, and selexipag because of potential or unknown teratogenicity.[359] Despite limited evidence, CCBs, PDE5is, and inhaled/i.v./subcutaneous (s.c.) prostacyclin analogues are considered safe during pregnancy.[356,360]

在过往的指南/共识中，妊娠患者罹患肺动脉高压的治疗策略基本均只强调“终止妊娠”，对药物治疗讳莫如深，这也使得实际临床工作中该类型患者难以得到充分合理的重视。在该版指南中，正式提出，**妊娠患者若主观上或客观上坚持妊娠，需要调整靶向药策略**，停用ERAs（安立生坦、马昔滕坦、波生坦等）及司来帕格，**改用静脉/皮下(吸入)前列环素类似物**以及PDE5is（西地那非等）。



FDA妊娠用药风险等级

药品类型	药品通用名	妊娠用药风险等级
PDE5i 五磷酸二酯酶抑制剂	西地那非	B
	他达拉非（尚未获适应症）	B
前列环素类似物	曲前列尼尔	B
前列环素受体激动剂	司来帕格	X
ERA内皮素受体拮抗剂	安立生坦	X
	波生坦	X
	马昔滕坦	X
sGCs鸟苷酸环化酶激动剂	利奥西呱	X

B级：在动物繁殖性研究中，未见到对胎儿的影响，可在密切观察下应用于孕产妇；
X级：在动物或人的研究中明确其会导致胎儿异常。本类药品禁用于妊娠或将妊娠的患者。

提示点

在**部分男性中，若可能有备孕准备，也需要强调靶向药的选择**，在多位专家的讲课中均提到，部分药物或会通过精液影响受孕过程，故需要避免使用X级药物。

结合指南以及国内重点肺动脉高压中心专家意见，对于妊娠期肺动脉高压的靶向药使用，在此强调以下推广要点：

- ☑ 告知肺动脉高压既往患者妊娠风险，建议避孕；对于已怀孕的肺动脉高压患者建议早期终止妊娠；
- ☑ 坚持妊娠的患者，一定要在肺动脉高压中心规律随访，且早期（孕中期）开始使用口服药（西地那非）；
- ☑ **超声评估重度肺动脉高压的患者，或已出现心衰症状的患者，无论轻重，均建议使用芮旎爾，尽快滴定至目标剂量后持续使用至产后42天，切勿在产后数天内就停药或降低剂量。**

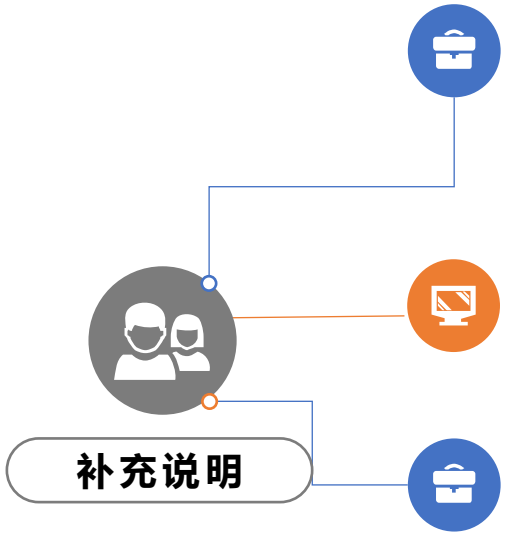
亮点五

对于低心排量的患者，无论其心功能等级、危险分层现况，均应考虑使用静脉或皮下前列环素类似物

亮点五

- 对于**低心排量**的患者，无论其心功能等级、危险分层现况，均应考虑使用静脉或皮下**前列环素类似物。**

Treating right HF should focus on treatable triggers such as infection, arrhythmia, anaemia, and other comorbidities. Fluid management is of utmost importance in these patients, most of whom require a negative fluid balance to reduce RV pre-load, thereby improving RV geometry and function.[468] Patients with a low CO may benefit from treatment with inotropes; dobutamine and milrinone are the most frequently used substances in this setting. Maintaining the mean systemic blood pressure >60 mmHg is a key objective when treating right HF, and patients with persistent hypotension may require vasopressors such as norepinephrine or vasopressin. Intubation and invasive mechanical ventilation should be avoided whenever possible in patients with advanced RV failure because of a high risk of further haemodynamic deterioration and death. Pulmonary arterial hypertension medication should be considered on an individual basis, taking into account underlying disease, comorbidities, and existing medication. In patients with newly diagnosed PAH presenting with low CO, combination therapy including i.v./s.c. prostacyclin analogues should be considered.[426]



