

# 中国大动脉炎相关高血压诊治多学科专家共识

大动脉炎相关高血压诊治多学科共识中国专家组<sup>△</sup>

**【摘要】** 大动脉炎(Takayasu's arteritis, TA)是好发于亚洲国家年轻女性的原发性血管炎症性疾病,大动脉炎相关高血压(Takayasu's arteritis-related hypertension, TARTH)常见且难治性比例高,导致的心、脑、肾、大血管等靶器官不良事件发生率高,严重影响TA患者的预后,是TA患者死亡的重要原因之一。目前尚无TARTH诊治的指南或共识,为此,我们联合国内风湿免疫科、心内科、肾内科、血管外科、神经内科等相关学科专家在国内首次制定了中国TARTH诊治多学科专家共识,旨在为相关临床科室提供治疗上的指导与建议。本共识的主要观点为:(1) TARTH常见,难治性比例高,需早期识别、早期诊断、早期治疗;(2)免疫炎症介导的血管壁水肿、顺应性降低是TARTH最主要的机制;(3)TA高危人群识别:40岁以下不明原因高血压、脉搏不对称或无脉、血管杂音、颈痛、胸腹痛、炎症指标升高、不明原因肾萎缩或两侧肾脏不对称、难治性或高血压急症;(4)大动脉炎常累及四肢血管,一经诊断需进行四肢血压和踝臂指数(ankle-brachial index, ABI)测定;(5)正确掌握血压测量方法、进行家庭自测血压有助于血压的长期随访和监测、调整和评估药物的疗效;(6)大动脉炎疾病急性活动期经过内科抗炎治疗可以改善血管壁的炎症,有助于控制高血压,因此应正确识别大动脉炎疾病活动和血管慢性损伤;(7)TARTH应全面评估疾病活动度、血压分级分期以及靶器官功能,对血管受累表型进行影像学分型;(8)TARTH的治疗应以风湿免疫科为主导进行多学科合作诊疗,尽快控制炎症和积极降压治疗,实现大动脉炎和高血压“双达标”的原则;(9)TA治疗以诱导疾病缓解和维持病情持续缓解为原则,内科治疗药物包括糖皮质激素和改善病情的抗风湿药(disease-modifying anti-rheumatic drugs, DMARDs),某些药物有引起血压升高的风险,须警惕药物相关性高血压;(10)TARTH应根据受累血管的病变程度选择降压药物,兼顾脑、心、肾的灌注水平,制定个体化的目标值和降压方案;(11)钙离子拮抗剂(calcium antagonists, CCB)、血管紧张素转化酶抑制剂(angiotensin-converting enzyme inhibitors, ACEI)、血管紧张素受体拮抗剂(angiotensin receptor antagonists, ARB)、利尿剂、β受体阻滞剂这5大类药物仍是TARTH的常用降压药物,均可作为起始治疗、维持治疗以及联合治疗的选择。难治性高血压还可以选择α受体阻滞剂和中枢性降压药等;(12)TARTH外科治疗强调内科积极抗炎控制稳定的前提下由多学科团队组成的专家组共同决策,充分权衡手术的获益与风险。

**【关键词】** 大动脉炎(TA); 高血压; 共识

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## Chinese multidisciplinary recommendations on the diagnosis and treatment of Takayasu's arteritis-related hypertension (TARTH)

Chinese Multidisciplinary Expert Task Force on TARTH<sup>△</sup>

**【Abstract】** Takayasu's arteritis (TA) is a primary vascular inflammatory disease that occurs primarily in young women of Asian countries. Takayasu's arteritis-related hypertension (TARTH) is common and has a high refractory proportion, leading to a high incidence of adverse events in target organs such as heart, brain,

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kidney, and large blood vessels, which seriously affects the prognosis of TA patients. To date, there is no guideline or consensus for the diagnosis and treatment of TARH. Therefore, a multi-disciplinary expert recommendations on the diagnosis and treatment of TARH has been established by the task force including Chinese experts from rheumatology, cardiology, nephrology, vascular surgery, neurology, aims to provide treatment guidance and advice to relevant clinical departments. The keypoints of this consensus include: (1) TARH is common and has a high refractory proportion, which require early recognition, early diagnosis, and early treatment; (2) Immune inflammation-mediated vascular wall edema and reduced compliance are the primary mechanisms of TARH; (3) Identification of high-risk population in patients with TA: unobviously caused hypertension under 40 years old, asymmetry or pulseless pulse, vascular murmur, neck pain, chest and abdomen pain, elevated inflammation indicators, unknown renal atrophy, or bilateral kidney asymmetry, refractory hypertension or hypertensive emergency; (4) Arteritis often involves the blood vessels of the extremities, once diagnosed with TARH, the blood pressure of the extremities and the ankle-brachial index (ABI) must be measured; (5) Properly mastering blood pressure measurement methods and self-test blood pressure at home are helpful for long-term follow-up, monitoring and adjustment of blood pressure and evaluate the efficacy of drugs; (6) Medical anti-inflammatory treatment during acute active stage of TA can improve the inflammation of the blood vessel wall and help control hypertension. Therefore, it is necessary to correctly identify the disease activity of aortic arteritis and chronic vascular damage; (7) TARH should be comprehensively assessed disease activity, blood pressure classification and staging, function of target organ, and performed imaging classification for vascular involvement; (8) Combined treatment of TARH should be dominated by rheumatologists, and inflammation and blood pressure should be controlled as soon as possible to achieve the principle of “double-reaching” for arteritis and hypertension; (9) TA treatment is based on the principle of inducing remission and maintaining remission by using the combined strategy of glucocorticoids and disease-modifying anti-rheumatic drugs (DMARDs). Be aware of certain drugs that cause high blood pressure; (10) Antihypertensive drugs should be selected according to the degree of the involved blood vessels, taking into account the perfusion level of brain, heart and kidney, and formulating individualized target values and antihypertensive programs; (11) Calcium antagonists (CCB), angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor antagonists (ARB), diuretics, beta blockers, these five major drugs are still commonly used to lower blood pressure in TARH.  $\alpha$ -receptor blockers and central antihypertensive drugs can be used in refractory hypertension; (12) Surgical treatment of TARH emphasizes the premise of full remission of the disease and weighs the benefits and risks of surgery, so as to an expert group composed of a multidisciplinary team makes decisions.

