ICS 11.020

SCM

世界中医药学会联合会

World Federation of Chinese Medicine Societies

SCM 0*-20**

国际中医临床实践指南 特发性肺纤维化

International Guideline for Clinical Practice of Chinese Medicine

Idiopathic Pulmonary Fibrosis

（征求意见草案）

（Committee Draft）

世界中联国际组织标准 20**-**-**发布实施

International Standard of WFCMS Issued and implemented on ***. **, 20**

目　次

前　言

请注意本文件的某些内容可能涉及专利。本文件的发布机构不承担识别这些专利的责任。

主要起草单位：河南中医药大学、河南中医药大学第一附属医院。

参与起草单位：河南中医药大学、河南中医药大学第一附属医院、兰州大学循证医学中心、北京中医药大学循证医学中心、北京大学人民医院、中日友好医院、天津中医药大学第二附属医院、广东省中医院、北京中医药大学东方医院、北京中医药大学第三附属医院、深圳市中医院、河北省中医院、河南省中医院、河南中医药大学第三附属医院、郑州市中医院、武汉市第一医院、江苏省中医院、江西中医药大学附属医院、辽宁中医药大学附属医院、辽宁中医药大学附属第二医院、青岛市中医院、陕西省中医院、昆明市中医院、上海中医药大学附属曙光医院、上海中医药大学附属龙华医院、浙江省中医院、贵州中医药大学第二附属医院、山东中医药大学附属医院、安徽中医药大学、北京中医药大学附属东直门医院。

指导专家委员会：王永炎、张伯礼、晁恩祥、孙塑伦。

主要起草人：李建生、余学庆、谢洋。

参与起草人及审阅专家（按姓氏笔画排序）：

中国：于雪峰、马战平、马艳芳、王成祥、王　琦、王明航、付　义、冯淬灵、曲妮妮、刘良倚、刘瑞新、孙子凯、孙增涛、李泽庚、李素云、李得民、李　猛、杨珺超、张立山、张　伟、张念志、张　炜、张洪春、张惠勇、陆学超、陈　生、陈　薇、陈耀龙、武　蕾、林　琳、孟　泳、封继宏、班承钧、徐立然、崔红生、鹿振辉、葛正行、薛汉荣；

中国香港：吕爱平；

中国澳门：吴其标；

英国：王多劳、陈涛。

本文件起草程序遵守了世界中医药学会联合会发布的 SCM 1.1-2021《标准化工作规范第 1 部分：标准制定与发布》。

引　言

特发性肺纤维化发病率逐年升高，致残率高，致死率高，生存质量差，疾病负担重，是严重危害公共健康的重大疾病。特发性肺纤维化发病率较高，在不同国家及地区略有差异[1]，其患病率可达 35.1/10 万人，而发病率也已上升到 11.2/10 万人[2]。疾病进展迅速，中位生存期短，约 3-5 年[3]， 3 年累积死亡率高达 50.2%[4]，预后极差。即使近年来给予积极抗纤维化等治疗，其 5 年生存率仍小于 50%[5]；伴随而来的是升高的病死率与致残率，严重影响患者生存质量。有研究显示，尽管抗纤维化治疗得以广泛推广，但患者病死率仍然处于上升趋势[6]，且病程超过 2 年的特发性肺纤维化患者生存质量低于慢阻肺肺功能 4 级患者[7]；严峻的疾病现状同时带来了严重的疾病负担。在英国，特发性肺纤维化病人年均直接医疗总费用高达 21732 美元[8]；在美国，特发性肺纤维化年医疗费用高达近 20 亿美元[9]；在中国，目前尚缺乏相关权威数据，基于医保支付数据的小样本流行病学调查显示，特发性肺纤维化患者次均住院费用高达 19645 元人民币[10]，相关合并症、急性加重事件将进一步增加特发性肺纤维化患者经济负担。

为更好的促进特发性肺纤维化防治工作，不同国际组织、国家间制定和发布了系列特发性肺纤维化诊断和/或治疗指南。

中医药治疗特发性肺纤维化具有一定的疗效，其优势环节可能在减少急性加重次数、提高运动耐力、改善生存质量及临床症状等方面[11]。目前对于特发性肺纤维化的中医诊疗方案缺乏统一认识、规范，影响研究成果的推广及整体临床疗效的提高。本文件的研究方法见附录B，其局限性与展望见附录C。

为适应中医、中西医结合临床应用及科研实践需求，参考、借鉴海内外特发性肺纤维化诊疗指南与专家共识，制定本文件，以期为中医药防治特发性肺纤维化的临床实践提供参考。

国际中医临床实践指南 特发性肺纤维化

1 范围

本文件规定了特发性肺纤维化的诊断标准、病因病机、辨证论治、中成药治疗、其他疗法等内容。

本文件适用于确诊为特发性肺纤维化的患者，可供呼吸科（中医、中西医、西医）临床医师参考使用。

2 规范性引用文件

下列文件中的内容通过文中的规范性引用而构成本文件必不可少的条款。其中，注日期的引用文件，仅该日期对应的版本适用于本文件；不注日期的引用文件，其最新版本（包括所有的修改单）适用于本文件。

GB/T16751.2-2020 中医临床诊疗术语 第 2 部分：证候

T/CACM1330-2019 特发性肺纤维化中医证候诊断标准

ICD-11 国际疾病分类第十一次修订本：传统医学证候

ATS/ERS/JRS/ALAT An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management

ATS/ERS An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation

3 术语及定义

下列术语及定义适用于本指南。

3.1

特发性肺纤维化

一种病因不明，慢性纤维化性间质性肺疾病，主要发病人群为中老年人，男性多见，以呼吸困难和肺功能进行性恶化为特征。

注：特发性肺纤维化急性加重为近 1 月内不明原因的呼吸困难，低氧血症、放射性肺泡渗透，并且不能用感染、肺栓塞、气胸或心脏病等解释[12]。

4 西医诊断标准

特发性肺纤维化的西医诊断标准、具体诊断分型、诊断流程参见附录 A。

5 病因病机

对于特发性肺纤维化的病因病机尚未形成统一认识。一种观点认为特发性肺纤维化基本病因病机为本虚标实，常由肺虚邪侵，气阴亏损，日久及肾，临床多见肺肾两虚、气阴不足

之虚症，或失治误治、或缠绵难愈而致久病入络、或毒邪损络而致毒痰瘀互结，脉络痹阻之实症。本虚多为肺、肾，标实则多为风、毒、痰、瘀[13]。另一种观点则认为特发性肺纤维化的病因不外虚、痰、瘀、毒，病理为痰瘀交阻，肺络不通，终致肺用无能[14]。还有一种观点认为特发性肺纤维化基本病机为正虚络痹积损，正虚指肺肾虚损、由肺及肾；络痹指肺络痹阻；积损指痰浊、瘀血稽留及其互结成积并日益损伤正气，积损难复终致肺失所用。肺肾虚损为本，肺络痹阻、痰瘀互结为标；积损成痿、痹痿并存、虚实错杂为其特征[15]。概括言之，特发性肺纤维化病因病机为本虚标实，虚实夹杂。以虚为本，主在肺肾之气虚、阴虚，甚则阳虚；以实为标，主在痰、瘀、毒等及其互结。

6 中医证候诊断标准

特发性肺纤维化常见证候包括主证类（阴虚肺燥证、肺气虚证、肺肾气虚证）、兼证类（痰湿证、血瘀证）二类五证候。痰湿证、血瘀证常兼见于虚证之中，表现为虚实兼夹，如兼于肺肾气虚证则为肺肾气虚痰湿证、肺肾气虚血瘀证，临床诊断时予以注意。特发性肺纤维化急性加重时常以阴虚肺燥证、肺气虚证兼痰湿证、血瘀证形式出现。证候辨证诊断标准应符合 T/CACM1330-2019 的相关要求[16]。

7 治则治法

特发性肺纤维化的治疗，以扶正祛邪为大法，体现于补、润、化、消。补即补益，包括补益肺气、补养肺阴、补益气阴、补益肺肾等；润即润肺，包括凉润清燥（热）、温润助阳；化即化痰、化瘀，包括清化痰热、燥湿化痰、活血化瘀；消即消积散结，常寓于活血通络化痰之中。祛邪者当分痰热、痰湿、瘀血，并注重浊毒，或清热化痰或燥湿化痰，时或佐以活血化瘀、解毒。伴痰瘀互结成积者，在活血化痰同时，佐以消积散结；扶正者在补益肺、肾时，应顾及气阴虚损之偏。在疾病中后期，痰瘀互结成积者，应在补益正气、佐以化痰活血的基础上，适当选用消积散结药物，包括活血通络类、化痰类、解毒类等[15]。

由于特发性肺纤维化病机复杂、不同疾病阶段的病机特点不同，临证用药时要注意辨病势缓急；辨邪之痰浊、瘀血、热毒；辨脏腑气血阴阳。在急性加重期应注意邪实的变化，注意在扶正的基础上加强祛邪之力，必要时以祛邪为主、兼以扶正；稳定期在补益肺肾的基础上、应佐以化痰、活血、散结。

8 辨证论治

8.1 主证类

8.1.1 阴虚肺燥证

主症：喘促，胸闷，气短，咳嗽，痰少，痰黏难咯，痰色黄，口干，咽干，口渴，苔少，苔黄，脉细，脉数。**次症：**干咳，痰质稠，手足心热，盗汗，神疲，乏力，舌红，苔剥。