- 指南中在阐述右心衰治疗时，强调了**外周循环血压的重要性**，提出：体循环平均压 > 60mmHg是右心衰治疗的关键目标。
- 紧接着，强调了血流动力学中，心排量对于外周循环的影响，提出：对于新诊断的低心排量肺动脉高压患者，联合治疗应该使用静脉/皮下前列环素类似物。
- **该推荐，强有力地说明了对于部分血压较低的患者，曲前列尼尔通过改善其血流动力学情况，不但不会加重血压下降，反而会对患者体循环起到保护、改善的积极作用！**

亮点六

靶向药治疗通过改善患者的血流动力学情况，可以为肝移植建立良好的手术条件

亮点六

靶向药治疗通过改善患者的血流动力学情况，可以为肝移植建立良好的手术条件。

7.4.2.1. Liver transplantation

Porto-pulmonary hypertension is not per se an indication for liver transplantation. Pulmonary arterial hypertension poses a major threat to patients who undergo liver transplantation when indicated for the severity of liver disease. In a historical series from the Mayo Clinic, severe PAH with mPAP ≥50 mmHg was associated with a 100% perioperative mortality rate. In patients with mPAP 35–50 mmHg and PVR >3.0 WU, mortality was still 50%.[550] In liver transplantation candidates with PAH, targeted medical therapy successfully improves haemodynamics and establishes eligibility for transplantation.[545,551–554] However, haemodynamic criteria for successful liver transplantation have not been firmly established. The International Liver Transplant Society proposed haemodynamic targets of mPAP <35 mmHg and PVR <5 WU, or mPAP ≥35 mmHg and PVR <3 WU in patients receiving PAH therapy, while acknowledging that these criteria need to be further validated.[175] An mPAP ≥45 mmHg is regarded as an absolute contraindication to liver transplantation.[175]

In patients with PoPH who successfully underwent liver transplantation, de-escalation or discontinuation of PAH medication is often feasible, but this has to be performed on an individual basis.[551,554]

- 该版指南中，不推荐门脉高压型肺动脉高压患者常规使用PAH靶向药治疗；
- 但强调：**严重的血流动力学障碍（mPAP≥50mmHg）与肝移植手术死亡率有密切的关系，所以对于肺动脉平均压较高、肺血管阻力较大的患者，应该使用靶向药治疗，以改善患者血流动力学，创造良好的肝移植手术条件。**

亮点七

对于口服药未能充分改善症状的艾森曼格患者，更推荐使用皮下（非静脉）前列环素类似物进行强化治疗

亮点七

- 对于口服药未能充分改善症状的艾森曼格患者，更推荐使用皮下（非静脉）**前列环素类似物**进行强化治疗。

with Eisenmenger syndrome (6MWD improved in both treatment and placebo arms), although decreases in NT-proBNP and PVR were noted in the macitentan arm.[575]

Experiences with other ERAs and PDE5is have shown favourable functional and haemodynamic results in Eisenmenger syndrome.[576] In a small, single-centre, pilot study, adding nebulized iloprost to a background of oral PAH therapy failed to improve 6MWD in Eisenmenger syndrome.[577] In case symptoms persist or in clinical deterioration, a sequential and symptom-orientated treatment strategy is recommended in Eisenmenger syndrome, starting with an oral ERA (or PDE5i) and escalating therapy. Should symptoms not adequately improve with oral therapies, i.v./s.c. options should be proactively considered.[578] There is a theoretical risk of paradoxical embolism in right-to-left shunt lesions with the presence of a central venous catheter for i.v. therapy; therefore, s.c. prostacyclin analogue infusion may be considered.

The effect of PAH therapies in patients with prevalent systemic-to-pulmonary shunts is less well established. Patients with small/coincidental defects should be treated with PAH medication.[557] This is also the case for patients with PAH after defect cor-

- 指南提出，对于口服药未能充分治疗改善症状的患者，考虑到艾森曼格患者右向左分流存在栓塞风险，应选用皮下前列环素类似物的强化治疗；
- **据此，在心外科或心内科CHD-PAH患者的芮旎爾用药中，应该更积极地推荐长期皮下治疗。**

