中国肾上腺衰老诊疗专家共识(2025 版)

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【摘要】 肾上腺衰老(adrenal aging)是指随年龄增长而出现的肾上腺结构与功能的渐进性改变,尤其表现为肾上腺皮质分泌谱的重塑:脱氢表雄酮(DHEA)及其硫酸酯(DHEAS)显著下降,醛固酮平均水平下降而皮质醇总体维持相对稳定或轻度升高,昼夜节律与分泌脉冲振幅减弱。这些激素改变与肌少症/骨量减少、代谢综合征、血压异常、免疫功能下降、情绪与认知障碍、衰弱与康复能力下降等多系统不良结局存在关联,提示肾上腺衰老是值得重视的临床问题。然而,迄今国内尚无关于“肾上腺衰老/肾上腺皮质衰老”的统一共识或指南。本共识在系统检索证据基础上,结合我国临床实践,首次提出肾上腺衰老的定义、诊断评估路径、实验室与影像学检测建议、鉴别诊断要点、分层管理与干预策略及随访规范,旨在规范我国肾上腺衰老的临床诊治与科研实践,促进健康老龄化。

【关键词】 肾上腺;衰老;肾上腺皮质;皮质醇;醛固酮;昼夜节律;衰弱
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Expert consensus on the diagnosis and management of adrenal aging in China (2025 **Edition**)

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【**Abstract**】 Adrenal aging refers to the progressive structural and functional changes of the adrenal glands that occur with advancing age, particularly characterized by a remodeling of the adrenal cortical secretory profile with a marked decline in dehydroepiandrosterone (DHEA) and its sulfate (DHEAS), a decrease in average aldosterone levels, and overall cortisol levels that remain relatively stable or are mildly elevated, with attenuation of circadian rhythms and secretory pulse amplitudes. These hormonal changes are associated with adverse outcomes across multiple systems, including sarcopenia/osteopenia, metabolic syndrome, blood pressure abnormalities, impaired immune function, mood and cognitive disorders, frailty, and reduced rehabilitation capacity, indicating that adrenal aging is a clinical issue warranting attention. However, there has been no unified national consensus or guideline in China on adrenal aging/adrenocortical aging to date. Based on a systematic review of the evidence and aligned with domestic clinical practice, this consensus for the first time proposes the definition of adrenal aging,

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pathways for diagnostic evaluation, recommendations for laboratory and imaging tests, key points for differential diagnosis, stratified management and intervention strategies, and follow-up standards, with the goal of standardizing clinical diagnosis, treatment, and research practice related to adrenal aging in China and promoting healthy aging.

【Key words】 adrenal gland; aging; adrenal cortex; cortisol; aldosterone; circadian rhythm; frailty

【推荐等级说明】

1A: 基于高水平证据(严格的 meta 分析或随机对照研究); 专家组一致

1B: 基于高水平证据; 专家组小争议

2A: 基于中低水平证据(前瞻性/回顾性队列、病例-对照、多中心观察等); 专家组一致

2B: 基于中低水平证据; 专家组少量争议

3: 主要基于专家共识或机制研究; 存在较大争议

随着人口老龄化的加速,越来越多的证据显示,肾上腺在老年期呈现特异的结构与功能变化,包括脱氢表雄酮(DHEA)及其硫酸酯(DHEAS)水平随年龄增长而显著下降、皮质醇昼夜节律与分泌脉冲振幅减弱,以及肾上腺皮质带区异质性改变等。这些变化与肌少症、骨量减少、代谢异常、免疫功能下降及脆弱状态等多系统结局显著相关,提示“肾上腺皮质衰老(adrenal cortex aging/senescence)”作为一种值得临床识别与分层管理的老年相关状态,具有潜在的临床意义[1]。需要强调的是,尽管分子层面的改变可能在中年阶段已逐步出现,本共识的诊断与管理聚焦于≥60 岁人群及具有相应表型或高危因素者,避免因诊断不明导致过度诊治。

2025 年我国团队发表的多组织人类蛋白质组研究,基于覆盖 13 种组织的“蛋白质组衰老时钟”,揭示了器官衰老的显著异质性与动态特征。深度分析发现,30 岁左右为衰老轨迹的初始分水岭——肾上腺组织率先呈现衰老特征,提示内分泌稳态失衡或为早期驱动力[2]。上述发现为理解器官层面的时序性与易感性提供了重要参照。

国际老年相关病理分类联盟(ICCARP)已提出老年相关病理的判定标准[3],并由内分泌与代谢工作组在 2025 年的观点性文章中,论证“肾上腺皮质衰老/腺皮质老年性功能下降”可作为老年相关病理的候选[4]。目前该议题处于证据评估与学术讨论阶段,尚无最终分类结论。因此,本共识以“工作诊断”与“风险分层管理”为导向,优先遵循既有内分泌指南与方法学规范,在充分排除可逆干扰与相关内分泌疾病的前提下,审慎解读激素学改变,并以改善与肾上腺衰老相关的功能结局为主要临床目标。国内尚无针对肾上腺衰老的共识或指南,临床实践中存在认识不足、评估不规范、干预不一致的问题。本共识旨在提出中国特色、可操作的肾上腺衰老的定义、检测、诊断、鉴别、管理与随访建议,填补空白。

1　肾上腺衰老的概念与发生率

1.1　定义　肾上腺衰老(狭义为“肾上腺皮质衰老”)是随年龄增长出现的肾上腺激素合成与分泌的年龄相关性改变,符合“老年相关病理”三个标准: 随年龄发展/进展; 与功能下降相关或导致功能下降; 有人类研究证据支持(2A)[1, 5]。典型激素谱: DHEA/DHEAS 显著下降(高峰期的 10%~20%,约 70 岁时),醛固酮下降(为人群平均趋势; 个体差异明显,受盐摄入、体位、肾功能与药物影响显著; 老年期原发性醛固酮增多症检出率上升与该趋势并存),皮质醇日均水平轻度升高或维持、昼夜振幅与脉冲减弱(2A)[6-14]。

共识 1:

建议在临床与研究中采用“肾上腺(皮质)衰老”作为实体概念,区分于“肾上腺功能不全/库欣综合征”等疾病(2A)。

1.2　流行病学与人群特征

1.2.1　生理性趋势: 第二至第三个十年(约 20~30 岁) DHEAS 达到峰值,随后呈年龄依赖性下降; 男性 DHEAS 水平高于女性但下降趋势一致(1A)[7, 10, 15]。

1.2.2　区域特异性: 灵长类单核转录组证据显示网状带(ZR)对衰老最敏感,表现为硫转移酶 2A1(SULT2A1)显著下调、脂质代谢紊乱、衰老标志物累积; 球状带(ZG)与束状带(ZF)亦有不同程度改变(2A)[16]。

1.2.3　患病负担: 肾上腺内分泌稳态丧失与肌少症、骨量减少、代谢异常、免疫下降、衰弱等相关(2A)[17-20]。

共识 2:

肾上腺衰老具有带状区域易感性与激素谱的“区域特异性重塑”,临床评估应关注 ZR 功能标志物(DHEAS)与昼夜节律(2A)。

2　生理与病理改变

2.1　分子/细胞层面　ZR 细胞出现衰老相关表型[细胞周期蛋白依赖性激酶抑制因子 1A(p21Cip1)、非转移性黑色素瘤糖蛋白 B(GPNMB)、脂褐素沉积、聚集体/β 淀粉样蛋白累积],胆固醇摄取与类固醇合成功能下降[低密度脂蛋白受体(LDLR)下调、SULT2A1 下调](2A)[16, 21-22]。

2.2　下丘脑-垂体-肾上腺(HPA)轴　HPA 轴是人体一个关键的神经内分泌系统,肾上腺衰老的患者 HPA 轴负反馈可能减弱,皮质醇昼夜节律变浅;伴有肾素-血管紧张素-醛固酮系统(RAAS)功能衰减与醛固酮合成细胞簇改变。该变化受共病与药物强烈影响,个体差异大,临床解读需结合表型与排除因素。该结论为趋势性观察,研究间存在异质性,需结合睡眠、情绪、药物等因素个体化解读(2B)[1, 8, 11, 13, 23-24]。

共识 3:

肾上腺衰老的核心机制包括胆固醇基质摄取与雄激素硫酸化通路受损,解释 DHEA/DHEAS 优先下降(2A)。

3　临床意义与高危人群

3.1　关联结局　情绪与认知障碍、睡眠紊乱、体成分异常(肌肉减少/脂肪分布改变)、骨量减少/骨折风险、血压调控异常、胰岛素抵抗/糖脂代谢异常、免疫功能下降与感染易感、体力与康复能力下降(2A)[1, 11, 13, 18-20, 25-35]。

3.2　高危人群　≥60 岁(≥65 岁风险更高)者,绝经后女性,衰弱与多病共存者,心血管代谢疾病与骨质疏松患者,慢性高血压、睡眠障碍、久坐者,长期/反复系统性糖皮质激素暴露后老年人(区分药源性抑制)。轮班/倒班、抑郁/焦虑、阻塞性睡眠呼吸暂停、慢性疼痛/阿片类使用等可影响皮质醇节律与 DHEAS,应优先识别与处理此类人群(2B)[9-10, 27, 36-41]。

共识 4:

对≥65 岁且合并衰弱、骨量减少、反复感染或代谢综合征/血压异常的患者,建议纳入肾上腺衰老评估(2A)。

4　评估与诊断路径(流程图)

本共识评估与诊断路径见文后流程图(第一、第二部分)。第一部分用于识别是否属于需评估的目标人群:具备高危特征或相关临床表现者进入下一步评估;不具备者以健康教育与常规随访为主,必要时结合临床变化重评。第二部分强调在进入“肾上腺衰老”评估前,应优先识别并分流可能存在的肾上腺相关疾病或其他需专病处理的情况;一旦提示,应转入相应专病诊疗路径而不进入本流程。完成分流后,再按以下分步评估完成基础检查、昼夜节律/动态检测及影像与相关功能评估,为后续分层干预与随访提供依据。

4.1　评估对象　有上述高危特征或相关临床表现者;老年综合评估(CGA)中出现衰弱/体成分异常/情绪认知问题者(2A)[1, 11, 42]。无相关临床提示者,可给予健康教育并常规随访,建议 12~24 个月或临床情况变化时重评。

4.2　评估步骤　初始评估时应首先识别是否存在需优先排除并转入专病路径的线索(流程图第二部分),包括但不限于:提示库欣综合征或隐匿性皮质醇增多的典型体征和(或)检验异常,提示肾上腺功能不全的临床表现或激素异常,提示原发性醛固酮增多症的临床与筛查结果,或影像学提示肾上腺占位/偶发瘤等。存在上述任一情形者,应优先按相应指南/规范进一步诊治,无明确分流指征者再进入以下分步评估。

4.2.1　病史与体格检查:年龄、应激与睡眠、药物(糖皮质激素/阿片类/抗癫痫药等)、合并症、肿瘤史;体格检查:血压体位性变化、肌力、体成分、皮肤毛发[1, 11, 36, 43-44]。

4.2.2　基础实验室指标(清晨空腹,08:00±30 min):DHEAS 与 DHEA[10, 45-48];皮质醇(总皮质醇,必要时测游离皮质醇)及促肾上腺皮质激素(ACTH)(口服雌激素可升高皮质醇结合球蛋白致总皮质醇假高,优先使用游离或唾液测定)[49-52];电解质(Na^+/K^+)、血浆肾素活性(PRA)或血浆肾素浓度(PRC)与醛固酮(必要时体位标准化)[53-55];25 羟维生素 D、甲状腺功能、性激素谱(绝经后女性/男性)[56-57]。

4.2.3　昼夜节律与动态:(1)晚间(23:00)唾液皮质醇或午夜血清皮质醇,若怀疑节律减弱或隐匿性过多(判定阈值依赖方法学与实验室参考标准,采用本实验室经验证的界值)[6, 58-60]。(2)24 h 尿游离皮质醇(用于排除库欣综合征;注意老年人肾功能影响,轻中度肾功能受损可致尿游离皮质醇假低,此情形下优先

采用深夜/午夜唾液或血清皮质醇)[6, 58-60]。(3) 可参考 DHEA 昼夜节律但以 DHEAS 为主(DHEA 存在日内变动,DHEAS 基本无明显昼夜节律)[10, 45-48]。

4.2.4　影像与其他:肾上腺 CT(如怀疑肿瘤/偶发瘤或激素异常无法解释)[61];骨密度、身体成分分析、血管评估(根据临床)[62-63]。

综合病史体征、基础实验室、昼夜节律/动态检测及必要影像与相关功能评估结果,在排除需专病处理的明确内分泌疾病及主要干扰因素后,判定是否达到"肾上腺衰老"诊断或高度疑似,并据此进入后续分层干预与随访路径。

共识 5:

DHEAS 是反映 ZR 功能与肾上腺衰老最稳健、可及的生物标志物,推荐作为首选化验指标,并结合年龄-性别分层解释(1B)。

共识 6:

评估应关注皮质醇水平与昼夜节律的"质量",而非单点水平,老年人群优先采用唾液/午夜采样等无创方法(2A)。

4.3　建议的工作诊断标准　(1) 基本条件:年龄≥60 岁;(2) 激素学特征(满足其二):①采用本机构年龄/性别分层参考区间或 Z 分数评估 DHEAS,DHEAS 低于同年龄/性别参考区间的下三分位或 Z 分数<-1,若缺乏本地参考区间,优先使用同地域/同方法建立的外部参考,并在报告中给出 Z 分数与分位点[64-67];② 清晨总皮质醇正常或偏高,且晚间唾液皮质醇相对升高或昼夜差值减小(同一实验室/方法学优先;需排除轮班/倒班、显著睡眠不足、重度抑郁/焦虑急性期、急性躯体疾病、显著肥胖、酒精滥用及相关药物干扰;如果存在异常,建议用相同方法重测确认)[17, 68];③血浆肾素-醛固酮轴提示醛固酮水平较低(建议在钠摄入与体位标准化、停用主要干扰药物的窗口期后解读,如无法实现,仅作'支持性线索'而非诊断依据);(3) 排除:原发/继发性肾上腺功能不全、库欣综合征、显性原醛、药源性激素影响、活动性严重系统疾病[69-70]。

分级:可按激素异常程度与临床表型(衰弱、骨量、代谢、认知/情绪)分为轻/中/重度用于管理(2B)[1, 6, 11, 58-60, 69-70]。

共识 7:

鉴于目前缺乏统一金标准,建议以"操作性工作诊断"指导分层管理与研究,同时强调排除明确内分泌疾病(2B)。

5　实验室与检测方法

5.1　DHEAS　日内稳定,优先;注意年龄、性别、实验室方法差异,建议机构建立本地参考区间或采用 Z 分数(1B)[71-72]。

5.2　皮质醇　清晨/晚间唾液或血清,重视节律性,唾液皮质醇优先,注意外源性类固醇(氢化可的松乳膏)/口腔污染干扰;24 h 尿游离皮质醇用于排除库欣综合征;口服雌激素可升高皮质醇结合球蛋白导致总皮质醇假高,优先使用游离或唾液测定;优先采用深夜唾液测定皮质醇(1B)[52, 73]。

5.3　外源性补充干扰　检测前停用含 DHEA/DHEAS 的保健品或药物至少 72 h(条件允许可延长至 1 周),以避免 DHEAS/类固醇谱假性升高。

5.4　RAAS　采血体位与时间标准化,评估醛固酮变化趋势;注意利尿剂、血管紧张素转换酶抑制剂/血管紧张素Ⅱ受体拮抗剂、β 受体阻滞剂影响(在条件允许时,参照指南停用主要干扰药物至建议的窗口期后再判读血浆醛固酮与肾素活性比(ARR)(2A)[74-78]。

5.5　动态试验　一般不推荐常规 ACTH 兴奋试验用于"衰老"评估,仅在鉴别肾上腺功能不全时使用(2A)[36, 79]。

5.6　影像　非增强 CT 可筛查偶发瘤并评估脂肪含量;MRI/功能影像检查按需实施(2B)[61]。

共识 8:

检测结果解读需严格控制前分析变量(采样时间、体位、药物影响),建议在报告中注明参考区间的年龄/性别分层(1B)。

6　鉴别诊断

与以下情况进行鉴别诊断,包括:原发/继发性肾上腺功能不全[36, 80];库欣综合征/轻型皮质醇增多症(MACS)[50, 61];原发性醛固酮增多症与药物影响的 RAAS 改变[54];肾上腺偶发瘤(含分泌性)与转移瘤[61];药源性/系统性疾病导致的激素改变[37, 54]。

共识 9:

在作出"肾上腺衰老"判断前,需系统排除肾上腺功能不全、库欣综合征与分泌性肿瘤等可治疗性疾病(1A)。

7　管理与干预

7.1　总体原则　目标:改善与肾上腺衰老相关的多系统功能与生活质量,降低衰弱、跌倒、骨折、感染与代谢

并发症风险(2A)[81-85]。对象:完成第 4 节评估、排除需转入专病路径的情况后,确诊或高度疑似肾上腺衰老者进入本节规范管理与干预。路径:生活方式为基础,合并症管理为核心,药物干预个体化,监测安全性与结局[81, 84, 86]。

7.2　生活方式与综合干预

7.2.1　运动:阻力+耐力+平衡训练(每周≥150 min 中等强度;阻力每周≥2 次),促进肌力、骨量、代谢(1A)[81-83, 85, 87]。

7.2.2　睡眠与昼夜节律:固定作息、光照管理、避免夜间强光与兴奋剂,优化皮质醇节律(2A)[88-91]。

7.2.3　营养:充足蛋白[1.0~1.2 g/(kg·d),合并疾病者个体化管理]、维生素 D 与钙、健康脂肪酸(以单/多不饱和为主);限制精制糖与反式脂肪酸摄入,倡导地中海式饮食(1B)[57, 86, 92-95]。

7.2.4　压力管理:认知行为疗法、正念/放松训练、社会支持(2A)[90, 96-97]。

7.2.5　药物审查:尽量减少长期系统性糖皮质激素与干扰 RAAS/皮质醇节律药物的非必要使用(2A)[37, 70, 74]。

共识 10:

建议所有确诊或高度疑似肾上腺衰老者实施规范的运动-营养-睡眠-减压"四联"基础干预(1B)。

7.3　药物与营养补充(谨慎选择)

7.3.1　DHEA 补充:研究显示,在部分人群(尤其绝经后女性或肾上腺源性低雄激素者)中补充 DHEA 可能改善性功能、情绪、骨代谢与血管顺应性,但整体证据不一致,长期结局与安全性(脂质改变、痤疮/多毛、激素敏感肿瘤风险)需警惕。禁忌证包括:激素敏感肿瘤、前列腺恶性肿瘤活动期、严重痤疮/雄激素性脱发倾向等。补充期间须监测血脂、肝功能、性激素结合球蛋白、雄激素谱、前列腺相关指标等。同时须警惕非处方渠道质量差异与不同批次间变异风险。我国尚无广泛规范适应证(2B)[19, 98-101]。

7.3.2　维生素 D/钙/蛋白补充:按骨健康与肌少症标准实施(1A)[57, 86, 92-95, 102]。

7.3.3　其他:目前无高质量证据支持常规使用适应原、褪黑素等可以改善肾上腺衰老结局,可按共病个体化管理(3)[89, 103-104]。

共识 11:

不建议将 DHEA 作为普遍一线干预;可在严格筛选(低 DHEAS、症状与风险-获益评估、排除禁忌证)与知情同意下短期试用,并监测不良反应与激素水平(2B)。

7.4　合并症管理

7.4.1　骨健康:按骨质疏松指南评估与干预(双膦酸盐/地舒单抗等);配合阻力训练(1A)[57, 85-86, 93-95, 102]。

7.4.2　代谢与血压:控制体重、血糖、血脂与血压;优先采用不干扰 RAAS/皮质醇节律的方案(2A)[37, 70, 74, 84]。

7.4.3　认知/情绪:筛查抑郁、焦虑与轻度认知障碍,纳入规范管理(2A)[96-97]。

共识 12:

强化合并症规范管理可显著改善与肾上腺衰老相关的功能结局(2A)。

8　随访与转诊

8.1　随访频率　基础干预后一般建议 3~6 个月复评;对轻症且指标/症状稳定者亦可 6~12 个月复评,稳定后每 6~12 个月随访;内容包括症状量表、体成分/骨密度、DHEAS 与皮质醇节律、血压、代谢指标(2A)[50, 61, 81, 94]。

8.2　转诊指征　出现可疑库欣综合征/肾上腺功能不全表现、进行性或异常激素改变、影像学提示肿瘤或增大、难治合并症(1A)[36-37, 42, 50, 61, 74]。

共识 13:

建议建立老年内分泌-老年医学-营养康复-心理医学多学科协作随访体系(2A)。

9　特殊人群

9.1　绝经后女性　肾上腺为主要性激素前体来源,更易受 DHEAS 下降的影响;评估与干预应关注骨与情绪/性健康(2A)[19, 98]。

9.2　高龄男性　与性腺轴共同衰退,关注肌少症、性功能与心血管代谢风险(2A)。

9.3　慢病与多药共用者　重视药物相互作用(利尿剂、血管紧张素转换酶抑制剂/血管紧张素Ⅱ受体拮抗剂、糖皮质激素等)对评估与治疗的影响(2A)[36-37, 74]。

共识 14:

特殊人群评估需结合性腺轴与药物因素,制定差异化目标与策略(2A)。

10　科研与未满足需求

10.1　制定标准　构建中国人群年龄/性别分层的 DHEAS、皮质醇日节律本地参考区间与判定阈值(1A-实践建议)[94]。

10.2　规范诊断　验证“工作诊断标准”的预测效度与结局相关性；开展干预研究（运动、睡眠、DHEA 等）与长期安全性评价（2A）[19, 81]。

10.3　机制研究　基于单细胞/空间组学，聚焦 LDLR-胆固醇摄取、SULT2A1 调控、带状细胞谱系分化与免疫微环境改变；探索潜在药物靶点（2A）[16,22]。

共识 15：

呼吁建立全国多中心队列与生物样本库，推动从机制到临床的转化研究（2A）。

11　结语

肾上腺衰老是一个全新的、尚未在我国形成指南共识但临床意义重大的概念。其核心表型为“ZR 主导的激素谱衰退（DHEAS 降低）+节律质量下降”，并与多系统功能受损密切相关。本共识倡导以规范的评估路径、分层管理和多学科随访，推进我国肾上腺衰老的标准化诊治与研究，服务健康老龄化国家战略。

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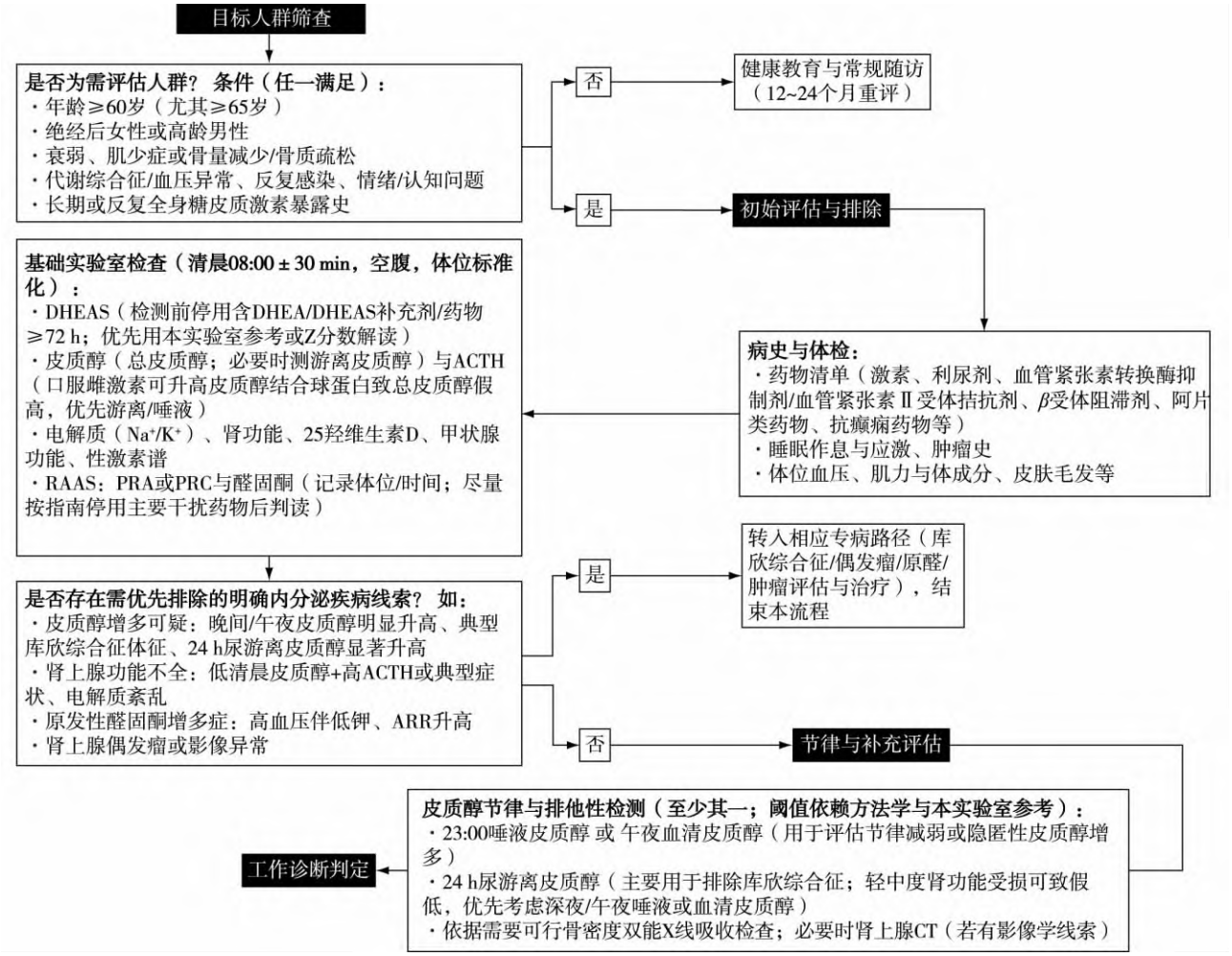
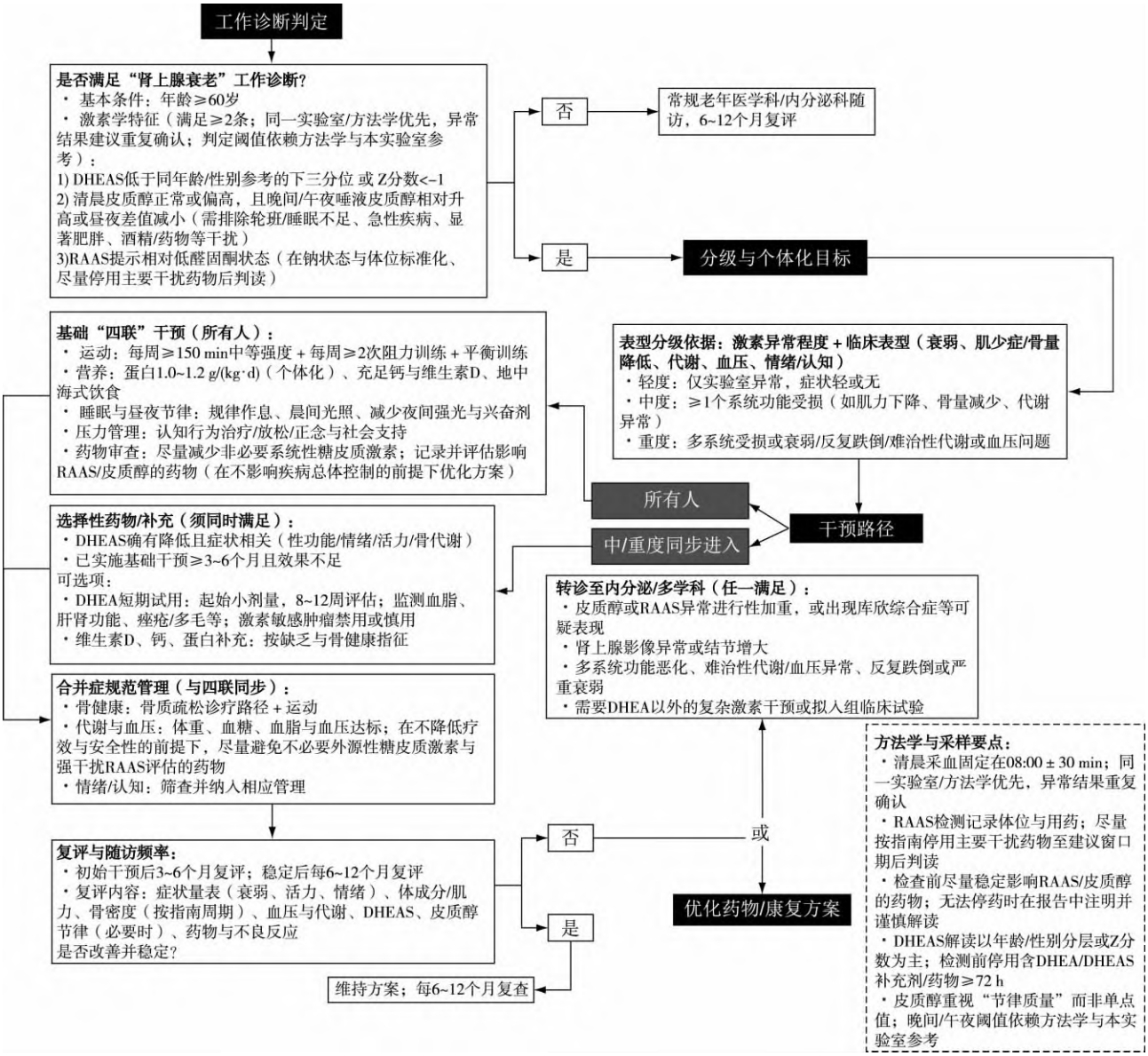
肾上腺衰老工作诊断及干预流程图(第一部分)