诊断条件:①喘促，或胸闷，或气短；②干咳，或痰少，或痰黏难咯，或痰色黄；③口干或咽干，或口渴；④手足心热；⑤盗汗；⑥舌红，或苔少或苔黄或苔剥，或脉细数。

诊断标准:具备①、②项，加③、④、⑤、⑥中 3 项。

治法：养阴润燥清热。

方药：麦门冬汤（《金匮要略》）合百合固金汤（《医方集解》）加减：南沙参 15g、麦冬 15g、地黄 15g、玄参 12g、白芍 15g、人参 6g、百合 15g、蜜百部 15g、浙贝母 9g、牡丹皮 12g、陈皮 12g、地龙 15g、炙甘草 9g。

加减：对于阴虚及气而致气阴两虚，症见咳或喘则汗出、恶风者，加五味子、绞股蓝、黄芪，或可选用百花煎丸（《鸡峰普济方》：人参、紫菀、阿胶、蜜百部、蜜款冬花、山药、天冬、麦冬、川贝母、炒苦杏仁、炙甘草）加减。干咳频作者，加蜜款冬花、炒蒌藜、麸炒僵蚕；热毒偏甚，症见咽痛、痰黄者，加黄芩、射干、炒牛蒡子；手足心热较重者，加知母、盐黄柏；盗汗明显者，加煅牡蛎、浮小麦；兼瘀血者，症见口唇紫绀、舌质紫暗或舌底脉络迂曲者，加土鳖虫、穿山龙、赤芍。

8.1.2 肺气虚证

主症：胸闷，气短，动则加重，咳嗽，神疲，乏力，自汗，易感冒，舌淡白，脉细。次症：痰色白，痰少，身体困倦，少气懒言，恶风，苔薄，苔白，脉沉，脉弱。

诊断条件：①胸闷，或气短，或咳嗽；②神疲，或乏力，动则加重；③自汗，动则加重；④恶风，或易感冒；⑤舌淡白，或脉沉细或细弱。

诊断标准：具备①项，加②、③、④、⑤中 2 项。

治法：补肺益气、化痰止咳。

方药：人参养肺汤（《杂症会心录》）合养肺煎（《鸡峰普济方》）加减：党参 15g、黄芪 15g、五味子 9g、核桃仁 15g、阿胶 6g（烊化）、蜜百部 15g、浙贝母 9g、炒紫苏子 9g、清半夏 12g、赤芍 9g、醋莪术 12 g、地龙 9g、夏枯草 12 g、陈皮 12g、炙甘草 9g。

加减：肺气虚甚损及阳气致肺气虚冷，症见畏风寒、痰清稀而冷者，加细辛、干姜、盐补骨脂，或选用补肺人参散（《太平圣惠方》：人参、蜜紫菀、鹿角胶、黄芪、肉桂、紫苏叶、麸炒白术、五味子、熟地黄、炒苦杏仁、干姜）合半夏汤（《备急千金方》：清半夏、生姜、肉桂、炙甘草、姜厚朴、人参、陈皮、麦冬）加减。兼阴虚，症见干咳或痰少难咯、咽干、舌红少苔甚至无苔者，加麦冬、南沙参；痰多、舌苔白腻者，减黄芪、麦冬，加橘红、麸炒白术、茯苓；痰黄、苔黄者，加黄芩、浙贝母、瓜蒌；自汗甚者，倍用黄芪，加浮小麦、煅牡蛎；兼瘀血者，症见口唇紫绀、舌质暗或舌底脉络迂曲者，选加炒桃仁、全蝎、烫水蛭、当归。

8.1.3 肺肾气虚证

主症：喘促，胸闷，气短，动则加重，咳嗽，神疲，乏力，自汗，易感冒，腰膝酸软，头昏，夜尿多，咳时遗尿，舌淡白，苔白，脉沉，脉细。次症：畏风寒，身体困倦，咳痰，痰质稀，泡沫痰，痰易咯出，耳鸣，小便频数，苔薄，脉弱。

诊断条件：①喘促，或气短，动则加重，或咳嗽；②神疲，或乏力，或自汗，动则加重；③畏风寒，或易感冒；④腰膝酸软；⑤头昏，或耳鸣；⑥小便频数，或夜尿多，或咳时遗尿；⑦舌淡白，或脉沉细或细弱。

诊断标准：具备①、②、③中2 项，加④、⑤、⑥、⑦中3项。

治法：补肺益肾，纳气平喘。

方药：参熟桃苏汤（《辨证录》）合补肺散（《普济方》）加减：人参6g、黄芪15g、核桃仁15g、麦冬12g、熟地黄15g、酒萸肉12g、五味子9g、盐补骨脂12g、炙淫羊藿9g、浙贝母9g、炒紫苏子9g、防己9、赤芍12g、地龙15g、全蝎6g、陈皮12g、炙甘草9g。

加减：对于气虚及阴而成肺肾气阴两虚者，症见干咳无力或痰少难咯、咽干、盗汗、舌红少苔者，减盐补骨脂，加酒黄精、天冬、阿胶。气损及阳致肺肾阳虚，症见畏寒、面浮、肢肿者，减麦冬，加炮附片、肉桂、茯苓；气短、喘息甚者，加蛤蚧、沉香；瘀血明显者，加醋莪术、土鳖虫、烫水蛭；痰黄者，加黄芩、浙贝母、瓜蒌；便秘者，加炒桃仁、酒大黄。

8.2 兼证类

8.2.1 痰湿证

主症：痰色白，痰易咳出，苔腻，脉滑。次症：痰多，食少，纳呆，痞满，腹胀，苔白，脉弦。

诊断条件：①痰色白，或痰易咯出；②纳呆，或食少；③痞满，或腹胀；④苔白或白腻，或脉滑或弦滑。

诊断标准：具备①项，加②、③、④中2项。

治法：燥湿化痰，宣降肺气。

方药：二陈汤（《医方集解》）合三子养亲汤（《杂病广要》引《皆效方》）加减：法半夏12g、茯苓15g、陈皮12g、白术12g、姜厚朴9g、炒白芥子9g、炒莱菔子9g、炒紫苏子9g、炙甘草6g。

8.2.2 血瘀证

主症：面色晦暗，口唇青紫，舌暗，舌青紫，舌有瘀斑或瘀点，舌下脉络迂曲。次症：胸闷，气短，脉涩。

诊断条件：①面色晦暗；②口唇青紫；③舌暗或青紫或有瘀斑或瘀点；④舌下脉络迂曲。

诊断标准：具备①、②、③、④中1项。

治法：活血化瘀。

方药：血府逐瘀汤（《医林改错》）加减：炒桃仁9g、红花9g、当归10g、川芎9g、赤芍12g、醋莪术9g、土鳖虫6g。

8.3 复杂证候

特发性肺纤维化证候多以复杂证候出现，即使是复杂证候，病机也有主次之分。如特发性肺纤维化证候以阴虚肺燥证、肺气虚证、肺肾气虚证为主，常兼有痰湿证、血瘀证。如肺气虚证兼有痰湿证则为肺气虚痰湿证，肺肾气虚证兼有痰湿证则为肺肾气虚痰湿证；瘀血常兼见各证候之中，如兼于肺气虚肺证则为肺气虚血瘀证、兼于肺肾气虚证则为肺肾气虚血瘀证等。若痰湿、血瘀同时兼有，如肺肾气虚证兼有痰湿、血瘀证则为肺肾气虚痰瘀证。

本文件难以将所有复杂证候全部列出，建议临床实践中，辨证为复杂证候时可参考本文件所列证候治法方药进行治疗，根据虚实主次而谴方用药。如肺肾气虚、痰瘀互结证者，应在补肺益肾、纳气平喘方药基础上，佐以化痰活血散结药物，如活血通络类的炒桃仁、醋莪术、烫水蛭、土鳖虫、蜈蚣等；化痰类的炒白芥子、川贝母（或浙贝母）、海蛤壳等。

9 中成药治疗

9.1 养阴清肺颗粒

口服，一次 1 袋，一日 2 次。功效：养阴润肺，清热利咽。用于咽喉干燥疼痛，干咳、少痰或无痰。

9.2 蛤蚧定喘胶囊

口服，一次 3 粒，一日 2 次。功效：滋阴清肺，止咳定喘。适用于肺肾两虚、阴虚肺热所致的咳喘、气短、胸闷、自汗、盗汗。

9.3 金水宝胶囊

口服，一次 3 粒，一日 3 次。功效：补益肺肾、秘精益气。适用于肺肾两虚，精气不足，久咳虚喘，神疲乏力等。

9.4 百令胶囊

口服，一粒 0.5g，一次 2~6 粒，一日 3 次。功效：补肺肾，益精气。适用于肺肾两虚引起的咳嗽、气喘等。

9.5 二陈丸

口服，一次 9-15g，一日 2 次。功效：燥湿化痰，理气和胃。用于痰湿停滞导致的咳嗽痰多等。

9.6 补肺活血胶囊

口服，一次 4 粒，一日 3 次。功效：益气活血，补肺固肾。适用于气虚血瘀证的咳喘、胸闷等。

9.7 血府逐瘀胶囊

口服，一次 6 粒，一日 2 次。功效：活血祛瘀，行气止痛。适用于气滞血瘀所致的胸闷、胸痛等。

10 其他疗法

针刺、离子导入、膏方、灸法等多种特色疗法治疗特发性肺纤维化均有一定的临床疗效。根据现有临床证据与专家共识，推荐使用膏方疗法[17-19]，具体处方用药及疗程需在中医临床医师辨证论治前提下开取和使用。