亮点八

儿童肺动脉高压的治疗策略，指南依然非常强调基于危险分层的充分治疗

亮点八

儿童肺动脉高压的治疗策略，指南依然非常强调基于危险分层的充分治疗。

Prostacyclin analogues (i.v./s.c.)			
Epoprostenol i.v.	Cohort studies, retrospective	No Suggested dosing: Starting dose: 1–2 ng/kg/min without a known maximum In children, a stable dose is usually 40–80 ng/kg/min Dose increases may be required	623–626
Treprostinil i.v./ s.c.	Cohort studies, retrospective: pharmacokinetics	No Suggested dosing: Starting dose: 2 ng/kg/min without a known maximum In children, a stable dose is usually 50–100 ng/kg/min Dose increases may be required	624,626,627
Other			
Iloprost (inhaled)	Insufficient data in children Small case series, retrospective	No	
Selexipag (oral)	Insufficient data in children Randomized, placebo-controlled, add-on, ongoing: safety, tolerability, pharmacokinetics in children aged 2–18 years	No	
Riociguat (oral)	Insufficient data in children Open-label, ongoing: safety, tolerability, pharmacokinetics in children aged 6–18 years	No	

© ESC/ERS 2022

i.v., intravenous; PAH, pulmonary arterial hypertension; RCT, randomized controlled trial; s.c., subcutaneous.

children with PH are currently not well defined.

Treatment of children with PAH is based on risk stratification.[599] Predictors of worse outcome in paediatric PAH are similar to those in adults, and include clinical evidence of RV failure, progression of symptoms, WHO-FC III–IV, certain echocardiographic parameters (e.g. TAPSE), and elevated serum NT-proBNP. A 6MWD <350 m has also been suggested as a predictor of worse outcome in paediatric PH, but its value in young children is less established. Further prognosticators identified in paediatric PAH are failure to thrive and haemodynamic variables, such as RAP >10 mmHg, the ratio of mean pulmonary-to-systemic blood pressure >0.75, and PVRI >20 WU·m^2.[602,606,607] Paediatric risk-assessment tools based on these parameters have been retrospectively validated in observational paediatric registries.[599,604a]

- 在儿童肺动脉高压的治疗策略中，指南依然非常强调基于危险分层的充分治疗；
- 同时，指南提出，**儿童用药剂量应该有更高的要求，通常应达到50-100ng/kg/min**（该指南推荐成人剂量为25-60ng/kg/min）。

03

指南对前列环素类似物（曲前列尼尔）的推荐

指南对前列环素类似物（曲前列尼尔）的推荐

- 指南中强调，治疗过程中“中高危”患者应该使用以静脉/皮下前列环素类似物为基础的靶向药治疗；
- 没有左心相关因素（左室舒张功能障碍，包括高血压、冠心病、糖尿病等）的第一大类肺动脉高压患者，对于高危患者应该在二联基础上，加用静脉/皮下前列环素类似物（曲前列尼尔）联合治疗；而对于中危及高危患者，则应该采用以静脉/皮下前列环素为基础的三联治疗；
- 对于有“严重”血流动力血障碍的中风险患者，也应该加用静脉/皮下前列环素类似物进行治疗；
- 在该版指南中，强调了曲前列尼尔皮下使用能改善CTEPH患者的六分钟步行距离等预后指标，同时指出，高剂量使用的获益会优于低剂量使用；
- 在不能手术（包括PEA外科手术及BPA内科介入）、或目前评估不适合做手术的患者中，以及已经做了手术但肺动脉高压复发或持续存在的患者中，该指南建议使用靶向药联合治疗，并且强调对于一些高危患者（这里的高危特指心功能III-IV级）应该使用曲前列尼尔进行治疗；
- 在该版指南中，正式提出，妊娠患者若主观上或客观上坚持妊娠，需要调整靶向药策略，停用ERAs（安立生坦、马昔滕坦、波生坦等）及司来帕格，改用静脉/皮下(或吸入）前列环素类似物以及PDE5is（西地那非等）；
- 对于新诊断的低心排量肺动脉高压患者，联合治疗应该使用静脉/皮下前列环素类似物（该推荐，强有力地说明了对于部分血压较低的患者，曲前列尼尔通过改善其血流动力学情况，不但不会加重血压下降，反而会对患者体循环起到保护、改善的积极作用）；
- 指南提出，对于口服药未能充分治疗改善症状的患者，考虑到艾森曼格患者右向左分流存在栓塞风险，应选用皮下前列环素类似物的强化治疗。据此，在心外科或心内科CHD-PAH患者的芮旋爾用药中，应该更积极地推荐长期皮下治疗。

谢谢关注！

thanks for your attention.