高血压与心房颤动的关系

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【摘要】高血压是心房颤动最常见的可逆危险因素。两者相互依存，显著增加心脑血管不良事件发生风险。越来越多的证据表明，控制可逆危险因素可能是心房颤动一级和二级预防的关键。虽然高血压和心房颤动的密切关系众所周知，但具体机制仍不完全清楚。现结合最新相关研究进展，拟从高血压合并心房颤动的发生风险、病理生理机制和血压控制对心房颤动患者预后的影响三方面，对高血压与心房颤动的关系进一步探讨，以期对临床诊疗提供理论支持。

【关键词】高血压；心房颤动；血压
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Hypertension and Atrial Fibrillation

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【**Abstract**】Hypertension is the most common and reversible risk factor for atrial fibrillation. Hypertension and atrial fibrillation are closely related and interdependent, which significantly increases the risk of cardiovascular and cerebrovascular adverse events. There is increasing evidence that controlling reversible risk factors may be the key to primary and secondary prevention of atrial fibrillation. Although the relationship between hypertension and atrial fibrillation is well known, the exact mechanism is still not entirely clear. Combined with the latest relevant research progress, this article intends to further explore the relationship between hypertension and atrial fibrillation from three aspects, namely the risk of hypertension associated with atrial fibrillation, the pathophysiological mechanism, and the influence of blood pressure control on the prognosis of patients with atrial fibrillation, in order to provide theoretical support for clinical diagnosis and treatment.

【**Key words**】Hypertension; Atrial fibrillation; Blood pressure

高血压和心房颤动（房颤）是中国重大的公共卫生问题。随着全球人口数目增长和老龄化进程，两者发病率逐年上升，影响人民健康，增加社会经济负担。房颤是临床最常见的心律失常。截至 2016 年，世界范围内约有 4 630 万的房颤/心房扑动患者[1]，年龄>75 岁的人群占其中的绝大部分，但由于临床上沉默型房颤患者的存在，房颤的患病率可能远超当前已知的数据。

高血压和房颤关系密切，相互依存。有 80% 的房颤患者合并高血压[2]，高血压也是房颤最常见的独立危险因素，占房颤病因的 15% 以上[3]。高血压合并房颤的危害具有叠加效应，可致脑卒中、心力衰竭、肾功能异常和死亡等不良事件的发生风险显著增加，致残率和致死率高。虽然高血压和房颤的关系有目共睹，但仍存疑问有待进一步研究。首先，高血压导致房颤发生的具体机制尚不完全清楚，血压水平与房颤风险之间呈线性还是非线性关系有待进一步研究明确；其次，高血压合并房颤患者的降压目标值、血压控制与房颤患者栓塞/出血风险以及射频导管消融术后房颤复发风险的关系，均是临床亟待解决的问题。现结合目前国内外相关研究，以期对上述疑问进行解答，为临床诊疗提供一定的帮助。

1　高血压合并房颤的发生风险

1.1　血压水平与房颤

高血压是房颤发生的重要危险因素，仅次于心力衰竭、年龄和心脏瓣膜病。一项队列研究显示，亚裔人群中高血压患者房颤患病率为 34.6%[4]。Framingham 心脏研究中心提出，高血压患者较健康人群房颤发生风险增加 1 倍[5]，同时，正常血压高值对房颤的发生也有促进作用。MESA 研究结果对其有明确的证实[6]。LIFE

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研究显示,收缩压每升高 10 mm Hg(1 mm Hg = 0.133 3 kPa),房颤的发生风险增加 6%。累积血压暴露对新发房颤也有一定的预测价值。王艳秀等[7]研究发现,累积收缩压暴露每增加 10 mm Hg·年,房颤的发生风险增加 3.4%,累积舒张压暴露每增加 5 mm Hg·年,房颤的发生风险增加 2.6%。其机制可能与长期左房压力增高、心房间质纤维化和炎性细胞浸润相关,但血压水平与房颤风险之间是否呈线性关系尚不明确。在一项接受降压治疗的人群研究中提到,血压水平与房颤事件之间存在"J"型曲线关系,血压波动在 120～130/60～69 mm Hg者房颤发生率最低[8]。另外,血压水平对房颤患者心血管预后也有一定预测作用。收缩压越高,卒中、心肌梗死和大出血等不良事件发生风险越高[9]。

1.2 脉压差与房颤

脉压增大与高血压患者房颤发生也有一定相关性。Mitchell 等[10]研究发现,脉压每升高 20 mm Hg,房颤的发病率增加约 26%。脉压主要反映动脉的弹性功能,压差越大,动脉硬化程度越严重,高血压患者发生心脑血管事件的风险越高。既往认为脉压波动较大,干扰因素多,测量数据误差较大。近年来,随着 24 小时动态脉压在临床的广泛应用,对进一步评价脉压对房颤发生的影响提供了帮助。

1.3 血压变异性与房颤

Hermida 等[11]研究指出,非杓型血压是预测高血压患者靶器官损害和心脑血管不良事件的重要因素。非杓型血压与高血压患者房颤发生有更强的相关性,其可能与交感神经系统和肾素-血管紧张素-醛固酮系统活性增加有关。近年有研究提出,血压变异性升高也是原发性高血压患者新发房颤的独立预测因子,尤其是收缩压变异性升高。Coulson[12]研究进一步表明,交感神经激活可能是血压变异性升高引起高血压患者房颤发生的主要机制。Proietti 等[13]在随访中发现,收缩压变异性升高也与出血和卒中等高风险事件的发生有关。因此,监测血压变化,降低血压变异性对防治房颤及其不良事件的发生有重要意义。