附录 A
（资料性）
特发性肺纤维化的临床诊断

A.1 临床诊断

A.1.1 临床表现

特发性肺纤维化患者的主要临床表现为不明原因的、进行性加重的劳力性呼吸困难、咳嗽和双侧肺底爆裂音，可伴有杵状指，一般无其他系统性疾病的临床表现。特发性肺纤维化的发病率与年龄增长呈正相关，典型表现为60~70岁起病，隐匿性呼吸困难，少数患者可以以急性加重形式起病，表现为数周内不明原因的、急剧加重的呼吸困难，且胸部高分辨率CT显示肺纤维化基础上新发磨玻璃影。

A.1.2 诊断措施

特发性肺纤维化诊断主要从胸部高分辨率 CT、肺活检组织病理学检查结果两方面进行组合诊断。特发性肺纤维化的影像学表型和组织病理学表型分为“UIP 型”、“可能 UIP 型”、“不确定型”、和“其他诊断” 4 个类型。

A.1.3 诊断标准

特发性肺纤维化的诊断需具备以下条件：①排除其他已知病因的间质性肺疾病（如居住、职业环境暴露，结缔组织疾病和药物影响等），以及出现下述第②或第③条表现。②UIP型高分辨率CT表现（见附录A.2）。③有肺组织病理的患者，符合高分辨率CT表型与肺脏病理表型的特定组合。

特发性肺纤维化急性加重诊断标准：对于已经诊断或当前诊断特发性肺纤维化者，如果满足以下条件，可做出诊断：①通常在 1 个月内出现了临床上显著的急性呼吸困难加重；②胸部高分辨率 CT 证实在原来 UIP 型改变基础上双肺新出现磨玻璃样改变和（或）实变影；③排除心力衰竭或液体负荷过重导致的呼吸功能恶化或急性肺水肿。

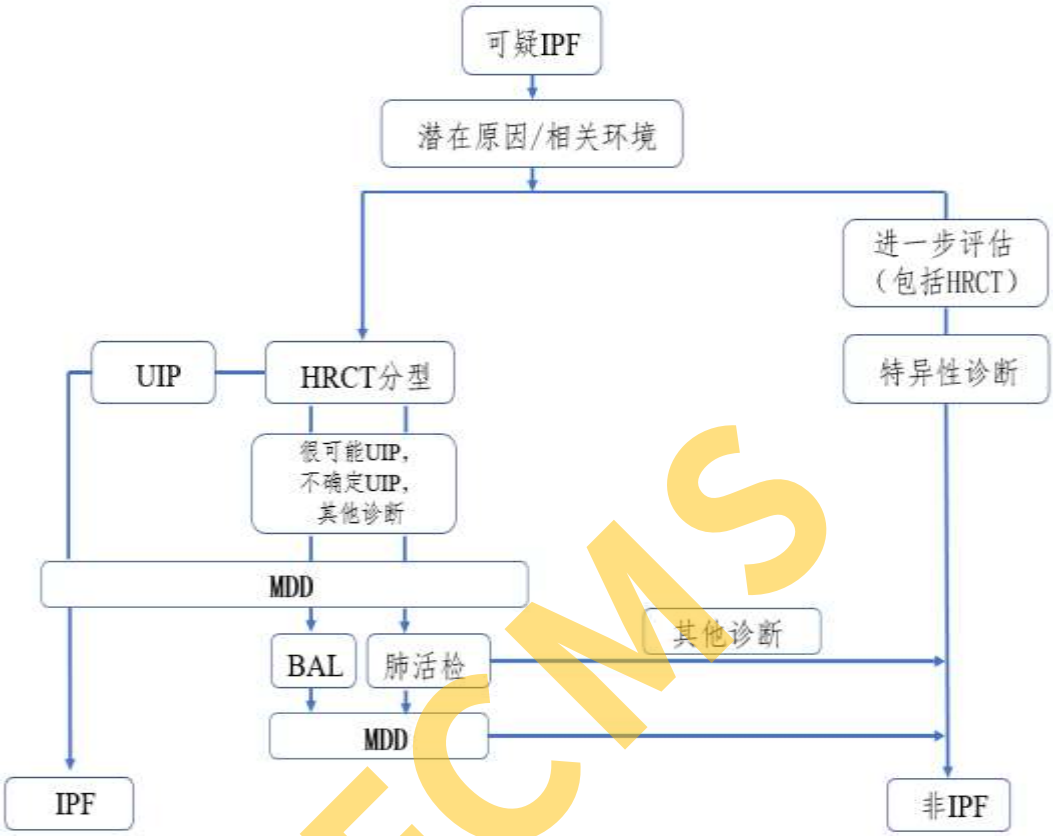
A.2 影像学表型和组织病理学表型特点

表A.1　影像学表型和组织病理学表型特点

	UIP型	可能UIP型	不确定型	其他诊断
影像学特点	1.病变主要位于下肺、胸膜下病变分布不均匀[a]，亦可见不对称分布。 2.蜂窝影，伴或不伴外周分布的牵张性支气管或细支气管扩张，小叶间隔增厚，通常伴随不同影像表现，可伴有轻度磨玻璃改变，可能有肺实变[b]。	1.病变主要位于下肺、胸膜下；病变分布不均匀。 2.网格影伴外周分布牵张性支气管或细支气管扩张。 3.可伴有轻微磨玻璃影。	1.缺少胸膜下集中分布的优势。 2.纤维化病灶特征和（或）分布不符合任一特性的间质性肺病的CT表型特点（真正意义上的“不确定型”）。	1.CT特征 （1）多发囊泡影；（2）弥漫马赛克征；（3）广泛磨玻璃影；（4）大量微结节；（5）小叶中心性结节（6）结节影实变。 2.病变分布 （1）沿支气管血管束分布；（2）沿淋巴管分布（考虑肺结节病）；（3）上或中肺野分布为主（考虑纤维化性HP、CTD-ILD及肺结节病）；（4）胸膜下分布为主（考虑NSIP或吸烟相关IP）。 3.其他 （1）囊肿（考虑LAM、PLCH、DIP）；（2）马赛克征（考虑HP）；（3）以磨玻璃为主要表现（考虑HP、吸烟相关性疾病、药物损伤及纤维化急性加重）；（4）大量小叶中心微结节（考虑HP或吸烟相关性疾病）；（5）结节（考虑结节病）；（6）肺实变（考虑机化性肺炎等）；（7）胸膜斑：多见于尘肺；（8）食管扩张：多见于结缔组织疾病；
组织病理特点	1.致密的纤维化伴肺结构明显破坏,即肺结构破坏、瘢痕形成，和（或）蜂窝形成； 2.纤维化病灶以胸膜下和（或）间隔旁分布为主； 3.肺纤维化病灶片状分布； 4.成纤维母细胞灶； 5.无其他疾病的特征性病理表现	1.UIP型病理特点中的部分表现，但不满足UIP 型病理表现的所有特点； 2.且无其他疾病的特征性病理表现； 3.或者只有蜂窝	1.肺纤维化，可有肺结构破坏，伴其他非UIP型的病理特点或表现[a]； 2.UIP型病理特点中的部分表现，同时有其他疾病的特征性病理表现[b]。	1.出现非UIP型IIP的病理学表现，如无成纤维母细胞灶或表现为疏松纤维化； 2.存在其他疾病的特征性病理表现，如过敏性肺炎、朗格汉斯组织细胞增生症、结节病、LAM等。

注：UIP：寻常型间质性肺炎；a 病变空间分布上存在多样性：偶尔呈弥漫性分布，也可两肺病变不对称；
b 合并其他CT表现：轻微磨玻璃影、网格影及肺实变。

A.3 特发性肺纤维化诊断流程图



图A.1　特发性肺纤维化诊断流程

注：MDD：多学科综合讨论；BAL：支气管肺泡灌洗

附录 B
（资料性）
指南研制方法

图 B.1 指南研制方法流程图

注：本指南制订过程性资料与编制说明可联系世界中联国际标准部获取。

附录 C
（资料性）
特发性肺纤维化指南局限性与展望

中医药治疗特发性肺纤维化临床研究证据数量有限，缺乏高质量临床研究证据。各证候推荐方药多为针对病机选定的经典名方，现代研究证据支撑不足；所推荐中成药在特发性肺纤维化临床治疗中应用广泛，尚需大样本、高质量的临床研究验证其治疗特发性肺纤维化疗效与安全性。

特发性肺纤维化急性加重是影响特发性肺纤维化自然病程的重要事件，预后差，中位生存期短，死亡率高。中医药参与治疗急性加重疗效显著，但现在研究证据相对匮乏，未能回答特发性肺纤维化急性加重中医药应用时机、治疗方案疗效等临床问题，建议亟待围绕特发性肺纤维化急性加重诊疗开展中医药临床研究，以明确中医药的疗效并提供高质量证据。

参考文献

[1] Maher TM, Bendstrup E, Dron L, et al. Global incidence and prevalence of idiopathic pulmonary fibrosis[J]. Respir Res, 2021,22(1):197.

[2] Cox IA, Otahal P, De Graaff B, et al. Incidence, prevalence and mortality of idiopathic pulmonary fibrosis in Australia[J]. Respirology, 2022,27(3):209-216.

[3] Strongman H, Kausar I, Maher TM. Incidence, Prevalence, and Survival of Patients with Idiopathic Pulmonary Fibrosis in the UK[J]. Adv Ther, 2018,35(5):724-736.

[4] Cottin V, Spagnolo P, Bonniaud P, et al. Mortality and Respiratory-Related Hospitalizations in Idiopathic Pulmonary Fibrosis Not Treated With Antifibrotics[J]. Front Med (Lausanne), 2021,8:802989.

[5] Gao J, Kalafatis D, Carlson L, et al. Baseline characteristics and survival of patients of idiopathic pulmonary fibrosis: a longitudinal analysis of the Swedish 特发性肺纤维化 Registry[J]. Respir Res, 2021,22(1):40.