**【Key words】** Takayasu's arteritis (TA); hypertension; recommendation

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大动脉炎(Takayasu's arteritis, TA)是一种累及主动脉及其主要分支的慢性非特异性炎症性疾病<sup>[1]</sup>,大动脉炎相关高血压(Takayasu's arteritis-related hypertension, TARH)常见,且以难治性和恶性高血压多见,发生心脑血管不良事件的风险显著增加,严重影响TA患者的预后,是TA患者死亡的

重要原因之一<sup>[2-3]</sup>。TARH临床诊治缺乏规范性,目前尚无相关的指南或共识。为此,我们全面搜索与整理文献资料,参考各相关指南和专家的意见,在国内首次制定大动脉炎相关高血压多学科专家共识,旨在为风湿免疫科、心内科、肾内科、血管外科、神经内科、心外科等相关科室提供治疗上的指导。

原发性高血压、其他继发性高血压及儿童高血压诊治不在此共识范围内。

**流行病学** 90%的TA患者在30岁以前发病<sup>[4]</sup>,女性多见,男女患病率约为1:4~9<sup>[5-6]</sup>。世界年发病率约2.6例/百万人群<sup>[1]</sup>,亚洲年发病率为1~2例/百万人群<sup>[7]</sup>,日本基于医院数据的年患病率为12.9~40例/百万人群<sup>[8-9]</sup>,我们中心统计的上海地区本地居民的患病率为7.01例/百万人群。世界范围内,TA患者中高血压发生率为32.5%~84%<sup>[10-13]</sup>,其中,亚洲国家45.3%~84%<sup>[11-12]</sup>,中国51%~84%<sup>[10-11]</sup>。TA以高血压起病者占3.9%~57.5%<sup>[13]</sup>,TA患者脑血管事件发生率为8%~20%<sup>[14-15]</sup>。复旦大学附属中山医院建立的华东地区大动脉炎(East China Takayasu arteritis, ECTA)队列中,TA相关高血压占比为33%,以高血压为首发症状起病者占16.2%,难治性高血压达52.5%,22%患者需要四联及以上降压药,血压达标率为46.3%,高血压急症占21.2%,高血压相关的心、脑、血管等不良事件发生率达32.1%,高血压患者10年死亡率为2.5%。

**定义** 高血压的诊断是在未使用降压药物的情况下,非同日多次重复测量后,诊室收缩压≥140 mmHg和/或舒张压≥90 mmHg(1 mmHg=0.133 kPa,下同);家庭自测血压收缩压≥135 mmHg和/或舒张压≥85 mmHg;动态血压24 h平均收缩压≥130 mmHg和/或舒张压≥80 mmHg,白天平均收缩压≥135 mmHg和/或舒张压≥85 mmHg,夜间平均收缩压≥120 mmHg和/或舒张压≥70 mmHg<sup>[16-17]</sup>。根据血压升高的水平对高血压进行分级,分级方法参考中国高血压防治指南(2018修订版)<sup>[17]</sup>。

TARH定义为TA患者因为血管炎症和损害引起的高血压,即大动脉炎继发性高血压<sup>[18]</sup>。

**TA相关难治性高血压:** TA患者合理并足量应用了3种或3种以上不同机制的降压药物(包括至少1种利尿剂)规范治疗4周后,诊室血压仍≥140/90 mmHg<sup>[19]</sup>。

**TA相关高血压急症:**既往称恶性高血压,是指在某些诱因作用下,血压突然和显著升高(一般超过180/120 mmHg),同时伴心、脑、肾等重要靶器官功能不全的表现。包括高血压脑病、高血压伴颅内出血(脑出血和蛛网膜下隙出血)、脑梗死、心力衰竭、急性冠状动脉综合征(不稳定型心绞痛、急性心肌梗死)、主动脉夹层、围手术期高血压、子痫前期

或子痫等。如血压显著升高但不伴急性靶器官损害则称高血压亚急症<sup>[20]</sup>。

**解剖和病理生理** TARH是在大动脉炎诊断的基础上,由免疫炎症介导的动脉炎症、血管狭窄,以及肾功能不全等引起的血压升高<sup>[3]</sup>。与高血压相关的血管病变包括肾动脉、腹主动脉、胸主动脉狭窄,主动脉扩张,主动脉瓣关闭不全等,可以单发或多发,还可以合并锁骨下动脉、颈动脉、冠状动脉等部位病变<sup>[3,18]</sup>。高血压的发生及严重程度通常与TA所累及的血管部位、数量和严重程度有关。