1.4 强化降压治疗与房颤

一项 meta 分析结果提示,强化血压控制与卒中、心肌梗死和心力衰竭等心血管疾病风险降低具有相关性[14],然而,由于研究的局限性,未能针对血压控制水平与房颤发生之间的关系进行分析。近期 *Hypertension* 杂志上发表的相关文章或许对此有一定指导意义。Soliman 等[15]发现,对存在心血管疾病高风险的高血压患者,强化降压治疗(收缩压目标值< 120 mm Hg)相比于标准降压治疗(收缩压目标值< 140 mm Hg),降低 26% 的新发房颤风险。对于老年高血压患者,强化降压治疗同样可降低房颤发生风险,对于预防左心室肥大(left ventricular hypertrophy, LVH)的进展也有益处。

2 病理生理机制

高血压与房颤关系密切,众多基础及临床研究致力于明确两者的发病机制,但仍不完全清楚。在高血压大鼠模型中发现左心房增大和纤维化改变等心肌重构迹象,加之传导延缓,除极异质性增加,有效不应期缩短和动作电位持续时间缩短等电生理改变[16]。此外发现,高血压肥胖大鼠相比消瘦大鼠,更易促进房颤的结构和功能改变,提示肥胖可能是促使房颤发生的另一危险因素[17]。

临床研究中,高血压患者房颤发生主要体现在血流动力学和非血流动力学改变方面。高血压患者长期血压控制不佳导致左心室舒张功能代偿性减低,出现 LVH,进而导致左心房压力升高,左心房增大,心房间质纤维化,顺应性减低,交感神经激活,出现结构性重构和电重构,促使房颤发生。一项涉及 27 141 例的 meta 分析结果提示,LVH 患者室上性心律失常的发生率为 11.1%,相比之下,无 LVH 者为 1.1%[18]。此外,由于左心房对刺激的敏感性,在 LVH 出现前,可能已有左心房扩大发生。左心房内径增大是房颤的独立危险因素,其每增加 5 mm,房颤的发生风险增加 1.4 倍[19]。

另外,神经激素的活化、自主神经系统失调、炎症和氧化应激也是促进房颤和高血压共存的主要机制,共同促进房颤的发生和进展。大量研究表明,肾素-血管紧张素-醛固酮系统通过促进高血压患者心肌炎症和纤维化,进而诱发心房和心室的电重构和结构重构,使离子和细胞连接改变,从而导致房颤的发展[20]。血管紧张素Ⅱ通过血管紧张素Ⅱ1 型受体激活肌成纤维细胞的纤维原通路,刺激一系列因子激活,导致心肌纤维化发生。此外,血管紧张素Ⅱ诱导的炎症反应也和高血压患者并发房颤具有相关性。醛固酮可能通过导致低钾血症、LVH 和舒张功能不全使得左房扩张、胶原沉积和心肌纤维化形成。与原发性高血压患者相比,原发性醛固酮增多症患者发生房颤的风险为 12 倍[21]。

3 血压控制对房颤患者预后的影响

3.1 改善心脏负荷和预后

2020 年 ESC 房颤管理指南再次强调房颤的综合管理,其中危险因素和合并症的识别与管理是房颤治疗中不可或缺的部分。尤其是对高血压、糖尿病和肥胖等可控因素的预防、控制和治疗。有研究结果提出

血压控制与心血管不良预后之间呈线性关系[22]。目前针对高血压合并房颤患者具体的降压目标尚无定论,但血压控制良好可明显降低动脉硬化和左心系统受累的概率[23-24]。

3.2 预防新发房颤和射频导管消融术后房颤复发

近年许多研究表明危险因素控制有助于维持窦性心律,减少房性心律失常的发生[25-26]。血压控制可降低新发房颤的发生风险。高血压也是预测射频导管消融术后房颤复发的独立危险因素。那么,控制血压是否可使这部分人群受益,使房颤复发率降低,结果有待进一步考证。一项随机对照研究结果提示,强化降压治疗相比于标准降压治疗,两组间射频导管消融术后的房颤复发率无明显差异(亚组分析中,仅年龄>61 岁的人群结果提示阳性),相反,强化降压治疗导致出现更多低血压患者[27]。关于肾交感神经去除术的 ERADICATE-AF 随机对照研究中,随访 12 个月,阵发性房颤合并高血压患者经肾交感神经去除术联合射频导管消融治疗,房颤复发率降低[28]。上述两项随机对照研究结果差异在于,或许只有在治疗严重顽固性高血压患者的血压时才取得显著的疗效。

3.3 预防脑卒中和痴呆

血压控制不佳与高血压合并房颤患者栓塞和出血事件风险增加相关,适当的降压治疗可预防卒中,减少抗凝出血等事件发生[29-30]。此外,高血压和房颤患者痴呆风险增加独立相关。Kim 等[31]研究发现,对于中年房颤患者,血压与痴呆风险之间呈 U 形曲线关系,血压波动于 120/80 mm Hg 左右时痴呆风险最低。高血压合并房颤患者降低高血压负荷,有助于降低痴呆风险。

3.4 降压要适度

血压控制是房颤综合管理的重要方面,但降压要适度!血压控制水平与房颤患者死亡风险之间仍具有不确定性。RELY 研究最新结果显示,接受抗凝治疗的房颤患者,控制血压 > 140/90 mm Hg 和 < 120/70 mm Hg,均增加全因死亡风险[32]。

高血压与房颤的关系紧密而复杂,需更多研究来探讨。考虑到高血压和房颤的患病率和二者临床症状的不典型,非常有必要对高血压患者进行房颤的机会性筛查,特别是在高危患者中,及时有效的治疗将明显改善不良事件的发生。

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(上接第 231 页)

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