[6] Dove EP, Olson AL, Glassberg MK. Trends in Idiopathic Pulmonary Fibrosis-related Mortality in the United States: 2000-2017[J]. Am J Respir Crit Care Med, 2019,200(7):929-931.

[7] Hopkins RB, Burke N, Fell C, et al. Epidemiology and survival of idiopathic pulmonary fibrosis from national data in Canada[J]. European Respiratory Journal, 2016,48(1):187-195.

[8] Raimundo K, Chang E, Broder MS, et al. Clinical and economic burden of idiopathic pulmonary fibrosis: a retrospective cohort study[J]. BMC Pulmonary Medicine, 2016,16(1).

[9] Collard HR, Chen SY, Yeh WS, et al. Health care utilization and costs of idiopathic pulmonary fibrosis in U.S. Medicare beneficiaries aged 65 years and older[J]. Ann Am Thorac Soc, 2015,12(7):981-987.

[10] 宣建伟, 卢永吉, 任懋东, 等. 中国特发性肺纤维化患者的直接经济负担[J].中国药物经济学, 2019,14(06):9-12.

[11] Li JS, Yu XQ, Xie Y, et al. Efficacy and Safety of Traditional Chinese Medicine Treatment for Idiopathic Pulmonary Fibrosis: An Exploratory, Randomized, Double-Blinded and Placebo Controlled Trial[J]. Frontiers in Pharmacology, 2022, 13.

[12] 中华医学会呼吸病学分会间质性肺病学组, 中国医师协会呼吸医师分会间质性肺疾病工作委员会. 特发性肺纤维化急性加重诊断和治疗中国专家共识[J]. 中华医学杂志. 2019,99(26):2014-2023.

[13] 鞠铮嵘. 肺痿理论—晁恩祥名老中医治疗肺纤维化经验总结[D]. 北京中医药大学, 2014.

[14] 张立山, 戴雁彦, 任传云. 武维屏教授治疗肺纤维化十法[J]. 中国中医药信息杂志, 2008, 15(4):94~95.

[15] 李建生. 特发性肺纤维化中医辨证治疗概要[J]. 中医学报, 2017, 32(06):929~931.
[16] 中华中医药学会内科分会，中国民族医药学会肺病分会，中华中医药学会肺系病分会. 特发性肺纤维化中医证候诊断标准(2019 版)[J]. 中医杂志, 2020, 61(18):1653~1656.
[17] 白文梅，马红霞，同立宏. 益气活血通络膏方治疗气虚血瘀型特发性肺纤维化 60 例疗效观察[J]. 新疆中医药, 2018, 36(06): 7-8.
[18] 杨柳，成淑芳，张树森，等. 康益膏方治疗特发性肺纤维化 60 例[J]. 光明中医，2015, 30(07): 1449-1450.
[19] 张树森，杨柳，董瑞. 珠及膏治疗特发性肺纤维化气阴两伤型临床观察[J]. 中国中医药现代远程教育, 2019, 17(23): 69-71.

Foreword

Attention is drawn to the possibility that some of the elements of this standard may be the subject of patent rights. WFCMS shall not be held responsible for identifying any or all such patent rights.

Main Drafting Units: Henan University of Chinese Medicine, The First Affiliated Hospital of Henan University of CM.

Drafting Units Participated: Henan University of Chinese Medicine, The First Affiliated Hospital of Henan University of CM, Lanzhou University Center for Evidence Based Medical and Clinical Research, Beijing University of Chinese Medicine Center for Evidence Based Medical and Clinical Research, Peking University People's Hospital, China-Japan Friendship Hospital, Second Teaching Hospital of Tianjin University of Traditional Chinese Medicine, Guangdong Provincial Hospital of Chinese Medicine, Dongfang Hospital Beijing University of Chinese Medicine, Beijing University of Chinese Medicine Third Affiliated Hospital, Shenzhen Hospital of Traditional Chinese Medicine, Hebei Provincial Hospital of Chinese Medicine, Henan Provincial Hospital of Chinese Medicine, The Third Affiliated Hospital of Henan University of Chinese Medicine, Zhenzhou TCM Hospital, Wuhan No.1 Hospital, Jiangsu Province Hospital of Chinese Medicine, Affiliated Hospital of Jiangxi University of TCM, The First Affiliated Hospital of Liaoning University of Traditional Chinese Medicine, The Second Affiliated Hospital of Liaoning University of Traditional Chinese Medicine, Qingdao Hospital of Traditional Chinese Medicine, Shaanxi Provincial Hospital of Chinese Medicine, Kunming Municipal Hospitalof Traditional Chinese Medicine, Shuguang Hospital.Shanghai University of Traditional Chinese Medicine, LongHua Hospital Shanghai University of Traditional Chinese Medicine, Zhejiang Provincial Hospital of Chinese Medicine, The Second Affiliated Hospital of Guizhou University of Traditional Chinese Medicine, Affiliated Hospital of Shandong University of Traditional Chinese Medicine, Anhui University of Chinese Medicine, Dongzhimen Hospital Beijing University of Chinese Medicine.

Advisory committee: WANG Yongyan, ZHANG Boli, CHAO Enxiang, SUN Sulun.

Main Drafters: LI Jiansheng, YU Xueqing, XIE Yang.

Drafters and reviewers(sorted by last name strokes):

Chinese mainland: YU Xuefeng, MA Zhanping, MA Yanfang, WANG Chengxiang, WANG Qi, WANG Minghang, FU Yi, FENG Cuiling, QU Nini, LIU Liangji, LIU Ruixin, SUN Zikai, SUN Zengtao, LI Zegeng, LI Suyun, LI Demin, LI Meng, YANG Junchao, ZHANG Lishan, ZHANG Wei, ZHANG Nianzhi, ZHANG Wei, ZHANG Hongchun, ZHANG Huiyong, LU Xuechao, CHEN Sheng, CHEN Wei, CHEN Yaolong,

WU Lei, LIN Lin, MENG Yong, FENG Jihong, BAN Chengjun, XU Liran, CUI Hongsheng, LU Zhenhui, GE Zhengxing, XUE Hanrong.

Hong Kong, China: LV Aiping.

Macao, China: WU Qibiao.

UK: WANG Duolao, CHEN Tao.

The drafting procedure of this document complies with the SCM1.1-2021 Directives for standardization—Part 1: Formulation and Publication of Standard issued by the World Federation of Chinese Medicine Societies (WFCMS).

Introduction

The incidence of idiopathic pulmonary fibrosis (IPF) is increasing year after year. With a high disability rate, high case fatality rate, low quality of life, and heavy burden of disease, IPF is a major disease that poses serious public health risks. The incidence rate of IPF is high and varies slightly across countries and regions [1]. The prevalence rate reaches 35.1/100,000 people, while the incidence rate has also increased to 11.2/100,000 people [2]. The disease progresses rapidly. It has a short median survival time of approximately 3-5 years [3], a high 3-year cumulative case fatality rate of 50.2% [4], and a dismal prognosis. Even with treatments such as aggressive anti-fibrotic therapy in recent years, the 5-year survival rate is still below 50% [5]. And with that comes higher case fatality rate and disability rate, which seriously affects the quality of life of the patients. Studies have shown that despite the wide use of anti-fibrotic treatment, the case fatality rate is still on the rise [6], and the quality of life with IPF after 2 years was lower than for Global Initiative for Chronic Obstructive Lung Disease stage IV chronic obstructive pulmonary disease [7]. The grim disease situation also brings a serious burden of disease. In the UK, the annual total direct medical costs for patients with IPF are $21,732 in average [8], and in the USA, the costs reach up to nearly $2 billion [9]. In China, there is a lack of authoritative data. But a epidemiological survey of small sample based on health insurance payment data showed that the average hospitalization costs per patient with IPF is as high as ¥19,645[10], and the comorbidities and acute exacerbation events will further increase the economic burden of patients with IPF.

In order to improve the prevention and treatment of IPF, a series of guidelines for the diagnosis and/or treatment of IPF have been developed and published by different international organizations and countries.

Chinese medicine is effective in treating IPF, and its advantages may be in reducing acute exacerbations, and improving exercise capacity, the quality of life, and clinical symptoms and signs for IPF[11]. However, there is a lack of uniform understanding and standardization of TCM treatment protocols for IPF, which affects the popularization of the researches and the improvement of overall clinical efficacy. See Annex B for the methodology of this document and Annex C for limitations and future directions.

To meet the needs of clinical use and research of TCM and integrated traditional Chinese and Western medicine, this document was made with reference to domestic and overseas guidelines and expert consensus on the treatment of IPF, hoping to provide a reference for the clinical prevention and treatment of IPF with Chinese medicine.

International Guideline for Clinical Practice of Chinese Medicine Idiopathic Pulmonary Fibrosis

1 Scope

This document specifies the diagnostic criteria, pathogenesis, syndrome differentiation, treatment with Chinese patent medicine, and other treatments of idiopathic pulmonary fibrosis (IPF).

This document applies to the patients with IPF, and can be used by respiratory clinicians (clinicians of TCM, integrated Chinese and Western medicine, and western medicine) for reference.

2 Normative references

The following referenced documents are indispensable for the application of this document. For dated references, only the dated edition applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

GB/T16751.2-2020 Clinic terminology of traditional Chinese medical diagnosis and treatment-Part 2:syndromes/patterns
T/CACM1330-2019 Syndrome Diagnostic Criteria of ldiopathic Pulmonary Fibrosis in Traditional Chinese Medicine
ICD-11 International Classification of Diseases 11th Revision：Traditional medicine conditions
ATS/ERS/JRS/ALAT An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management
ATS/ERS An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

3.1
Idiopathic pulmonary fibrosis

a chronic, fibrotic, and interstitial lung disease of unknown cause. IPF occurs primarily in middle-aged and elderly people, and is more common in males. And it's characterized by dyspnea and progressive worsening of lung function.