TARH的机制包括<sup>[3,18,21-23]</sup>:(1)免疫炎症介导的血管壁水肿、顺应性降低是TARH最主要机制;(2)主动脉-肾动脉血管狭窄导致肾脏血流量减少,从而激活肾素-血管紧张素-醛固酮系统(renin aniotension aldosterone system, RAAS),导致水钠潴留和血压升高;(3)肾脏灌注不足引起肾实质缺血、肾单位丧失引起血压升高;(4)主动脉瓣关闭不全引起收缩期高血压;(5)颈动脉病变一方面引起颈动脉窦压力感受器敏感性降低从而不能调节血压;另一方面,颈动脉狭窄引起颅脑灌注降低,导致脑缺血、缺氧,反射性激活交感神经系统,引起血压升高。

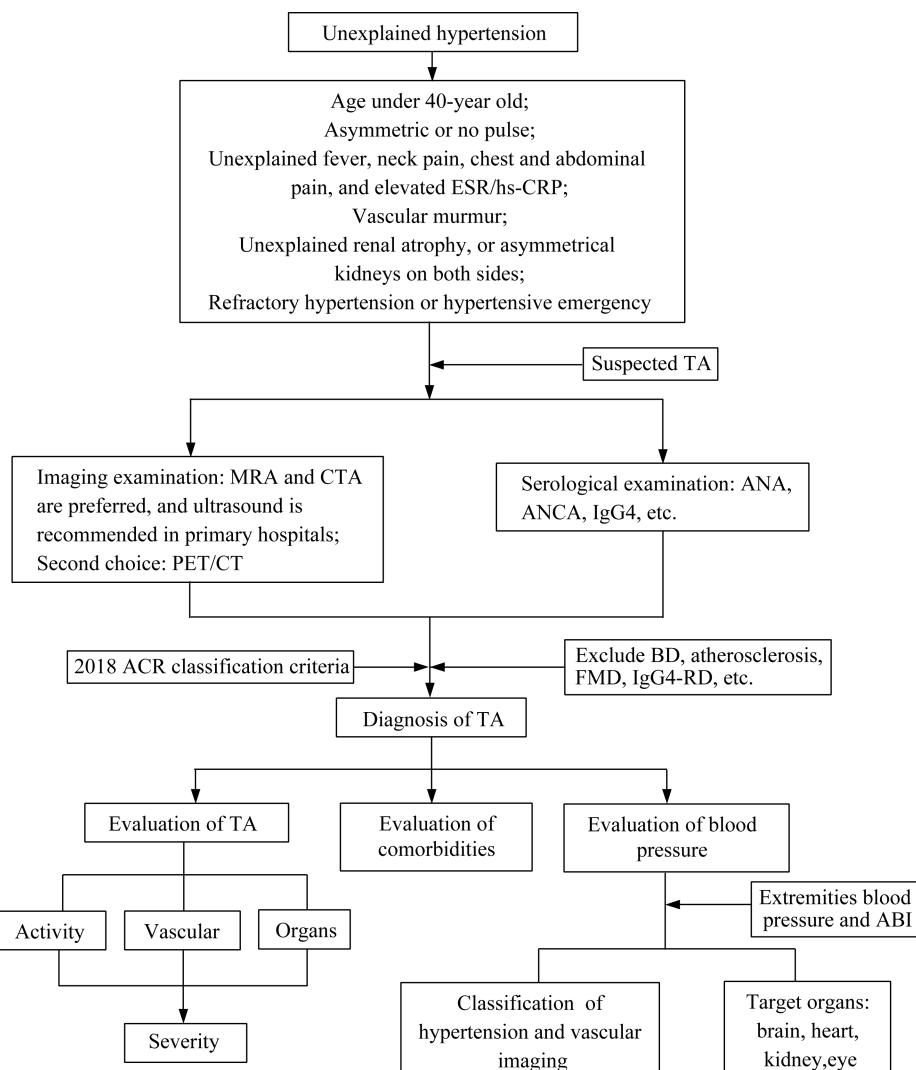
TARH发生机制复杂,难治性比例高,因此,高血压导致的心、脑、肾、大血管等靶器官不良事件发生率高。TA具有多发血管受累的特点,在ECTA队列中,主动脉-肾动脉同时受累比例为33.3%,颈动脉和肾动脉同时受累比例为39.6%,导致了TARH治疗的难度。TA疾病活动可导致血压升高控制不佳,急性活动期经过内科抗炎治疗可以改善血管壁的炎症,有助于控制高血压。

### TARH的诊断

**高危人群** (1)40岁以下不明原因的高血压;(2)脉搏不对称或无脉;(3)血管杂音;(4)伴原因不明的发热、颈痛、胸腹痛、血沉/C反应蛋白升高;(5)不明原因肾萎缩,或两侧肾脏不对称;(6)难治性或高血压急症。具体诊治流程见图1。

### 血压测量

**测量部位** 由于TA常累及四肢血管,在ECTA队列中,脉搏减弱或无脉患者占11%,腹主动脉狭窄者占32.2%,因此,TA初次诊断后须进行四肢血压及踝臂指数(ankle brachial index, ABI)测



ESR: Erythrocyte sedimentation rate; hs-CRP: High sensitivity C-reactive protein; TA: Takayasu's arteritis; BD: Behcet's disease; MRA: Magnetic resonance angiography; CTA: Computed tomography angiography; PET/CT: Positron emission computed tomography; ANA: Antinuclear antibody; ANCA: Antineutrophil cytoplasmic antibodies; IgG4: Immunoglobulin G 4; FMD: Fibro-muscular dysplasia; IgG4-RD: IgG4-related disease; ABI: Ankle brachial index.

