标准与规范。

【编者按】 痴呆是当今威胁老年人健康的重大疾病之一,对其进行规范诊治是全世界关注的一个焦点问题。我国人口多,痴呆患者基数大,目前已有700万以上老年性痴呆患者,约占全世界总病例数的1/4,且每年约30万人加入这个行列。痴呆防治直接关系着我国的国计民生。

虽然我国痴呆的临床研究起步较晚,但近十年呈现出越来越多神经和精神科医师投身于痴呆防治的态势。通过他们的努力,不仅提高了痴呆的防治水平,也增强了民众对痴呆的防治意识。但目前我国在痴呆诊治方面仍缺乏系统认识,水平参差不齐,因此我们急需加强痴呆及相关认知障碍诊治知识的普及和规范化工作。

《中国痴呆与认知障碍诊治指南》由中华医学会神经病学分会痴呆与认知障碍学组和中国阿尔茨海默病协会组织编写。专家们参考国际最新痴呆及其相关研究成果,结合多年临床诊疗实践,以循证医学结果为依据,制定出了我国第一部痴呆与认知障碍临床诊疗指南。指南采用国际欧洲神经科学联合会(EFNS)通用编写模式,但在内容方面较国外已发表痴呆指南更为全面和贴近临床实践,指南中不仅包括痴呆概念、病史收集、神经心理评估、辅助检查、诊断标准以及治疗,还包括轻度认知功能障碍诊疗及痴呆护理和对照料者咨询等,极大增强了临床实用性和可行性。

为了让更多临床医师能系统掌握痴呆诊治知识,本杂志精选了《中国痴呆与认知障碍诊治指南》 中缩编后的痴呆诊断流程、痴呆分型及诊断标准、神经心理评估的量表选择、辅助检查及其选择、痴呆 治疗、痴呆患者护理、照料咨询及相关伦理等重要章节进行系列连载,相信对加快我国痴呆与认知障 碍诊治的规范化进程并逐渐与国际同步起到重要的推动作用。

中国痴呆与认知障碍诊治指南(一):痴呆诊断流程

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痴呆是一组综合征,病因多种,表现多样。为规 范临床对痴呆的诊断,写作组参考了国内外近期发 表的痴呆相关临床研究、荟萃分析和系统性综述,以 循证医学结果为依据,并结合我国实际情况,编写了 痴呆诊断流程指南。

本指南本着科学性、实用性和可行性对痴呆临床诊断思路、临床实践(病史、体格检查及神经心理评估)进行叙述、希望能为临床医师提供参考。

一、证据来源、分级及推荐强度

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- 1. 证据来源: 通过检索 Medline、Cochrane Library、以及 Science Direct、Ovid 和中国期刊全文数据库,获取 1998—2010 年间的痴呆相关文献。
- 2. 证据分级:根据研究的证据力度标为不同的 等级(Ⅰ、Ⅱ、Ⅲ和Ⅳ级),并依据证据级别确定证据 推荐级别(A、B、C级和专家共识),具体为: I级:有 力的前瞻性、随机、对照的临床研究,人群具有代表 性,结果评价明确可靠;或者基于以上资料的系统性 综述。可满足以下条件:(a)随机、盲法:(b)主要观 察指标明确;(c)纳入标准和排除标准明确;(d)脱 失率低,不会告成结果的偏倚:(e)明确描述人群基 线期的特征,而且基线期的特征在治疗组和对照组 匹配。Ⅱ级:前瞻性的、匹配的队列研究,人群具有 代表性,结果评价明确可靠,符合以上【级证据中 a~e点;或者一个随机、对照研究,人群具有代表 性.但不符合 a~e 中的某一条件。Ⅲ级:其他对照 研究(包括描述明确的自然病程对照研究或自身对 照研究),人群具有代表性。Ⅳ级:非对照研究,病 例分析,个案报道,专家意见。
- 3. 推荐强度: A 级(结果确定): 至少1个有说服力的 I 级证据,或者至少2个结论一致的、有说服

力的Ⅱ级证据。B级(结果很可能):至少1个有说服力的Ⅱ级证据,或大量的Ⅲ级证据。C级(结果可能):至少2个有说服力的Ⅲ级证据。专家共识:不符合上述推荐标准,但与临床治疗紧密相关的研究结论。