Note: Acute exacerbations of IPF (AEIPF) are defined as dyspnea, hypoxemia, radiation-induced alveolar infiltration occurred within the last month of unidentifiable cause that cannot be explained by infection, pulmonary embolism, pneumothorax, heart disease, etc. [12].

4 Western diagnostic criteria

See Annex A for the western diagnostic criteria, classification, and process of IPF.

5 Pathogenesis

There is no uniform understanding of the pathogenesis of IPF. One view is that the basic pathogenesis of IPF is the deficiency in origin and excess in superficiality, which is often caused by lung deficiency and evil invasion that harm qi, yin, and the kidney over time. The following syndromes are common in clinical practices: asthenia syndromes including deficiency of both lung and kidney, and deficiency of qi and yin; or sthenia syndromes including chronic diseases transforming to collaterals due to mistreatment or long-standing illness, or toxic phlegm and blood stasis and collaterals obstruction due to toxic evil damaging the collaterals. The deficiency in origin often manifests as lung deficiency and kidney deficiency, while excess in superficiality often manifests as wind, toxin, phlegm, and stasis [13]. Another view believes that the basic pathogenesis of IPF is no more than deficiency, phlegm, stasis, and toxin. And the pathology is phlegm and blood stasis leading to lung collateral obstruction and eventually the loss of lung function. The other view believes healthy qi depletion, collaterals obstruction, and constraints accumulation are the basic pathogenesis of IPF. Healthy qi depletion refers to the deficiency of the lung causing the deficiency of the kidney. Collaterals obstruction refers to lung collateral obstruction. And constraints accumulation refers to the accumulation of phlegm turbidity and blood stasis irreversibly damaging the healthy qi over time and eventually leading to the loss of lung function. The root cause of IPF is lung and kidney deficiency, the symptoms are lung collateral obstruction and phlegm and blood stasis, and its characteristics are constraints accumulation resulting in the loss of functions, the combination of loss of functions and obstruction, and a mixture of asthenia syndromes with asthenia syndromes. In conclusion, the pathogenesis of IPF are deficiency in origin and excess in superficiality, and a mixture of asthenia syndromes with asthenia syndromes. The root causes of IPF are asthenia syndromes with lung-qi and kidney-qi deficiency, yin deficiency, and even yang deficiency being the main syndromes. And the symptoms of IPF are asthenia symptoms with phlegm, stasis, toxin and their combinations being the

main symptoms.

6 TCM diagnostic criteria

The common syndromes of IPF include two types: main syndromes (yin deficiency and lung dryness syndrome, lung-qi deficiency syndrome, and lung-qi and kidney-qi deficiency syndrome) and accompanied syndromes (phlegm dampness syndrome and blood stasis syndrome). It should be noted that phlegm dampness syndrome and blood stasis syndrome are often accompanied by deficiency syndromes and manifest as a mixture of asthenia syndromes with asthenia syndromes. For example, when accompanied by lung and kidney deficiency syndromes, the patient will have lung-qi and kidney-qi deficiency with phlegm dampness syndrome, or lung-qi and kidney-qi deficiency with blood stasis syndrome. Acute exacerbations of IPF often manifest as yin deficiency and lung dryness syndrome, lung-qi and kidney-qi deficiency with phlegm dampness syndrome, and blood stasis syndrome. The diagnostic criteria of the syndromes should meet the requirements in T/CACM1330-2019.

7 Therapeutic principles and methods

The main therapeutic method of IPF is supporting healthy qi to eliminate evils, which means nourishing, moistening, resolving, and eliminating. Nourishing includes nourishing the lung-qi, lung-yin, qi and yin, lung and kidney, etc. Moistening refers to moistening the lung, including clearing heat by moistening with the cold and supporting yang by moistening with the warm. Resolving refers to resolving phlegm and stasis, covering clearing the phlegm-heat, drying dampness and resolving phlegm, and promoting blood circulation and removing blood stasis. Eliminating means eliminating accumulated hard masses, which is often included in the methods of quickening the blood, freeing the collaterals, and resolving phlegm. In terms of eliminating evils, distinguish the evils between phlegm-heat, phlegm dampness, or blood stasis, and pay particular attention to turbidity and toxin. Based on the syndromes, treat by clearing heat and resolving phlegm, or drying dampness and resolving phlegm, or with promoting blood circulation, removing blood stasis, and detoxifying sometimes. For patients with accumulated phlegm and blood stasis, quicken the blood, resolve phlegm, and eliminate accumulated hard masses. In terms of supporting healthy qi, while nourishing the lung and the kidney, consider which deficiency is more serious, qi or yin. At the middle and late stages of IPF, patients with accumulated phlegm and blood stasis should be treated by nourishing healthy qi, resolving phlegm, quickening the blood, and with medicines that eliminate accumulated hard

masses, such as those with the functions of quicken the blood and free the collaterals, resolve phlegm, detoxify, etc. [15].

Given the pathogenesis of IPF is complex and varies at different stages, the degree of seriousness, whether the evil is phlegm turbidity, blood stasis, or heat toxin, and the qi-blood and yin-yang of visceral organs should be differentiated in clinical medicine use. The changes in excess evil should be paid attention to at acute exacerbation stage, when the method of eliminating evils should be enhanced, or used as the main treatment when necessary while supporting healthy qi. At stable stage, resolve phlegm, quicken the blood, and eliminate accumulated hard masses on the basis of nourishing the lung and the kidney.

8 Syndrome differentiations

8.1 Main syndromes

8.1.1 Yin deficiency and lung dryness syndrome

Main symptoms: dyspnea, chest tightness, shortness of breath, cough, scant phlegm, sticky and difficult-to-expectorate phlegm, yellow phlegm, dry mouth, dry throat, thirst, little tongue fur, yellow tongue fur, fine pulse, rapid pulse. Secondary symptoms: dry cough, thick phlegm, heat in the heart of the palms and soles, night sweats, mental fatigue, physical fatigue, red tongue, peeling tongue fur.

Diagnostic conditions: ①dyspnea, chest tightness, or shortness of breath; ②dry cough, scant phlegm, sticky and difficult-to-expectorate phlegm, or yellow phlegm; ③dry mouth, dry throat, or thirst; ④heat in the heart of the palms and soles; ⑤night sweats; ⑥red tongue, little tongue fur, yellow tongue fur, peeling tongue fur, or fine and rapid pulse.

Diagnostic criteria: having both ①② and three of ③④⑤⑥.

Treating methods: nourish yin, moisten dryness, and clear heat.

Prescriptions: Modified Maimendong decoction (from Synopsis of Prescriptions of the Golden Chamber) combined with Baihe Gujin decoction (from Collected Exegesis of Recipes): Radix Adenophorae 15g, Radix Ophiopogonis 15g, Rehmannia Glutinosa 15g, Radix Scrophulariae 12g, Paeoniae Radix Alba 15g, Ginseng 6g, Bulbus Lilii 15g, Stemonae fried with honey 15g, Bulbus Fritillariae Thunbergii 9g, Cortex Moutan 12g, Citri Reticulatae Pericarpium 12g, earthworm 15g, baked Radix Glycyrrhiza 9g.

Modified prescriptions: for some patients, yin-deficiency will affect qi to cause

qi-yin deficiency, resulting in the symptoms of cough or dyspnea with sweating, and aversion to wind. Add Fructus Schisandrae, Gynostemma Pentaphyllum, and Radix Astragali to their prescriptions. Or use modified Baihuajian pills (from Jifeng's Formularies for Universal Relief: Ginseng, Tartarian Aster, Colla Corii Asini, Stemonae fried with honey, Flos Farfarae fried with honey, Rhizoma Dioscoreae, Radix Asparagi, Radix Ophiopogonis, Bulbus Fritillariae Cirrhosae, stir-fried bitter Apricot seed, baked Radix Glycyrrhiza). For patients with frequent dry cough, add Flos Farfarae fried with honey, stir-fried Fructus Tribuli, and Bombyx Batryticatus stir-fried with bran to their prescriptions. For patients with excess heat toxin and with symptoms of sore throat and yellow phlegm, add Scutellaria Baicalensis, Rhizoma Belamcandae, and stir-fried Fructus Arctii to their prescriptions. For patients with severe heat in the heart of the palms and soles, add Anemarrhenae Rhizoma and salt-fried Phellodendri Chinensis Cortex to their prescriptions. For patients with obvious night sweats, add Calcined Oyster and light wheat to their prescriptions. For patients with blood stasis and with symptoms of cyanotic lips, dark purple tongue, or sublingual varicose veins, Add woodlouse, Rhizoma Dioscoreae Nipponicae, and Radix Paeoniae Rubra to the prescriptions.

8.1.2 Lung-qi deficiency syndrome

Main symptoms: chest tightness and shortness of breath that worsen in movements, cough, mental fatigue, physical fatigue, spontaneous sweating, being susceptible to colds, pale and white tongue, fine pulse. Secondary symptoms: white phlegm, scant phlegm, physical fatigue, asthenic breathing and disinclination to talk, aversion to wind, thin tongue fur, white tongue fur, deep pulse, weak pulse.

Diagnostic conditions: ①chest tightness, shortness of breath, or cough. ②mental fatigue, or fatigue that worsens in movements; ③spontaneous sweating that worsens in movements; ④aversion to wind, or being susceptible to colds; ⑤pale and white tongue, deep and fine pulse, or fine and weak pulse.