图1 TA高危人群诊治流程

Fig 1 Diagnosis and treatment process of people with high-risk in TA

定。根据影像学结果选择相应的测量部位,一侧肢体血管受累时,建议测健侧肢体;当双上肢血管均受累,建议测双下肢血压;四肢血管均受累时应进行中心血压测定。

**测量方法** 血压测量是评估血压水平、诊断高血压以及观察降压疗效的基本方法。主要包括诊室血压、动态血压监测和家庭血压监测,后两者可以避免白大衣效应。指导家庭血压监测是主要方法,动态监测一天内不同时段血压,有助于血压的长期随访和监测、调整和评估药物的疗效<sup>[24-26]</sup>。

(1) 测量仪器:电子血压计和水银血压计均可。

电子血压计:使用通过国际标准方案认证(ESH、BHS 和 AAMI)的上臂式医用电子血压计。

(2) 测量部位:常用部位有上肢肱动脉和下肢腘动脉,也可以测踝动脉。血压测量前30 min内,避免吸烟、摄入咖啡因和运动,排空膀胱,安静环境中休息至少5 min。

(3) 上肢血压测量方法:①测量时取坐位,手臂放在桌子上,上臂中点与心脏同高,后背靠在椅子上,双腿自然下垂、双足平放在地上;②上肢裸露伸直并轻度外展,肘部置于心脏同一水平,将气袖均匀紧贴皮肤缠于上臂,使其下缘在肘窝以上约2.5 cm,

气袖中央位于肱动脉表面。正常双上肢压差达5~10 mmHg,超过此范围时须进行四肢血压测定。

(4) 下肢血压测量方法:测量时患者取俯卧位,趴在床上,下肢肌肉放松,裤口宽松,袖带平整缚于大腿下部,下缘距离腘窝4 cm,气囊纵轴中线压于腘动脉上。正常情况下,同侧下肢血压比上肢血压高20~40 mmHg。

**高血压的监测和随访** 每次去医院就诊前1周或改变治疗方案后2周需要连续监测血压。每天晨起后1 h内(服药前)和睡前1 h内测量,休息3 min测量第1次,再休息1 min,测量第2次。如果这2次测量值相差大,测量第3次。血压控制良好者,每月至少连续测量1周<sup>[27]</sup>。

**TA及TARH的评估** 对TA患者进行密切监测和全面系统的病情评估十分重要,有助于了解病情进展情况,及时干预,防止不良事件的发生,改善患者预后。

评估包括以下内容:(1)TA疾病活动性、严重性及慢性损伤的评估;(2)根据血压水平、危险因素、靶器官损害以及并发症,进行心血管风险评估,判断可能影响预后的重要因素;(3)评估疗效和安全性。

**TA的评估** TA一经诊断,需要对疾病的活动性,全身血管包括病变的部位、范围、程度、性质、严重性以及合并症进行评估。TA活动性评估常用方法包括症状、体征<sup>[1]</sup>、血清学标志物<sup>[28-30]</sup>、影像学评价<sup>[31-32]</sup>以及美国国立卫生研究院(National Institutes of Health, NIH)评分<sup>[33]</sup>。全身血管的评估建议采用磁共振血管造影(magnetic resonance angiography, MRA)和计算机断层血管造影(computed tomography angiography, CTA),TA严重性根据血管受累的情况及重要脏器功能进行评估,分为轻、中、重度,详见《中国大动脉炎性肾动脉炎诊治多学科专家共识》<sup>[34]</sup>。

正确识别TA疾病活动和血管损伤对治疗决策的选择、避免过度治疗造成的治疗相关毒性反应有重要意义。

**活动性评估** 早期识别TA疾病活动性,积极控制血管炎症,一方面可以恢复受累脏器的血流灌注,另一方面也能对血压起到一定的控制作用。评估方法见参考文献<sup>[34]</sup>。

**慢性损伤的评估** 慢性损伤定义为血管炎症继发出现的不可逆的疤痕样损害。

对于症状持续大于6个月,经治疗后不改善或维持原状,均应考虑损伤引起的临床症状。损伤评分标准可以采用血管炎损伤指数(vasculitis damage index, VDI)及大动脉炎损伤指数(Takayasu arteritis damage score, TADS)评分表进行评分<sup>[35-36]</sup>。

**影像学分型** 基于ECTA队列患者血管受累的分布,将TARH患者的动脉受累表型分为3种影像学表型:I型,累及腹主动脉和/或肾动脉;II型,累及升主动脉,主动脉弓及其分支,胸主动脉;III型,同时累及I型和II型。I型和III型难治性高血压常见,心脑血管事件发生率增加。