Flowchart for the diagnosis and intervention of adrenal aging (Part 1)



肾上腺衰老工作诊断及干预流程图(第二部分)

Flowchart for the diagnosis and intervention of adrenal aging (Part 2)



[参考文献]

[1] YIALLOURIS A, TSIOUTIS C, AGAPIDAKI E, et al. Adrenal aging and its implications on stress responsiveness in humans[J]. Front Endocrinol: Lausanne, 2019, 10: 54.

[2] DING Y, ZUO Y, ZHANG B, et al. Comprehensive human proteome profiles across a 50-year lifespan reveal aging trajectories and signatures[J]. Cell, 2025, 188(20): 5763-5784.e26.

[3] SHORT E, CALIMPORT S, BENTLEY B. Defining an ageing-related pathology, disease or syndrome: International Consensus Statement[J]. Geroscience, 2025, 47(2): 1713-1720.

[4] SHORT E, AJJAN R, BARBER T M, et al. Adrenal cortex senescence: an ageing-related pathology? [J]. J Endocrinol Invest, 2025, 48(7): 1515-1524.

[5] MAZZIOTTI G, GIUSTINA A. Glucocorticoids and the regulation of growth hormone secretion[J]. Nat Rev Endocrinol, 2013, 9(5): 265-276.

[6] ADAM E K, KUMARI M. Assessing salivary cortisol in large-scale, epidemiological research[J]. Psychoneuroendocrinology, 2009, 34(10): 1423-1436.

[7] FELDMAN H A, LONGCOPE C, DERBY C A, et al. Age trends in the level of serum testosterone and other hormones in middle-aged men: longitudinal results from the Massachusetts male aging study[J]. J Clin Endocrinol Metab, 2002,

87(2): 589-598.

[8] FERRARI E, CRAVELLO L, MUZZONI B, et al. Age-related changes of the hypothalamic-pituitary-adrenal axis: pathophysiological correlates [J]. Eur J Endocrinol, 2001, 144(4): 319-329.

[9] LABRIE F. Intracrinology [J]. Mol Cell Endocrinol, 1991, 78(3): C113-C118.

[10] ORENTREICH N, BRIND J L, RIZER R L, et al. Age changes and sex differences in serum dehydroepiandrosterone sulfate concentrations throughout adulthood [J]. J Clin Endocrinol Metab, 1984, 59(3): 551-555.

[11] VAN CAUTER E, LEPROULT R, KUPFER D J. Effects of gender and age on the levels and circadian rhythmicity of plasma cortisol [J]. J Clin Endocrinol Metab, 1996, 81(7): 2468-2473.

[12] PENG N, ZHANG Z, XIAO Y, et al. Effect of age on aldosterone-renin ratio in screening primary aldosteronism [J]. J Clin Hypertens: Greenwich, 2025, 27(3): e70014.

[13] WEIDMANN P, DE MYTTENAERE-BURSZTEIN S, MAXWELL M H, et al. Effect of aging on plasma renin and aldosterone in normal man [J]. Kidney Int, 1975, 8(5): 325-333.

[14] MA L, SONG Y, MEI M, et al. Age-related cutoffs of plasma aldosterone/renin concentration for primary aldosteronism screening [J]. Int J Endocrinol, 2018, 2018: 8647026.

[15] NAFZIGER A N, BOWLIN S J, JENKINS P L, et al. Longitudinal changes in dehydroepiandrosterone concentrations in men and women [J]. J Lab Clin Med, 1998, 131(4): 316-323.

[16] WANG Q, WANG X, LIU B, et al. Aging induces region-specific dysregulation of hormone synthesis in the primate adrenal gland [J]. Nat Aging, 2024, 4(3): 396-413.