Diagnostic criteria: having ① and two of ②③④⑤.

Therapeutic methods: nourish the lung, boost qi, resolve phlegm and relieve cough.

Prescriptions: Modified Renshen Yangfei decoction (from Records of Insights into Miscellaneous Diseases) combined with Yangfei decocted extract (from Jifeng's Formularies for Universal Relief): Radix Codonopsis 15g, Radix Astragali 15g, Fructus Schisandrae 15g, English walnut seed 15g, Colla Corii Asini 6g (melted in

hot solution), Stemonae fried with honey 15g, Bulbus Fritillariae Thunbergii 9g, stir-fried Fructus Perillae 9g, Alum Processed Pinellia 12g, Radix Paeoniae Rubra 9g, vinegar-processed Curcumae Rhizoma 12g, earthworm 9g, Spica Prunellae 12g, Citri Reticulatae Pericarpium 12g, baked Radix Glycyrrhiza 9g.

Modified prescriptions: for some patients, severe lung-qi deficiency will affect yang-qi to cause lung-qi deficiency and cold, resulting in the symptoms of fear of wind and cold, and clear and cold phlegm. Add Asarum Sieboldii Miq, Rhizoma Zingiberis, salt-processed Psoraleae Fructus to their prescriptions. Or use modified Bufei Renshen powder (from Taiping Royal Prescriptions: Ginseng, Tartarian Aster fried with honey, deerhorn glue, Radix Astragali, Cinnamon, Folium Perillae, Rhizoma Atractylodis Macrocephalae stir-fried with bran, Fructus Schisandrae, prepared Rehmanniae root, fried bitter Apricot seed, Rhizoma Zingiberis) combined with Banxia decoction (from Valuable Prescriptions for Emergency: Alum Processed Pinellia, ginger, Cinnamon, baked Radix Glycyrrhiza, ginger mix-fried Cortex Magnoliae Officinalis, Ginseng, Citri Reticulatae Pericarpium, Radix Ophiopogonis). For patients with yin deficiency and with symptoms of dry cough or scant and difficult-to-expectorate phlegm, dry throat, red tongue with little or even no tongue fur, add Radix Ophiopogonis and Radix Adenophorae to their prescriptions. For patients with copious phlegm and white and slimy tongue fur, remove Radix Astragali and Radix Ophiopogonis, and add Citri Grandis Exocarpium, Rhizoma Atractylodis Macrocephalae stir-fried with bran, and Poria Cocos. For patients with yellow phlegm and yellow tongue fur, add Scutellaria Baicalensis, Bulbus Fritillariae Thunbergii, and Trichosanthes Kirilowii Maxim to their prescriptions. For patients with severe spontaneous sweating, double the amount of Radix Astragali, and add light wheat and Calcined oyster to their prescriptions. For patients with blood stasis and with the symptoms of cyanotic lips, dark tongue color or sublingual varicose veins, selectively add stir-fried peach kernel, scorpion, hirudo scalded with talc powder, and Angelica Sinensis.

8.1.3 Lung-qi and kidney-qi deficiency syndrome

Main symptoms: dyspnea, chest tightness, and shortness of breath that worsen in movements, cough, mental fatigue, physical fatigue, spontaneous sweating, being susceptible to colds, waist-knee soreness, dizziness, frequent urination at night, enuresis when coughing, pale white tongue, white tongue fur, deep pulse, fine pulse. Secondary symptoms: fear of wind and cold, fatigue, cough with phlegm, dilute phlegm, easy-to-expectorate phlegm, tinnitus, frequent urination, thin tongue fur, weak pulse.

Diagnostic conditions: ①dyspnea, or shortness of breath that worsens in movements, or cough; ②mental fatigue, physical fatigue, or spontaneous sweating that worsen in movements; ③fear of wind and cold, or being susceptible to colds; ④waist-knee soreness; ⑤dizziness or tinnitus; ⑥frequent urination, frequent urination at night, or enuresis when coughing; ⑦pale white tongue, deep and fine pulse, or fine and weak pulse.

Diagnostic criteria: having two of ①②③ and three of ④⑤⑥⑦.

Therapeutic methods: nourish the lung and the kidney, help the kidney to control qi to prevent asthma.

Prescriptions: Modified Shenshu Taosu decoction (from Bianzheng Lu) combined with Bufei powder (from Prescriptions for Universal Relief): Ginseng 6g, Radix Astragali 15g, English walnut seed 15g, Radix Ophiopogonis 12g, prepared Rehmanniae root 15g, wine-steamed Corni Fructus 12g, Fructus Schisandrae 9g, salt-processed Psoraleae Fructus 12g, processed Epimedii Folium 9g, Bulbus Fritillariae Thunbergii 9g, stir-fried Fructus Perillae 9g, Radix Stephaniae Tetrandrae 9g, Radix Paeoniae Rubra 12g, earthworm 15g, scorpion 6g, Citri Reticulatae Pericarpium 12g, baked Radix Glycyrrhiza 9g.

Modified prescriptions: For some patients, qi deficiency will affect yin to cause qi-yin deficiency in both lung and kidney, resulting in the symptoms of weak dry cough, or scant and difficult-to-expectorate phlegm, dry throat, night sweats, red tongue with little moss. Remove salt-processed Psoraleae Fructus from their prescriptions and add wine-steamed Rhizoma Polygonati, Radix Asparagi, and Colla Corii Asini. For some patients, qi damage will affect yang to cause yang deficiency in both lung and kidney, resulting in the symptions of fear of cold, puffy face, and swollen limbs. Remove Radix Ophiopogonis from their prescriptions and add processed Aconiti Lateralis Radix Praeparata, Cinnamon, and Poria Cocos. For patients with shortness of breath and heavy gasping, add Gecko and Lignum Aquilariae Resinatum to their prescriptions. For patients with obvious blood stasis, and add vinegar-processed Curcumae Rhizoma, woodlouse, and hirudo scalded with talc powder to their prescriptions. For patients with yellow phlegm, add Scutellaria Baicalensis, Bulbus Fritillariae Thunbergii, and Trichosanthes Kirilowii Maxim to their prescriptions. For patients with constipation, add stir-fried peach kernel and wine-steamed Rhubarb to their prescriptions.

8.2 Accompanied syndromes

8.2.1 Phlegm dampness syndrome

Main symptoms: white phlegm, easy-to-expectorate phlegm, slimy tongue fur, slippery pulse. Secondary symptoms: copious phlegm, low food intake, anorexia, distention and fullness, abdominal distension, white tongue fur, string-like pulse.

Diagnostic conditions: ①white phlegm, or easy-to-expectorate phlegm; ②anorexia or low food intake; ③distention and fullness or abdominal distension; ④white tongue fur, white-and-slimy tongue fur, slippery pulse, or string-like and slippery pulse.

Diagnostic criteria: having ① and two of ②③④.

Therapeutic methods: dry dampness and resolve phlegm, diffuse and downbear lung qi.

Prescriptions: Modified Erchen decoction (from *Collected Exegesis of Recipes*) combined with Sanzi Yangqin decoction (from *Za Bing Guang Yao*): Pinellia Ternate 12g, Poria Cocos 15g, Citri Reticulatae Pericarpium 12g, Rhizoma Atractylodis Macrocephalae 12g, ginger mix-fried Cortex Magnoliae Officinalis 9g, stir-fried Semen Brassicae 9g, stir-fried Semen Raphani 9g, stir-fried Fructus Perillae 9g, baked Radix Glycyrrhiza 6g.

8.2.2 Blood stasis syndrome

Main symptoms: dull face, green-blue or purple lips, dark tongue, green-blue or purple tongue, ecchymosis and petechiae on tongue, sublingual varicose veins. Secondary symptoms: chest tightness, shortness of breath, rough pulse.

Diagnostic conditions: ①dull face; ②green-blue or purple lips; ③dark tongue, green-blue or purple tongue, ecchymosis or petechiae on tongue; ④sublingual varicose veins.

Diagnostic criteria: having one of ①②③④.

Therapeutic methods: promote blood circulation and remove blood stasis.

Prescriptions: Modified Xuefu Zhuyu Decoction (from *Correction on Errors in Medical Classics*): stir-fried peach kernel 9g, Carthamus Tinctorius L. 9g, Angelica Sinensis 10g, Chuanxiong Rhizoma 9g, Radix Paeoniae Rubra 12g, vinegar-processed Curcumae Rhizoma 9g, woodlouse 6g.

8.3 Complex syndromes

The syndromes of IPF are mostly complex syndromes, which still have a

difference between the main syndromes and secondary syndromes. For example, the main syndromes of IPF are yin deficiency and lung dryness syndrome, lung-qi deficiency syndrome, and lung and kidney qi deficiency syndrome. And the common secondary syndromes are phlegm dampness syndrome and blood stasis syndrome. If lung-qi deficiency syndrome is combined with phlegm dampness syndrome, it turns into lung-qi deficiency and phlegm dampness syndrome. If lung and kidney qi deficiency syndrome is combined with phlegm dampness syndrome, it turns into lung and kidney qi deficiency and phlegm dampness syndrome. Blood stasis is common in all syndromes. When it's combined with lung-qi deficiency syndrome, it turns into lung-qi deficiency and blood stasis syndrome. And if it's combined with lung and kidney qi deficiency syndrome, it turns into lung and kidney qi deficiency and blood stasis syndrome. If phlegm dampness and blood stasis both appear, for example, when lung and kidney qi deficiency syndrome is combined with both syndromes, it turns into lung and kidney qi deficiency and phlegm stasis syndrome.