**靶器官评估** TA患者因受累血管的狭窄/闭塞引起供应器官的缺血、缺氧等病变,如合并高血压会进一步加重靶器官损害<sup>[14,36]</sup>,主要是心脏、大脑、肾脏、眼底和血管的结构或功能变化,因此早期全面的靶器官评估对TARH病情严重性判断及制定治疗方案具有重要价值。对颅脑受累的患者,客观评价脑血管灌注水平、代偿程度等,评价有无急性脑血管事件等危象,有无颅脑血管受累或者颈动脉狭窄等潜在风险;对心脏受累患者,需评估心脏结构和功能状态、冠状动脉有无严重狭窄病变等心脏缺血风险;对肾脏受累患者,应全面评估肾动脉病变(包括单侧/双侧)、有无RAAS系统激活以及有无急慢性肾功能损伤等。相关脏器的具体评估方法参见原发性高血压指南<sup>[16-17]</sup>。

**TARH的治疗** 主要是以风湿免疫科为主导的多学科合作诊疗,早期诊断、全面评估、分层治疗。

**治疗原则:**(1)尽快控制炎症,积极诱导疾病缓解,维持病情持续缓解,有助于减少严重并发症;(2)积极降压治疗,高血压及靶器官评估的基础上合理选择降压药物,规律监测血压,定期随访;(3)对于血压不能达标者,在炎症控制期,选择外科干预;(4)TA和高血压均要达标治疗,实现“双达标”的原则。

**TA的治疗** TA的治疗目标是积极控制疾病活动,诱导疾病缓解,在全面评估的基础上,根据疾病的活动性和严重性,制定个性化治疗方案。根据病情,治疗分为诱导缓解、维持缓解和预防复发。治疗药物包括糖皮质激素(glucocorticoid, GC)<sup>[38-41]</sup>和改善病情的抗风湿药(disease-modifying anti-rheumatic drugs, DMARDs),GC是基本用药,

DMARDs 包括化学合成的改善病情抗风湿药 (conventional synthetic disease-modifying anti-rheumatic drugs, cDMARDs), 如环磷酰胺 (cyclophosphamide, CTX)<sup>[40,42-45]</sup>、甲氨蝶呤 (methotrexate, MTX)<sup>[39,41,44-45]</sup>、霉酚酸酯 (mycophenolate mofetil, MMF)<sup>[45-46]</sup>、来氟米特 (leflunomide, Lef)<sup>[42-43,45,47]</sup>等, 以及生物合成的改善病情抗风湿药 (biological disease-modifying anti-rheumatic drugs, bDMARDs), 如托珠单抗 (tocilizumab, TCZ)<sup>[39-41,45,48]</sup>、肿瘤坏死因子 $\alpha$ 抑制剂 (tumor necrosis factor- $\alpha$  inhibitor, TNFi)<sup>[39,41,45,49]</sup>等。

其他治疗包括抗血小板、抗凝、调脂治疗<sup>[34]</sup>。TA 若处于活动期, 经积极抗炎治疗后血压可得到一定的改善, 疾病维持持续缓解有助于稳定血压。

TA 的一些治疗药物有引起血压升高的风险, 需要警惕药物相关性高血压(表1)。当血压升高与所用药物有一定的时间相关性或所用药物的药理作用有致血压升高的可能时, 均应考虑药物相关性高血压。一旦诊断药物相关的高血压, 建议及时调整治疗方案。对合并有肾脏损害的患者谨慎应用环孢素 A(cyclosporin A, CyA)等治疗 TA。

表1 大动脉炎相关治疗药物引起高血压的发病机制

Tab 1 Pathogenesis of hypertension caused by drugs for treatment of TA

Type of drug	Drug name	Mechanisms cause blood pressure to rise	Precautions
NSAIDs	Ibuprofen, indometacin, celecoxib, meloxicam, diclofenac sodium	Water and sodium retention; Reduce the prostaglandin content in the circulation; Kidney damage	Affect the antihypertensive effect of antihypertensive drugs (such as ACEI/ARB, $\beta$ -blockers); aspirin has no effect on blood pressure
Glucocorticoids	Such as prednisone, methylprednisolone, hydrocortisone, etc.	Has mineralocorticoid-like effect, can cause water and sodium retention, activate sympathetic nerves, promote the synthesis of angiotensinogen in the liver, and increase RAAS activity	Pay attention to changes in blood potassium
cDMARDs	Leflunomide, cyclosporine A, tacrolimus	Activate sympathetic nerves; NO-mediated impaired vasodilation and increased endothelin release; Inhibit the synthesis and release of prostaglandins	Leflunomide, cyclosporine A, tacrolimus increase blood pressure
bDMARDs	TNF, anti-CD20 antibody, IL-6 receptor antagonist, JAK inhibitor	The mechanism is unclear	Anti-CD20 can cause hypertension or hypotension, blood pressure needs to be closely monitored

NSAIDs: Non-steroidal anti-inflammatory drugs; cDMARDs: Conventional synthetic disease-modifying anti-rheumatic drugs; bDMARDs: Biological disease-modifying anti-rheumatic drugs; TNF: Tumor necrosis factor; CD20: Cluster of differentiation 20; IL-6: Interleukin-6; JAK: Janus-activated kinase; RAAS: Renin aniotension aldosterone system; NO: Nitric oxide; ACEI: Angiotensin converting enzyme inhibitors; ARB: Angiotensin receptor blocker.