[17] KUMARI M, SHIPLEY M, STAFFORD M, et al. Association of diurnal patterns in salivary cortisol with all-cause and cardiovascular mortality: findings from the Whitehall II study [J]. J Clin Endocrinol Metab, 2011, 96(5): 1478-1485.

[18] LUPIEN S J, DE LEON M, DE SANTI S, et al. Cortisol levels during human aging predict hippocampal atrophy and memory deficits [J]. Nat Neurosci, 1998, 1(1): 69-73.

[19] NAIR K S, RIZZA R A, O'BRIEN P, et al. DHEA in elderly women and DHEA or testosterone in elderly men [J]. N Engl J Med, 2006, 355(16): 1647-1659.

[20] OHLSSON C, LABRIE F, BARRETT-CONNOR E, et al. Low serum levels of dehydroepiandrosterone sulfate predict all-cause and cardiovascular mortality in elderly Swedish men [J]. J Clin Endocrinol Metab, 2010, 95(9): 4406-4414.

[21] LÓPEZ-OTÍN C, BLASCO M A, PARTRIDGE L, et al. The hallmarks of aging [J]. Cell, 2013, 153(6): 1194-1217.

[22] MILLER W L, AUCHUS R J. The molecular biology, biochemistry, and physiology of human steroidogenesis and its disorders [J]. Endocr Rev, 2011, 32(1): 81-151.

[23] NISHIMOTO K, NAKAGAWA K, LI D, et al. Adrenocortical zonation in humans under normal and pathological conditions [J]. J Clin Endocrinol Metab, 2010, 95(5): 2296-2305.

[24] NISHIMOTO K, TOMLINS S A, KUICK R, et al. Aldosterone-stimulating somatic gene mutations are common in normal adrenal glands [J]. Proc Natl Acad Sci USA, 2015, 112(33): E4591-E4599.

[25] BARRETT-CONNOR E, VON MÜHLEN D, LAUGHLIN G A, et al. Endogenous levels of dehydroepiandrosterone sulfate, but not other sex hormones, are associated with depressed mood in older women: the rancho bernardo study [J]. J Am Geriatr Soc, 1999, 47(6): 685-691.

[26] BRUNNER E J, HEMINGWAY H, WALKER B R, et al. Adrenocortical, autonomic, and inflammatory causes of the metabolic syndrome: nested case-control study [J]. Circulation, 2002, 106(21): 2659-2665.

[27] GREENDALE G A, EDELSTEIN S, BARRETT-CONNOR E. Endogenous sex steroids and bone mineral density in older women and men: the Rancho Bernardo Study [J]. J Bone Miner Res, 1997, 12(11): 1833-1843.

[28] HILDRETH K L, GOZANSKY W S, JANKOWSKI C M, et al. Association of serum dehydroepiandrosterone sulfate and cognition in older adults: sex steroid, inflammatory, and metabolic mechanisms [J]. Neuropsychology, 2013, 27(3): 356-363.

[29] KARLAMANGLA A S, SINGER B H, CHODOSH J, et al. Urinary cortisol excretion as a predictor of incident cognitive impairment [J]. Neurobiol Aging, 2005, 26(Suppl 1): 80-84.

[30] KHORRAM O, VU L, YEN S S. Activation of immune function by dehydroepiandrosterone (DHEA) in age-advanced men [J]. J Gerontol A Biol Sci Med Sci, 1997, 52(1): M1-M7.

[31] LENG S X, CAPPOLA A R, ANDERSEN R E, et al. Serum levels of insulin-like growth factor-I (IGF-I) and dehydroepiandrosterone sulfate (DHEA-S), and their relationships with serum interleukin-6, in the geriatric syndrome of frailty [J]. Aging Clin Exp Res, 2004, 16(2): 153-157.

[32] STRAUB R H, CUTOLO M. Involvement of the hypothalamic—pituitary—adrenal/gonadal axis and the peripheral nervous

system in rheumatoid arthritis: viewpoint based on a systemic pathogenetic role [J]. Arthritis Rheum, 2001, 44(3): 493-507.

[33] VALENTI G, FERRUCCI L, LAURETANI F, et al. Dehydroepiandrosterone sulfate and cognitive function in the elderly: the InCHIANTI Study [J]. J Endocrinol Invest, 2009, 32(9): 766-772.

[34] VGONTZAS A N, BIXLER E O, LIN H M, et al. Chronic insomnia is associated with nyctohemeral activation of the hypothalamic-pituitary-adrenal axis: clinical implications [J]. J Clin Endocrinol Metab, 2001, 86(8): 3787-3794.

[35] WOLKOWITZ O M, REUS V I, KEEBLER A, et al. Double-blind treatment of major depression with dehydroepiandrosterone [J]. Am J Psychiatry, 1999, 156(4): 646-649.

[36] BORNSTEIN S R, ALLOLIO B, ARLT W, et al. Diagnosis and treatment of primary adrenal insufficiency: an endocrine society clinical practice guideline [J]. J Clin Endocrinol Metab, 2016, 101(2): 364-389.

[37] BROERSEN L H A, PEREIRA A M, JØRGENSEN J O L, et al. Adrenal insufficiency in corticosteroids use: systematic review and meta-analysis [J]. J Clin Endocrinol Metab, 2015, 100(6): 2171-2180.

[38] FLESERIU M, HASHIM I A, KARAVITAKI N, et al. Hormonal replacement in hypopituitarism in adults: an endocrine society clinical practice guideline [J]. J Clin Endocrinol Metab, 2016, 101(11): 3888-3921.

[39] FRIED L P, TANGEN C M, WALSTON J, et al. Frailty in older adults: evidence for a phenotype [J]. J Gerontol A Biol Sci Med Sci, 2001, 56(3): M146-M156.

[40] HAMER M, STAMATAKIS E. Physical activity and risk of cardiovascular disease events: inflammatory and metabolic mechanisms [J]. Med Sci Sports Exerc, 2009, 41(6): 1206-1211.

[41] LABRIE F, BÉLANGER A, LUU-THE V, et al. DHEA and the intracrine formation of androgens and estrogens in peripheral target tissues: its role during aging [J]. Steroids, 1998, 63(5/6): 322-328.

[42] ELLIS G, GARDNER M, TSIACHRISTAS A, et al. Comprehensive geriatric assessment for older adults admitted to hospital [J]. Cochrane Database Syst Rev, 2017, 9(9): CD006211.

[43] HUSEBYE E S, PEARCE S H, KRONE N P, et al. Adrenal insufficiency [J]. Lancet, 2021, 397(10274): 613-629.

[44] JOSEPH R M, HUNTER A L, RAY D W, et al. Systemic glucocorticoid therapy and adrenal insufficiency in adults: a systematic review [J]. Semin Arthritis Rheum, 2016, 46(1): 133-141.

[45] ARLT W. Dehydroepiandrosterone and ageing [J]. Best Pract Res Clin Endocrinol Metab, 2004, 18(3): 363-380.