It's impossible to list each complex syndrome in the document. Therefore, in clinical practices, it's recommended to refer to the listed prescriptions in this document to treat patients diagnosed with complex syndromes, and modify the prescriptions based on whether the syndromes are asthenia or sthenia, and whether the syndromes are main or secondary syndromes. For example, for patients with lung and kidney deficiency syndrome and intermingled phlegm and blood stasis syndrome, on the basis of using prescriptions that nourish the lung and the kidney and help the kidney to control qi to prevent asthma, herbs with the effect of resolving phlegm, quickening the blood, and eliminating hard masses should be added, such as those quicken the blood and free the collaterals (stir-fried peach kernel, vinegar-processed Curcumae Rhizoma, hirudo scalded with talc powder, woodlouse, scolopendra, etc.) and those resolve phlegm (stir-fried Semen Brassicae, Bulbus Fritillariae Cirrhosae or Bulbus Fritillariae Thunbergii, clam shell, etc.).

9 Treatment with Chinese patent medicine

9.1 Yangyin Qingfei granule

1 sachet orally, 2 times a day. Effect: nourishing yin, moistening the lung, clearing heat, and good for the throat. Used for dry and sore throat, dry cough, and scant or no phlegm.

9.2 Gejie Dingchuan capsule

3 capsules orally, 2 times a day. Effect: nourishing yin, clearing the lung, relieving

cough, and preventing asthma. Used for cough and asthma, shortness of breath, chest tightness, spontaneous sweating, and night sweats caused by lung and kidney deficiency, and lung heat due to yin deficiency.

9.3 Jinshuibao capsule

3 capsules orally, 3 times a day. Effects: nourishing both lung and kidney, containing essence and boosting qi. Used for lung and kidney deficiency, essential qi deficiency, enduring cough, dyspnea of deficiency type, mental and physical fatigue, etc.

9.4 Bailing capsule

0.5g for each capsule, 2-6 capsules orally, 3 times a day. Effects: nourishing both lung and kidney, and boosting essential qi. Used for cough, asthma, ect caused by lung and kidney deficiency.

9.5 Erchen pill

9-15g orally, 2 times a day. Effects: drying dampness, resolving phlegm, rectifying qi, and harmonizing the stomach. Used for cough and copious phlegm caused by phlegm dampness obstruction.

9.6 Bufei Huoxue capsule

4 capsules orally, 3 times a day. Effects: boosting qi, quickening the blood, nourishing the lung, and securing the kidney. Used for cough, chest tightness, ect caused by qi deficiency and blood stasis.

9.7 Xuefu Zhuyu capsule

6 capsules orally, 2 times a day. Effects: quickening the blood, dispelling stasis, moving qi, and relieving pain. It is used for chest tightness, chest pain, etc. caused by qi stagnation and blood stasis.

10 Other treatments

Multiple TCM treatment including acupuncture, iontophoresis, cream formula, and moxibustion have certain efficacy on IPF. Based on existing clinical evidences and expert consensus, cream formula therapy is recommended [17-19]. The detailed prescriptions and treatment should be used after the patient's syndromes are differentiated by TCM physicians.

Annex A
(Informative)

Clinical Diagnosis of IPF

A.1 Clinical diagnosis

A.1.1 Clinical manifestations

IPF usually manifests as progressive dyspnea on exertion, cough, and crackles on the base of lung of unidentifiable cause, and may be accompanied by clubbing digits. There are generally no clinical manifestations of other systemic diseases. The incidence rate of IPF is positively correlated with the growth of age. Typically, a patient will have his onset at the age of 60-70 with occult dyspnea. Few patients may start with acute exacerbation, which manifests as acute exacerbation dyspnea of unidentifiable cause within a few weeks, and newly detected ground-glass opacity on chest HRCT on the basis of pulmonary fibrosis.

A.1.2 Diagnostic measures

IPF is mainly diagnosed by both chest HRCT and histopathological examination by lung biopsy. There are 4 patterns of IPF based on imaging findings and histopathological examination: UIP pattern, probable UIP pattern, indeterminate for UIP, and alternative diagnoses.

A.1.3 Diagnostic criteria

The diagnosis of IPF should: ①rule out other interstitial lung diseases of identifiable cause (including residential exposure, occupational exposure, connective tissue disease, influence of drugs, etc.) and fit ② or ③ below. ② UIP pattern on HRCT (see Annex A.2). ③Patients with lung pathological manifestations meet specific combinations of HRCT phenotype and lung pathological phenotype.

Diagnostic criteria for AEIPF: patients diagnosed with IPF can be diagnosed with AEIPF if they ①show significant acute dyspnea exacerbation usually within a month; ②on the basis of UIP pattern changes, see newly detected lung ground-glass opacity and/or lung consolidation on chest HRCT; ③rule out deteriorated respiratory function or acute pulmonary edema caused by heart failure or fluid overload.

A.2 Features of patterns on imaging findings and histopathological examination

Table A.1 Features of patterns on imaging findings and histopathological examination

	UIP pattern	Probable UIP pattern	Indeterminate for UIP	Alternative diagnoses
Features of imaging findings	1. Distribution: lower lung–predominant and subpleural-predominant. Often heterogeneous and may be asymmetric. 2. Honeycombing with or without peripheral traction bronchiectasis/bronchiolectasis. Presence of thickening of interlobular septa with varied imaging findings usually. May have mild GGO and lung consolidation.	1. Distribution: lower lung–predominant and subpleural-predominant. Often heterogeneous. 2. Reticular pattern with peripheral traction bronchiectasis/bronchiolectasis. 3. May have mild GGO.	1. Distribution: without subpleural-predominance. 2. The features and distribution of lung fibrosis do not fit any CT features of any interstitial lung disease (truely indeterminate for UIP.)	1. CT features: (1) Multiple cysts; (2) diffuse mosaic attenuation; (3) predominant GGO; (4) profuse micronodules; (5) centrilobular nodules; (6) nodules consolidation. 2. Distribution: (1)peribronchovascular predominant; (2)perilymphatic distribution (consider sarcoidosis); (3)upper or mid lung (consider fibrotic HP, CTD-ILD, and sarcoidosis); (4)subpleural-predominance (consider NSIP or smoking-related IP). 3. Other features: (1)cysts (consider LAM, PLCH, and DIP); (2)mosaic attenuation (consider HP); (3)predominant GGO (consider HP, smoking-related disease, drug toxicity, and acute exacerbation of fibrosis); (4)profuse centrilobular micronodules (consider HP or smoking-related disease); (5)nodules (consider sarcoidosis); (6)consolidation (consider organizing pneumonia, etc.); (7)pleural plaques (consider pneumoconiosis); (8)dilated esophagus (consider CTD).
Histopat	1. Dense fibrosis	1. Have some but not	1. Pulmonary	1. Presence of pathological

hologica l features	with significant architectural distortion (i.e., destructive scarring and/or honeycombing). 2. A predilection for subpleural and/or paraseptal fibrosis. 3. Patchy pulmonary fibrosis. 4. Fibroblast foci. 5. The absence of features that suggest an alternative diagnosis.	all features in UIP pattern. 2. The absence of features that suggest an alternative diagnosis. 3. Or have honeycombing alone.	fibrosis. May be architectural distortion, with other pathological features of non-UIP patterns [a]. 2. Some features in UIP pattern and of other diseases [b].	features of IIP of non-UIP patterns, such as without fibroblast foci, or loose fibrosis. 2. Presence of pathological features of other diseases, such as hypersensitivity pneumonitis, pulmonary Langerhans cell histiocytosis, sarcoidosis, LAM, etc.

*UIP: usual interstitial pneumonia; a: Varied distribution (diffuse distribution, or asymmetric in the two lobes); b: Combined with other CT features (mild ground-glass opacity, reticular pattern, and consolidation).

A.2 Diagnostic algorithm for IPF

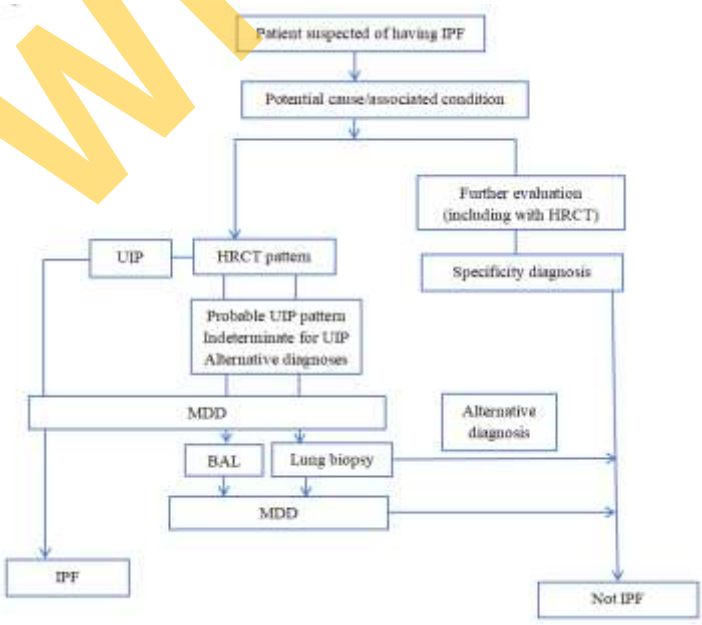


Figure A.1 Diagnostic algorithm for IPF

*MDD: multidisciplinary discussion; BAL: bronchoalveolar lavage.