二、老年期痴呆临床诊断思路

- 1. 首先,根据痴呆的定义和诊断标准明确是否为痴呆:对于既往智能正常,之后出现获得性认知能力下降(记忆力障碍,并有失语、失用、失认和抽象思维或判断力中至少一项障碍),妨碍患者的社会活动或日常生活,可拟诊痴呆(建议认知功能损害最好由神经心理评估客观证实)。最后还应排除意识障碍、谵妄,排除假性痴呆(抑郁等导致)以及短暂意识混乱和智能下降(药物、毒物等导致)等后方可确立诊断。
- 2. 其次,确定痴呆类型(病因诊断):诊断为痴呆后,要结合患者认知障碍起病形式、各认知域和精神行为损害的先后顺序、病程发展特点以及既往病史和体格检查提供的线索,对痴呆的病因做出初步判断,然后选择合适的辅助检查,最终确定痴呆综合征的病因。病因学诊断步骤可分为几步(图1):(1)皮质性特征还是皮质下特征;(2)有无多发性缺血发作特征;(3)有无运动障碍;(4)有无明显的情感障碍;(5)有无脑积水。根据上述痴呆诊断步骤,可确定大多数痴呆患者的病因。各型痴呆应根据相应国际通用诊断标准进行诊断,详见本指南系列刊

痴呆 皮质性特征 皮质下特征 阿尔茨海默病 皮克病等 多发性缺血,发作特征 无明显缺血发作 多发梗塞性痴呆 运动障碍 无运动障碍 锥体外系综合征痴呆 明显情感障碍 无明显情感障碍 抑郁性痴呆综合征 帕金森病痴呆 慢性进行性舞蹈病痴呆 肝豆状核变性痴呆 脑积水 无脑积水 进行性核上性麻痹痴呆 脊髓小脑变性痴呆 脑积水痴呆 慢性意识混乱状态 代谢性疾病 中毒性疾病 脱髓鞘性疾病 其他

图 1 痴呆流程诊断鉴别

载中的诊断标准一节内容。

3. 最后,依据临床表现、日常能力受损情况、认知评估等确定痴呆的严重程度。常用临床痴呆评定量表(CDR)或总体衰退量表(GDS)做出严重程度的诊断。

三、病史询问、体格检查和神经心理评估

(一)病史

临床应重视获取知情者提供信息(由于患者本人有认知损害)。病史包括现病史和既往史,伴随疾病、家族史、职业、受教育水平等。现病史采集着重询问认知障碍的发病时间、起病形式、具体表现,进展方式(力求全面了解各认知域的损害情况),诊治经过及转归;注意了解认知障碍是否对患者有知。日常能力、自理能力产生影响;是否伴有精神行为和人格改变,精神行为与认知障碍发生的先后顺序以及精神行为的具体表现(如淡漠、抑郁、反社会行为如偷窃、幻觉等);追问可能的诱发因或事件。既往病史询问亦应详细,尤其注意询问可能导致痴呆的疾病(如脑血管病、帕金森病、外伤等)。根据现病史和既往史可初步诊断患者是否有痴呆以及初步判定痴呆的可能原因。

【推荐】

应详细采集患者的病史,在可能的情况下,除患者本人提供的病史外,尽量获得知情者提供的病史 信息【A级推荐】。

(二)体格检查

【推荐】

对所有患者都应当进行一般查 体和神经系统查体【专家共识】。

(三)神经心理评估

包括认知评估、精神行为症状的评估、日常能力评估、伴随疾病评估,在痴呆诊断过程中占重要地位。以下分别叙述:

1. 认知评估:包括总体认知功能评估、记忆力、 执行功能、语言、运用、视空间和结构能力等。通过 对认知评估为痴呆诊断提供客观证据(如记忆障 碍、执行功能障碍等);帮助判断痴呆的类型及原 因:诵讨定期评估,评价认知障碍与痴呆的治疗效果 及转归:(1)总体认知功能:研究发现:简易精神状 态检查(MMSE),对识别正常老人和痴呆有较好的 价值,但对区别 MCI 和痴呆作用有限[1](I 级证 据)。蒙特利尔认知评估(MoCA)可用于区别正常 老人和轻度 AD,但该量表在国内尚缺乏公认的年 龄和文化程度校正的常模。Mattis 痴呆评估量表 (DRS),对额叶-皮质下痴呆敏感[24],可识别帕金森 病痴呆(敏感度和特异度分别为92.65%和 91.4%)^[4](Ⅱ级证据),可正确区别 85% 的 AD 和 76%的 FTD 患者^[5](Ⅱ级证据)。阿尔茨海默病评 估量表认知部分(ADAS-cog)常用于轻中度 AD 的 疗效评估(通常将改善4分作为临床上药物显效的 判断标准)[6-7]。血管性痴呆认知评估量表(VaDAScog)对脑白质病变具有更好的识别能力[8](I 级证 据),但该量表应用尚不广泛。(2)记忆力:不同类 型痴呆记忆力受损各有其特点。AD 患者情景记忆 障碍重,而 VaD 和皮质下性痴呆(DLB、PDD等)主 要累及信息的提取[9-12],语义性痴呆病程初期可出 现语义记忆障碍,AD 患者也可出现(晚于情景记忆 障碍)。临床工作中往往通过词语学习和延迟回忆 测验对情景记忆进行检查。研究发现应用词语延迟 回忆能够鉴别抑郁和痴呆[13](【级证据),可区别轻 度 AD 和正常老人(正确率 90% 以上)[14](Ⅱ级证 据),可预测临床前 AD 转化成 AD[15-16](I 级证 据)。Mattis 痴呆评定量表可区别 AD 和 PDD(准确 率为86%)[11](Ⅱ级证据)。韦氏记忆量表可区别 AD 和 VaD(准确率 80.6%)^[12](Ⅱ级证据),并可区 别 AD 和 DLB(敏感度和特异度为 81% 和 76%)[17] (Ⅱ级证据)。临床常用语言流畅性等评估语义记 忆障碍。(3)执行功能:执行功能异常见于多种痴 呆,其中额叶皮质下性痴呆,包括 VaD、额颞叶痴呆 (FTD)、路易体痴呆(DLB)和帕金森病痴呆(PDD) 等损害相对更突出。研究发现 PDD 和 DLB 的注意 执行功能损害突出[17:22], 患者的 DRS 量表中启动与 保持因子得分低于 AD 患者[19-21], 韦氏成人智力量

表的数字符号亚测验和连线测验也较 AD 患者 差[17,22]。其他评估方法侧重执行功能不同环节,如 韦氏成人智力量表相似性亚测验侧重抽象概括能 力、连线测验 A 侧重信息处理速度等, 临床可根据 评估侧重点的不同选用。(4)语言: AD 患者早期出 现找词困难、语言空洞,最后发展为缄默[23]。 VaD 患者可出现各种类型的失语。语义性痴呆的国际通 用诊断标准中,语言障碍是诊断的核心特征[24]。临 床上.区别语义性痴呆和 AD 患者可选用波士顿命 名测验联合 MMSE,正确率 96.3% [25](Ⅲ级证据)。 区别语义性痴呆、额颞叶痴呆和 AD 可选择波士顿 命名测验联合其他检查,总正确率为89.2% [26](Ⅲ 级证据)。国内汉语失语成套测验(ABC)应用也比 较广泛。此外 MMSE、ADAS-cog、韦氏智力量表中评 估语言的项目也可选用。(5)运用:研究发现皮质 性痴呆和皮质下性痴呆均存在失用[27],有失用的 AD 患者病情发展更快^[28]。皮质基底节变性(CBD) 以失用为突出症状[29-30],患者可出现各种类型的失 用,临床评估主要让患者做一些动作或模仿一些动 作,或者使用一些道具来完成某些操作和指令进行 评价。(6)视空间和结构能力:额颞叶痴呆的视空 间技能损害较轻。AD 患者,其早期即可出现视空 间功能障碍(表现不能准确地临摹立体图形,不能 正确的按照图示组装积木)。至中期,患者临摹简 单的二维图形错误,生活中不能判断物品的确切位 置。损害最重的为路易体痴呆。在路易体痴呆的诊 断中,显著的注意力、执行功能和视空间能力损害是 核心特征[31]。研究发现用临摹交叉五边形测验可 区别路易体痴呆患者与 AD 患者(敏感度 70%~ 88%, 特异度为 57% ~ 59%) [32-33] (分别为 Ⅱ 和 Ⅲ 级证据)。用积木测验联合记忆测验、词语流畅性测 验可区别额颞叶痴呆和 AD[34](Ⅲ级证据)。此外临 床评价视空间结构技能还包括画钟测验、Rev-Osterreith 复杂图形测验和重叠图形测试等。