[46] FOSTER P A, MUELLER J W. SULFATION PATHWAYS: Insights into steroid sulfation and desulfation pathways [J]. J Mol Endocrinol, 2018, 61(2): T271-T283.

[47] NGUYEN A D, CONLEY A J. Adrenal androgens in humans and nonhuman Primates: production, zonation and regulation [J]. Endocr Dev, 2008, 13: 33-54.

[48] RABIJEWSKI M, PAPIERSKA L, BINKOWSKA M, et al. Supplementation of dehydroepiandrosterone (DHEA) in pre- and postmenopausal women - position statement of expert panel of Polish Menopause and Andropause Society [J]. Ginekol Pol, 2020, 91(9): 554-562.

[49] DE CASTRO M, MOREIRA A C. Screening and diagnosis of Cushing's syndrome [J]. Arq Bras Endocrinol Metabol, 2007, 51(8): 1191-1198.

[50] NIEMAN L K, BILLER B M K, FINDLING J W, et al. The diagnosis of Cushing's syndrome: an endocrine society clinical practice guideline [J]. J Clin Endocrinol Metab, 2008, 93(5): 1526-1540.

[51] RAFF H. Cushing's syndrome: diagnosis and surveillance using salivary cortisol [J]. Pituitary, 2012, 15(1): 64-70.

[52] RAFF H, CARROLL T. Cushing's syndrome: from physiological principles to diagnosis and clinical care [J]. J Physiol, 2015, 593(3): 493-506.

[53] AZIZAN E A B, DRAKE W M, BROWN M J. Primary aldosteronism: molecular medicine meets public health [J]. Nat Rev Nephrol, 2023, 19(12): 788-806.

[54] FUNDER J W, CAREY R M, MANTERO F, et al. The management of primary aldosteronism: case detection, diagnosis, and treatment: an endocrine society clinical practice guideline [J]. J Clin Endocrinol Metab, 2016, 101(5): 1889-1916.

[55] ROSSI G P, SECCIA T M, PESSINA A C. Primary aldosteronism - part I: prevalence, screening, and selection of cases for adrenal vein sampling [J]. J Nephrol, 2008, 21(4): 447-454.

[56] CRUZ-JENTOFT A J, BAHAT G, BAUER J, et al. Sarcopenia: revised European consensus on definition and diagnosis [J]. Age Ageing, 2019, 48(1): 16-31.

[57] SHOBACK D, ROSEN C J, BLACK D M, et al. Pharmacological management of osteoporosis in postmenopausal women: an endocrine society guideline update [J]. J Clin Endocrinol Metab, 2020, 105(3): dgaa048.

[58] CARROLL T, RAFF H, FINDLING J W. Late-night salivary cortisol for the diagnosis of Cushing syndrome: a meta-

analysis[J]. Endocr Pract, 2009, 15(4): 335-342.

[59] CASTRO M, ELIAS P C, QUIDUTE A R, et al. Out-patient screening for Cushing's syndrome: the sensitivity of the combination of circadian rhythm and overnight dexamethasone suppression salivary cortisol tests [J]. J Clin Endocrinol Metab, 1999, 84(3): 878-882.

[60] RESTITUTO P, GALOFRÉ J C, GIL M J, et al. Advantage of salivary cortisol measurements in the diagnosis of glucocorticoid related disorders [J]. Clin Biochem, 2008, 41(9): 688-692.

[61] FASSNACHT M, TSAGARAKIS S, TERZOLO M, et al. European Society of Endocrinology clinical practice guidelines on the management of adrenal incidentalomas, in collaboration with the European Network for the Study of Adrenal Tumors [J]. Eur J Endocrinol, 2023, 189(1): G1-G42.

[62] DOGRA P, ŠAMBULA L, SAINI J, et al. High prevalence of frailty in patients with adrenal adenomas and adrenocortical hormone excess: a cross-sectional multi-centre study with prospective enrolment [J]. Eur J Endocrinol, 2023, 189(3): 318-326.

[63] SCHOUSBOE J T, SHEPHERD J A, BILEZIKIAN J P, et al. Executive summary of the 2013 International Society for Clinical Densitometry Position Development Conference on bone densitometry [J]. J Clin Densitom, 2013, 16(4): 455-466.

[64] ARIBAS E, ROETERS VAN LENNEP J E, DE RIJKE Y B, et al. Sex steroids and sex steroid-binding globulin levels amongst middle-aged and elderly men and women from general population [J]. Eur J Clin Invest, 2022, 52(12): e13866.

[65] DAMGAARD-OLESEN A, JOHANNSEN T H, HOLMBOE S A, et al. Reference ranges of 17-hydroxyprogesterone, DHEA, DHEAS, androstenedione, total and free testosterone determined by TurboFlow-LC-MS/MS and associations to health markers in 304 men [J]. Clin Chim Acta, 2016, 454: 82-88.

[66] KUNZ S, WANG X, FERRARI U, et al. Age- and sex-adjusted reference intervals for steroid hormones measured by liquid chromatography-tandem mass spectrometry using a widely available kit [J]. Endocr Connect, 2023, 13(1): e230225.

[67] YOUNG D G, SKIBINSKI G, MASON J I, et al. The influence of age and gender on serum dehydroepiandrosterone sulphate (DHEA-S), IL-6, IL-6 soluble receptor (IL-6 SR) and transforming growth factor beta 1 (TGF-beta1) levels in normal healthy blood donors [J]. Clin Exp Immunol, 1999, 117(3): 476-481.

[68] KARL S, JOHAR H, LADWIG K H, et al. Dysregulated diurnal cortisol patterns are associated with cardiovascular mortality: findings from the KORA-F3 study [J]. Psychoneuroendocrinology, 2022, 141: 105753.

[69] CHAROENSRI S, AUCHUS R J. A contemporary approach to the diagnosis and management of adrenal insufficiency [J]. Endocrinol Metab, 2024, 39(1): 73-82.

[70] FLESERIU M, AUCHUS R, BANCOS I, et al. Consensus on diagnosis and management of Cushing's disease: a guideline update [J]. Lancet Diabetes Endocrinol, 2021, 9(12): 847-875.

[71] KOAL T, SCHMIEDERER D, PHAM-TUAN H, et al. Standardized LC-MS/MS based steroid hormone profile-analysis [J]. J Steroid Biochem Mol Biol, 2012, 129(3-5): 129-138.

[72] SAINI J, SALAMA B, YU K, et al. Dehydroepiandrosterone sulfate in diagnosing mild autonomous cortisol secretion and adrenal insufficiency [J]. J Endocr Soc, 2025, 9(9): bvaf136.

[73] NIEMAN L K, BILLER B M K, FINDLING J W, et al. Treatment of Cushing's syndrome: an endocrine society clinical practice guideline [J]. J Clin Endocrinol Metab, 2015, 100(8): 2807-2831.