### 高血压治疗

**血压控制目标** 高血压患者的血压应控制在 $<140/90\text{ mmHg}$ 。若患者耐受, 建议进一步降至 $<130/80\text{ mmHg}$ <sup>[16,50-51]</sup>。

TARH 应根据受累血管的病变程度选择降压药物, 兼顾脑、心、肾的灌注水平, 并注意降压速度, 制定个体化的目标值。如合并弓上分支受累患者, 降压治疗需充分保证脑灌注, 急性脑梗死时谨慎使用快速强力降压方案。一侧颈动脉狭窄 $\geq 70\%$ 时, 收缩压控制在 $130\sim 150\text{ mmHg}$ ; 双侧颈动脉狭窄 $\geq 70\%$ 时, 收缩压控制在 $150\sim 170\text{ mmHg}$ ; 颈动脉狭窄 $<70\%$ 的高血压患者, 降压目标同一般人群<sup>[52]</sup>。肾动脉狭窄合并其他脏器受损时以保护其他靶器官灌

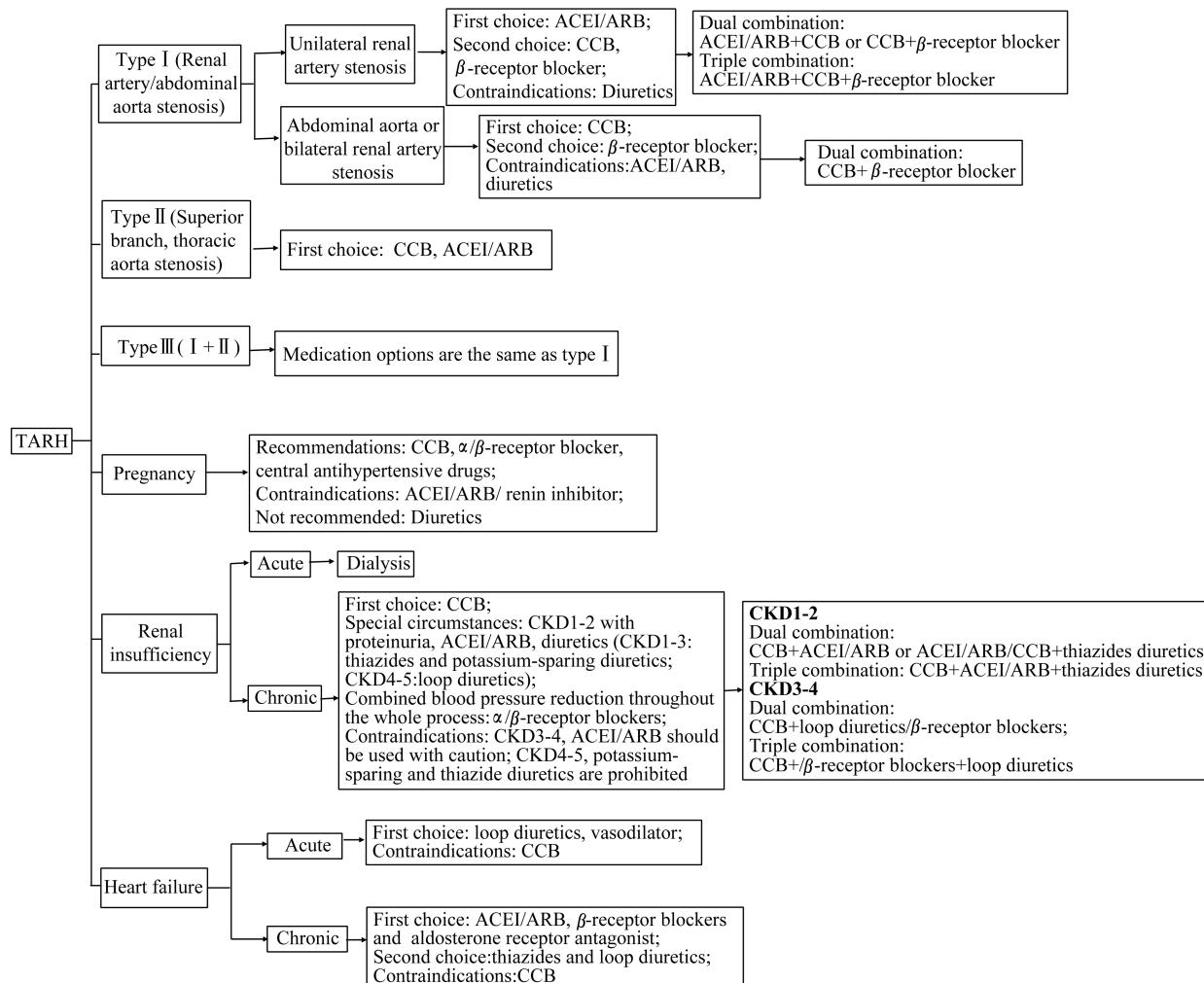
注优先。若同时存在多个系统受累, 建议多学科团队(multidisciplinary team, MDT)进行协调诊治。

**一般治疗** TA 是一种慢性病, 高血压也是慢性病, 因此治疗需要长期坚持。健康的生活方式(如合理膳食、忌酗酒、戒烟、控制体重、避免过度焦虑和恐慌等)是 TA 患者和高血压患者治疗的基本要求。

**药物治疗** TARH 患者常用的降压药物包括钙离子拮抗剂 (calcium channel blockers, CCB)、血管紧张素转化酶抑制剂 (angiotensin converting enzyme inhibitors, ACEI)、血管紧张素受体拮抗剂 (angiotensin receptor blocker, ARB)、利尿剂、 $\beta$ 受体阻滞剂。这 5 大类药物均可作为起始治疗及维持治疗。联合治疗应该成为 TA 相关高血压治疗的基本

原则。除 ACEI 和 ARB 不能联合应用外, 多采用不同作用机制的药物联合治疗。难治性高血压还可

以选择  $\alpha$  受体阻滞剂、中枢性降压药等。详见图 2。



TARH: Takayasu's arteritis-related hypertension; ACEI: Angiotensin converting enzyme inhibitors; ARB: Angiotensin receptor blocker; CCB: Calcium channel blockers; CKD: Chronic kidney disease.