2. 精神行为症状的评估:痴呆的精神行为症状 (BPSD) 几乎在所有痴呆患者病程的某一阶段都会 出现^[35]。精神行为症状在不同的痴呆类型中表现不同,如人格改变和行为异常是 FTD 最早、最突出的症状,而且贯穿于疾病的全程,是该病的核心特征之一^[24,36]。AD 患者淡漠、抑郁和焦虑出现较早,而 幻觉和激越出现在病程的中晚期。反复发作的视幻觉是 DLB 的核心特征之一^[31]。临床上常通过对精神行为症状的评估鉴别痴呆类型:额叶行为问卷区别 FTD 和其他类型痴呆(AD、VaD)敏感度和特异度

分别为97%和95%[37](Ⅲ级证据),神经精神问卷 有助于区别 FTD 和 AD[38](Ⅱ级证据)。刻板行为、 饮食习惯改变、社会规范意识丧失区别 FTD 和 AD 的准确率为71.4% [39](Ⅲ级证据)。视幻觉对区别 DLB 和 AD 特异度 99% [40] (Ⅱ 级证据)。视幻觉诊 断路易体病(包括 DLB 和 PD)的特异度达 92.9%, 但敏感度偏低(51.7%)[41](Ⅱ级证据)。视幻觉有 助于鉴别帕金森病和非路易体的帕金森综合征[41] (Ⅱ级证据)。此外,阿尔茨海默病行为病理评定量 表 (BEHAVE-AD), Cohen-Mansfield 激越问券 (CMAI)和神经精神症状问卷(NPI)在临床 BPSD 评估中亦常应用。在评定抑郁情绪时应该询问抑郁 的核心症状(悲观忧愁、无用感、绝望感、希望死亡 或自杀等),而不要依赖于体重减轻、食欲改变、睡 眠障碍和精神迟缓。注意肺部或泌尿系感染,肝肾 疾病等伴随的躯体疾病可能引起或加重 BPSD。

- 3. 日常能力评估:日常能力减退是痴呆的核心症状之一,是诊断痴呆的必须条件^[42],日常能力评估能够帮助痴呆诊断的建立。在临床评估中,常用阿尔茨海默病协作研究日常能力量表(ADCS-ADL)、Lawton 工具性日常能力量表(instrumental ADL scale of Lawton)、社会功能问卷(FAQ)等。日常能力评估更适用于农村及低教育程度人群中痴呆的筛查^[43](I级证据)。FAQ和工具性日常活动能力量表适用于较轻患者的评价。重度痴呆患者应该另选相应的评定量表,如阿尔茨海默病协作研究重度患者日常能力量表(ADCS-ADL-severe)。此外还有进行性恶化评分(PDS)和痴呆残疾评估(DAD)等量表,可根据情况选用。
- 4. 伴随疾病的评估:共病在老年期痴呆患者中尤为常见,往往会加重患者的认知及其他功能障碍(N级证据),如糖尿病患者的血糖水平与其认知功能密切相关^[44]。要注意检查患者是否伴有高血压病、糖尿病、心血管病、肾脏疾病等全身性内科疾病。伴有相关疾病要进行控制,如果发现既往有脑血管病病史或神经系统体检及神经影像学检查发现有脑血管病证据的患者,应注意二级预防,血压控制的达标及小剂量阿司匹林的运用有利于防止认知功能下降^[45]。随着患者痴呆程度的加重,营养不良的发生率增高,可应用简易营养评估表(MNA-SF)、皇家医学院营养筛查系统(INSYST)及时评价,因需要体重指数,适合有运动障碍的患者使用^[4647]。伴有 BPSD 的患者,注意区分精神症状是一种临床

症状(如 DLB 患者以视幻觉为突出临床特征)还是治疗药物引发的不良反应。临床上常用抑郁自评量表(SDS)和汉密尔顿抑郁量表(HAMD)对痴呆早期的淡漠、焦虑及抑郁进行评估。常用 AD 病理性行为评估量表(BEHAVE-AD)和神经精神问卷(NPI)等对中晚期痴呆出现的幻觉、妄想及激惹等病理性行为进行测评。

【推荐】

在痴呆诊断过程中应对认知、精神行为、日常能力和伴随疾病进行全面评估【A级推荐】。

评价认知时应尽可能全面,应包括总体认知功能、记忆力、执行功能、语言、运用、视空间和结构能力等[A级推荐]。

应尽可能对所有痴呆患者评估是否存在共病, 并做相应的处理【专家共识】。

志谢 本指南由中华医学会神经病学分会痴呆与认知障碍学组和中国阿尔茨海默病协会(ADC)组织撰写

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中国痴呆与认知障碍诊治指南(一):痴呆诊断流程



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