[74] ADLER G K, STOWASSER M, CORREA R R, et al. Primary aldosteronism: an endocrine society clinical practice guideline [J]. J Clin Endocrinol Metab, 2025, 110(9): 2453-2495.

[75] CHENG J Y, WONG F C, CHOW E W, et al. Chinese normotensive and essential hypertensive reference intervals for plasma aldosterone and renin activity by liquid chromatography-tandem mass spectrometry [J]. Clin Chem Lab Med, 2022, 60(10): 1640-1647.

[76] CONSTANTINESCU G, GRUBER S, FULD S, et al. Steroidomics-based screening for primary aldosteronism: impact of antihypertensive drugs [J]. Hypertension, 2024, 81(10): 2060-2071.

[77] JĘDRUSIK P, SYMONIDES B, LEWANDOWSKI J, et al. The effect of antihypertensive medications on testing for primary aldosteronism [J]. Front Pharmacol, 2021, 12: 684111.

[78] MULATERO P, RABBIA F, MILAN A, et al. Drug effects on aldosterone/plasma renin activity ratio in primary aldosteronism [J]. Hypertension, 2002, 40(6): 897-902.

[79] MARTIN-GRACE J, DINEEN R, SHERLOCK M, et al. Adrenal insufficiency: physiology, clinical presentation and diagnostic challenges [J]. Clin Chim Acta, 2020, 505: 78-91.

[80] BANCOS I, HAHNER S, TOMLINSON J, et al. Diagnosis and management of adrenal insufficiency [J]. Lancet Diabetes Endocrinol, 2015, 3(3): 216-226.
[81] BULL F C, AL-ANSARI S S, BIDDLE S, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour [J]. Br J Sports Med, 2020, 54(24): 1451-1462.
[82] NIEMAN D C, WENTZ L M. The compelling link between physical activity and the body's defense system [J]. J Sport Health Sci, 2019, 8(3): 201-217.
[83] PIERCY K L, TROIANO R P, BALLARD R M, et al. The physical activity guidelines for Americans [J]. JAMA, 2018, 320(19): 2020-2028.
[84] SHERRINGTON C, MICHALEFF Z A, FAIRHALL N, et al. Exercise to prevent falls in older adults: an updated systematic review and meta-analysis [J]. Br J Sports Med, 2017, 51(24): 1750-1758.
[85] LIU C J, LATHAM N K. Progressive resistance strength training for improving physical function in older adults [J]. Cochrane Database Syst Rev, 2009, 2009(3): CD002759.
[86] DEUTZ N E P, BAUER J M, BARAZZONI R, et al. Protein intake and exercise for optimal muscle function with aging: recommendations from the ESPEN Expert Group [J]. Clin Nutr, 2014, 33(6): 929-936.
[87] FRAGALA M S, CADORE E L, DORGO S, et al. Resistance training for older adults: position statement from the national strength and conditioning association [J]. J Strength Cond Res, 2019, 33(8): 2019-2052.
[88] AUGER R R, BURGESS H J, EMENS J S, et al. Clinical practice guideline for the treatment of intrinsic circadian rhythm sleep-wake disorders: advanced sleep-wake phase disorder (ASWPD), delayed sleep-wake phase disorder (DSWPD), non-24-hour sleep-wake rhythm disorder (N24SWD), and irregular sleep-wake rhythm disorder (ISWRD). An update for 2015: an American Academy of Sleep Medicine clinical practice guideline [J]. J Clin Sleep Med, 2015, 11(10): 1199-1236.
[89] AULD F, MASCHAUER E L, MORRISON I, et al. Evidence for the efficacy of melatonin in the treatment of primary adult sleep disorders [J]. Sleep Med Rev, 2017, 34: 10-22.
[90] BURKE H M, DAVIS M C, OTTE C, et al. Depression and cortisol responses to psychological stress: a meta-analysis [J]. Psychoneuroendocrinology, 2005, 30(9): 846-856.
[91] O'BYRNE N A, YUEN F, BUTT W Z, et al. Sleep and circadian regulation of cortisol: a short review [J]. Curr Opin Endocr Metab Res, 2021, 18: 178-186.
[92] BAUER J, BIOLO G, CEDERHOLM T, et al. Evidence-based recommendations for optimal dietary protein intake in older people: a position paper from the PROT-AGE Study Group [J]. J Am Med Dir Assoc, 2013, 14(8): 542-559.
[93] DINU M, PAGLIAI G, CASINI A, et al. Mediterranean diet and multiple health outcomes: an umbrella review of meta-analyses of observational studies and randomised trials [J]. Eur J Clin Nutr, 2018, 72(1): 30-43.
[94] GREGSON C L, ARMSTRONG D J, AVGERINOU C, et al. The 2024 UK clinical guideline for the prevention and treatment of osteoporosis [J]. Arch Osteoporos, 2025, 20(1): 119.
[95] KANIS J A, COOPER C, RIZZOLI R, et al. European guidance for the diagnosis and management of osteoporosis in postmenopausal women [J]. Osteoporos Int, 2019, 30(1): 3-44.
[96] ANG L, LEE M S, SONG E, et al. Psychotherapeutic treatments for depression in older adults [J]. Cochrane Database Syst Rev, 2024, 11(11): CD015976.
[97] ROGERSON O, WILDING S, PRUDENZI A, et al. Effectiveness of stress management interventions to change cortisol levels: a systematic review and meta-analysis [J]. Psychoneuroendocrinology, 2024, 159: 106415.
[98] LABRIE F, LABRIE C. DHEA and intracrinology at menopause, a positive choice for evolution of the human species [J]. Climacteric, 2013, 16(2): 205-213.
[99] PANJARI M, DAVIS S R. DHEA therapy for women: effect on sexual function and wellbeing [J]. Hum Reprod Update, 2007, 13(3): 239-248.
[100] VEGUNTA S, KLING J M, KAPOOR E. Androgen therapy in women [J]. J Womens Health: Larchmt, 2020, 29(1): 57-64.
[101] VILLAREAL D T, HOLLOSZY J O. Effect of DHEA on abdominal fat and insulin action in elderly women and men: a randomized controlled trial [J]. JAMA, 2004, 292(18): 2243-2248.
[102] FINGER D, GOLTZ F R, UMPIERRE D, et al. Effects of protein supplementation in older adults undergoing resistance training: a systematic review and meta-analysis [J]. Sports Med, 2015, 45(2): 245-255.
[103] BUSCEMI N, VANDERMEER B, HOOTON N, et al. The efficacy and safety of exogenous melatonin for primary sleep disorders. A meta-analysis [J]. J Gen Intern Med, 2005, 20(12): 1151-1158.
[104] PANOSSIAN A, WIKMAN G. Evidence-based efficacy of adaptogens in fatigue, and molecular mechanisms related to their stress-protective activity [J]. Curr Clin Pharmacol, 2009, 4(3): 198-219.

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