Annex B
(Informative)

Guideline development

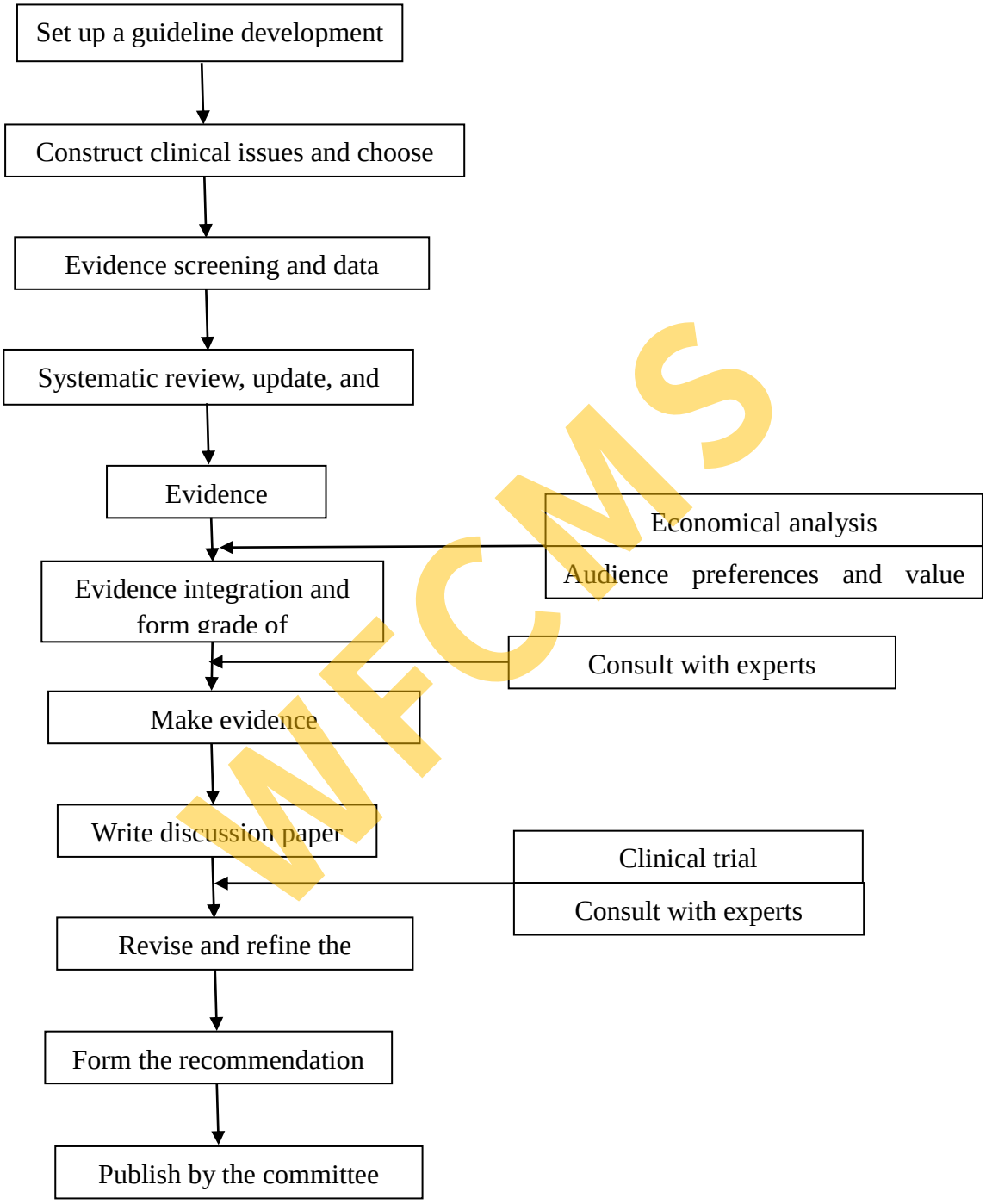


Figure B.1 Guideline development algorithm

*The process data and instructions of this guideline can be obtained from the International Standards Department of WFCMS.

Annex C
(Informative)

Limitations and future directions of the IPF guideline

The evidence of clinical research on the treatment of idiopathic pulmonary fibrosis with traditional Chinese medicine is limited and lacking in high-quality clinical research evidence. Most of the recommended prescriptions for various syndromes are classic and famous prescriptions selected based on the pathogenesis, lacking in modern research evidence; The recommended Chinese patent medicines are widely used in the clinical treatment of IPF; and large sample sized and high-quality clinical research is needed to verify their efficacy and safety.

The acute exacerbation of IPF, with a dismal prognosis, short median survival time, and a high case fatality rate, is an vital incidence that affects the natural course of IPF. Traditional Chinese medicine has a significant effect in the treatment of acute exacerbation of IPF, but is lacking research evidence at the present and unable to solve the clinical problems such as the application time of traditional Chinese medicine and the effect of treatment. It is recommended to carry out clinical research on the diagnosis and treatment to clarify the effect of traditional Chinese medicine and provide high-quality evidence.

Bibliography

[1] Maher TM, Bendstrup E, Dron L, et al. Global incidence and prevalence of idiopathic pulmonary fibrosis[J]. Respir Res, 2021,22(1):197.

[2] Cox IA, Otahal P, De Graaff B, et al. Incidence, prevalence and mortality of idiopathic pulmonary fibrosis in Australia[J]. Respirology, 2022,27(3):209-216.

[3] Strongman H, Kausar I, Maher TM. Incidence, Prevalence, and Survival of Patients with Idiopathic Pulmonary Fibrosis in the UK[J]. Adv Ther, 2018,35(5):724-736.

[4] Cottin V, Spagnolo P, Bonniaud P, et al. Mortality and Respiratory-Related Hospitalizations in Idiopathic Pulmonary Fibrosis Not Treated With Antifibrotics[J]. Front Med (Lausanne), 2021,8:802989.

[5] Gao J, Kalafatis D, Carlson L, et al. Baseline characteristics and survival of patients of idiopathic pulmonary fibrosis: a longitudinal analysis of the Swedish Idiopathic Pulmonary Fibrosis Registry[J]. Respir Res, 2021,22(1):40.

[6] Dove EP, Olson AL, Glassberg MK. Trends in Idiopathic Pulmonary Fibrosis-related Mortality in the United States: 2000-2017[J]. Am J Respir Crit Care Med, 2019,200(7):929-931.

[7] Hopkins RB, Burke N, Fell C, et al. Epidemiology and survival of idiopathic pulmonary fibrosis from national data in Canada[J]. European Respiratory Journal, 2016,48(1):187-195.

[8] Raimundo K, Chang E, Broder MS, et al. Clinical and economic burden of idiopathic pulmonary fibrosis: a retrospective cohort study[J]. BMC Pulmonary Medicine, 2016,16(1).

[9] Collard HR, Chen SY, Yeh WS, et al. Health care utilization and costs of idiopathic pulmonary fibrosis in U.S. Medicare beneficiaries aged 65 years and older[J]. Ann Am Thorac Soc, 2015,12(7):981-987.

[10]Xuan Jianwei, Lu Yongji, Ren Maodong, etc. Direct Economic Burden of Patients in ldiopathic Pulmonary Fibrosis in China[J]. China Journal of Pharmaceutical Economics,2019,14(06):9-12.

[11] Li JS, Yu XQ, Xie Y, et al. Efficacy and Safety of Traditional Chinese Medicine Treatment for Idiopathic Pulmonary Fibrosis: An Exploratory, Randomized, Double-Blinded and Placebo Controlled Trial[J]. Frontiers in Pharmacology, 2022, 13.

[12]ILD Group of Chinese Thoracic Society,ILD Committee of Chinese Association of Chest Physicians.Chinese Expert Consensus on the Diagnosis and

Treatment of Acute Exacerbation of IPF[J].National Medical Journal of China.2019,99(26):2014-2023.

[13]Ju Zhengrong. Fei Wei Theory--Treatment Experiences of Doctor Chao Enxiang on Pulmonary Fibrosis[D]. Beijing University of Chinese Medicine, 2014.

[14]Zhang Lishan, Dai Yanyan, Ren Chuanyun. Ten Methods of Professor Wu Weiping in treating Pulmonary Fibrosis[J].Chinese Journal of Information on Traditional Chinese Medicine.2008,15(4):94~95.

[15]Li Jiansheng. General Situation of ldiopathic Pulmonary Fibrosis Treated by Chinese Medicine[J].Acta Chinese Medicine.2017,32(06):929~931.

[16]Internal Medicine Branch of China Association of Chinese, Pulmonary Disease Branch of China Medical Association of Minorities, Pulmonary Disease Branch of China Association of Chinese Medicine.Medicine Syndrome Diagnostic Criteria of ldiopathic Pulmonary Fibrosis in TraditionaChinese Medicine (2019 edition)[J].Journal of Traditional Chinese Medicine.2020, 61(18):1653~1656.

[17]Bai Wenmei, Ma Hongxia, Tong Lihong, Observation of Curative Effect of YiQiHuoXueTongLuo Herbal Paste in Treatmentof 60 Cases of ldiopathic Pulmonary Fibrosis with Qi Deficiency and Blood Stasis Syndrome[J].Xinjiang Journal of Traditional Chinese Medicine. 2018, 36(06): 7-8.

[18]Yang Liu, Cheng Shufang, Zhang Shusen, etc. Kangyi Herbal Paste in Treatmentof 60 Cases of ldiopathic Pulmonary Fibrosis[J].Guangming Journal of Chinese Medicine.2015,30(07): 1449-1450.

[19]Zhang Shusen, Yang Liu, Dongrui.Clinical Observation on Zhuji Ointment in the Treatment of ldiopathic Pulmonary Fibrosis of lmpairment of both Qi and Yin Type[J].Chinese Medicine Modern Distance Education of China.2019, 17(23): 69-71.