图 2 大动脉炎特殊人群降压药物选择

Fig 2 Selection of antihypertensive drugs for special populations with TA

常用降压药种类、不良反应及禁忌证:(1) CCB, 包括二氢吡啶类和非二氢吡啶类。TA 相关高血压患者中由肾动脉狭窄引起血压升高者达 76.2%<sup>[11]</sup>, 对于不适宜使用 ACEI/ARB 的患者(如双侧肾动脉狭窄), CCB 类是安全有效的药物, 且能降低高血压患者发生脑卒中事件的风险<sup>[53]</sup>。(2) ACEI/ARB, 通过抑制 RAAS 系统的活化发挥降压作用, 是肾动脉狭窄引起高血压的有效降压药物。且降压同时有靶器官保护作用, 减少心血管重构、降低蛋白尿等。若单侧肾动脉狭窄时优先选择 ACEI/ARB, 注意监测肾功能、尿量和电解质, 血肌酐 > 165 μmol/L 时慎用。严重胸腹主动脉狭窄、双

侧肾动脉狭窄、单功能肾、高血钾、妊娠、血管神经性水肿禁用。(3)利尿剂, 通过促进水钠排泄、降低细胞外容量、降低外周血管阻力发挥降压作用。常用利尿剂包括噻嗪类、袢利尿剂和保钾利尿剂, 以及螺内酯。各种利尿剂均可通过降低有效循环血容量激活交感神经和 RAAS 系统, 从而引起肾血管收缩, 肾缺血缺氧, 因此, 肾动脉狭窄性高血压慎用利尿剂。(4)β受体阻滞剂, 由于β受体阻滞剂具有抑制肾素释放的作用, 肾动脉狭窄性高血压可以选用或联合用药, 尤其是合并慢性心功能不全者; 此外, 适用于高血压合并快速性心律失常、心绞痛/心肌梗死、慢性心力衰竭患者。禁用于哮喘、心动过缓、

心脏传导阻滞的患者。(5)其他如 $\alpha$ 受体阻滞剂、中枢降压药、直接血管扩张剂等在高血压难以控制时可作为选择。

**合并妊娠** 建议血压 $\geq 140/90$  mmHg 的妊娠期高血压患者启动降压药物治疗<sup>[16,54]</sup>,降压的目的是保障母婴安全和顺利分娩,注意保持血压平稳和避免过度降压。常用的降压药物有CCB类、 $\alpha$ 和 $\beta$ 肾上腺素能受体阻滞剂和中枢性降压药。推荐常用的口服降压药有甲基多巴、拉贝洛尔、硝苯地平和硝苯地平缓释片等;静脉降压药有拉贝洛尔、酚妥拉明。 $\beta$ 肾上腺素能受体阻滞剂可能引起胎儿心动过缓,因此种类和剂量应有所选择,避免使用阿替洛尔。不推荐妊娠期使用利尿剂,防止血液高凝状态。禁止使用ACEI、ARB和直接肾素抑制剂。

**影像学分型治疗** (1) I型(腹主动脉/肾动脉受累):单侧肾动脉受累,首选ACEI/ARB,需监测肾功能和血钾,血肌酐 $>165$   $\mu\text{mol/L}$ 时慎用;当双侧肾动脉血供均受影响如严重胸腹主动脉狭窄、双侧肾动脉狭窄以及单个功能肾脏,慎用ACEI/ARB,透析患者例外;CCB是治疗双侧肾动脉狭窄性高血压安全有效的药物,推荐首选CCB; $\beta$ 受体阻滞剂有抑制肾素释放的作用,可用于联合降压;利尿剂可激活RAAS系统,在高肾素时避免选用。(2) II型(弓上分支、胸主动脉受累):降压的同时要保证颅脑的灌注,急性缺血性脑卒中时谨慎使用快速强力降压方案。本共识推荐使用CCB及ACEI/ARB降压治疗。(3) III型(I+II型):降压方案选择同I型。

**特殊情况降压药物选择** 在TA治疗过程中,应对急性的合并症进行积极而有针对性的应急治疗。

(1) 高血压急症:高血压急症患者应该收住院,首先去除引起血压急剧升高的诱因。降压原则是在保证重要脏器灌注的基础上渐进降压。发病初始1 h内血压控制目标为治疗前平均动脉压的25%,之后2~6 h内将血压降至较安全水平,一般为160/100 mmHg。可选用方便调节的静脉降压药,当血压平稳后改用口服降压药<sup>[17]</sup>。(①急性冠脉综合征(acute coronary syndrome, ACS):对急性冠脉事件者,建议迅速将收缩压降至 $<140$  mmHg,首选静脉用硝酸甘油和拉贝洛尔,次选乌拉地尔<sup>[55-57]</sup>。②急性主动脉病变(动脉瘤破裂或主动脉夹层):控制心室率、抑制心脏收缩,保证脏器灌注的前提下,迅速

降低血压和心率,使收缩压 $<120$  mmHg,心率 $<60$ 次/min。首选静脉途径的 $\beta$ 受体阻滞剂、非二氢吡啶类CCB<sup>[56,58-59]</sup>。③脑卒中:急性脑出血患者应根据血压水平决定是否降压治疗,收缩压 $\geq 220$  mmHg时应积极使用静脉降压药,使收缩压 $<180$  mmHg;收缩压 $<220$  mmHg时不建议立即降压。缺血性脑卒中患者不建议通过降压药常规降低血压,以下情况除外:静脉溶栓患者溶栓后24 h内维持血压在 $<180/105$  mmHg;血压持续升高(收缩压 $\geq 220$  mmHg或舒张压 $\geq 120$  mmHg)伴严重心功能不全、主动脉夹层、高血压脑病者可予降压治疗。可选择拉贝洛尔、尼卡地平等降压药<sup>[16,56,60-62]</sup>。

## (2) 合并症

**肾功能不全:**肾功能不全合并蛋白尿时首选ACEI/ARB,但慢性肾脏病(chronic kidney disease, CKD)3~4期谨慎使用ACEI/ARB,剂量减半,严密监测血肌酐、血钾和估算肾小球滤过率(estimated glomerular filtration rate, eGFR)。二氢吡啶类CCB主要经肝脏排泄,对肾功能无影响,推荐用于明显肾功能异常的高血压患者。噻嗪类和保钾利尿剂可用于CKD1~3期( $e\text{GFR} \geq 30 \text{ mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$ ,当 $e\text{GFR} < 30 \text{ mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$ 时选择袢利尿剂。 $\beta$ 受体阻滞剂可用于肾功能不全不同时期的联合降压。发生急性肾功能不全时,可考虑透析治疗<sup>[63-65]</sup>。

**心功能不全:**急性心衰时控制心衰的同时积极降压,推荐静脉给予袢利尿剂和血管扩张剂,包括硝酸甘油、硝普钠或乌拉地尔。不推荐CCB、 $\alpha$ 受体阻滞剂和中枢降压药。慢性心衰首选ACEI(不能耐受者可用ARB)、沙库巴曲缬沙坦钠片(诺心妥)、 $\beta$ 受体阻滞剂和醛固酮受体拮抗剂。也可使用噻嗪类和袢利尿剂。如血压仍未控制,可选择CCB类降压药<sup>[66-68]</sup>。

**外科干预** 原则:经内科积极治疗TA控制稳定、充分权衡手术的获益与风险、由多学科团队组成的专家组共同决策、与患者充分沟通的前提下可考虑外科治疗。

**目标:**改善高血压、降低心脏负荷的同时保证脑肾等重要脏器的灌注、降低高血压所致心脑肾等并发症、解除血管狭窄所致器官缺血症状,减少降压药物的使用。

**适宜人群:**多种降压药物不能控制的高血压(血压持续升高Ⅱ~Ⅲ级)或药物不能耐受、血管严重病变并伴血流动力学不稳定、靶器官严重缺血。

经内科治疗后仍需二联及以上降压药物,血压未能达标,尤其是年轻患者,在充分沟通的情况下,手术作为可选择的治疗手段。

**干预方式:**血管腔内治疗(PTA、PTA+支架)及开放性手术。

由肾动脉狭窄导致的高血压外科治疗原则、适应证、手术时机、手术方式的选择等内容详见相关共识<sup>[34]</sup>。

对大动脉炎性肾动脉狭窄(Takayasu's arteritis-induced renal artery stenosis, TARAS)血管重建术的疗效和安全性进行的系统综述<sup>[62]</sup>表明,在再狭窄发生率、血管通畅率、晚期并发症等方面,开放手术均优于血管内干预治疗。而血管内干预治疗中,经皮血管成形术(percutaneous transluminal angioplasty, PTA)与支架植入术相比,前者肾动脉再狭窄率更低、血管通畅率更高。

**腹主动脉狭窄手术适应证和禁忌证**<sup>[69-70]</sup>:(1)手术适应证为血管狭窄直径>70%,或跨狭窄部位的收缩压峰值>20 mmHg;临床指征:难治性高血压、药物治疗不能耐受、严重的下肢跛行、肠缺血或坏死。经内科治疗疾病已无明显活动。(2)疗效判断标准:支架植入术后病变动脉直径残余狭窄<30%;血管直径比治疗前>50%;跨狭窄压力梯度<20 mmHg,并且至少比手术前降低15 mmHg。临床治愈:不用降压药的情况下血压降至正常;改善:收缩压至少降低15%,或者服用更少的降压药使收缩压<90 mmHg;失败:血压没有改善。(3)手术方式:血管腔内治疗——PTA、支架植入;开放性手术——血管置换术、旁路移植术。腹主动脉由于血管壁弹性大,PTA术后血管弹性回缩导致再狭窄概率高,故不作为常规治疗方法。支架植入可以有效抵抗狭窄血管的弹性回缩,成为腔内治疗的主要方法<sup>[69]</sup>。

**结语** TARH是一种少见的,以系统性免疫炎症为基础的继发性高血压,难治性是其特点。早期发现、早期诊断、积极干预可以诱导大动脉炎的缓解,逆转血管病变,从而控制高血压,保护靶器官,减少心血管风险。多学科共同诊治,是实现大动脉炎和高血压“双达标”的积极措施。尽快开展国内随机对照临床研究以制定中国大动脉炎相关高血压的临床诊治方案十分重要和必要。

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