

脉压的影响因素及其与靶器官损害的研究进展

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【摘要】 脉压为收缩压与舒张压差值,根据测量位置差异又分周围脉压与中心脉压,影响两者因素较多,且不尽相同,目前对脉压影响因素描述缺乏统一性,临床研究也缺乏考虑两种脉压综合效果。在与多靶器官损害关系上,脉压能预示多靶器官损害,尤其是心脑系统,多年来作为独立危险因素倍受研究者们青睐,但对周围脉压和中脉压与多靶器官损害关系研究欠全面,且存在争议,阐述上各有利弊,说法不一。

【关键词】 周围脉压;中心脉压;机制;影响因素;靶器官损害

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Influential factors of pulse pressure and its research progress on target organ damage. CUI Lu-lu. Graduate School, Zunyi Medical University, Zunyi 563000, Guizhou, CHINA

【Abstract】 The pulse pressure is the difference between systolic blood pressure and diastolic blood pressure. It is divided into peripheral pulse pressure and central pulse pressure, according to the difference of measurement position. There are many factors affecting the two, and they are not the same. At present, there is no uniformity in describing the factors affecting pulse pressure. Clinical studies also lack the comprehensive effect of considering two pulse pressures. In relation to multi-target organ damage, pulse pressure can predict multi-target organ damage, especially in the cardiovascular system, which has been favored by researchers for many years as an independent risk factor. But it is not comprehensive in the study of damage relations between peripheral pulse pressure and central pulse pressure and multi-target organs, and there are controversies. There are various advantages and disadvantages in the elaboration, and there are different opinions.

【Key words】 Peripheral pulse pressure; Central pulse pressure; Mechanism; Influencing factors; Target organ damage

高血压是一种最常见的慢性病,也是心脑血管疾病的重要危险因素,可伴靶器官损伤,如心、脑、肾等,最终导致器官衰竭,给家庭及社会带来严重负担。目前全球高血压患者数超过 11 亿人^[1],而我国现患患者数占全球患患者数超过 1/4^[2],据最新研究显示 2012—2015 年我国成人高血压患病率高达 27.8%,且逐年呈上升趋势^[3]。诊断高血压有赖于收缩压或舒张压,但近年来二者差值,即脉压作为描述血压的指标备受关注,既往研究报道脉压增大能更好地反应高血压,且与靶器官损害密切相关^[4]。脉压根据测量部位的不同分为周围动脉脉压和中心动脉脉压,而影响两种脉压的影响因素不同。本文旨在复习相关文章,描述两种脉压的不同影响因素及其与靶器官损害的研究进展,以期给临床诊疗及科研提供新思路。

1 脉压增大的机制

脉压增大目前存在两种说法,一种认为随着年龄的增加,动脉顺应性降低(即,动脉僵硬度增加)导致大动脉缓冲功能受损,压力将血液向外周传送过程中。因外周或局部血管弹性差,使该点反射波提前反射回大动脉,而此时大动脉仍处于收缩期,压力与之重叠

使收缩期时间延长及峰值增高,到舒张期时因提前反流,动脉储存血液增多,使舒张压降低,导致脉压增大。另一种观点认为,脉压增大与全身炎症有关,高血压危险因素可诱导血管内皮功能受损,发生炎症反应,致使血管平滑肌增生,弹性纤维的退化和胶原纤维的增加,最终导致动脉弹性下降和僵硬度增加,脉压发生变化^[5-7]。此外,随着年龄增加,血管内皮功能退化,一氧化氮释放逐渐减少,血管蛋白流失、弹性纤维减少,也加快动脉硬化,导致脉压增宽^[8]。

2 脉压的影响因素

周围脉压和中心脉压的影响因素不同。外周脉压通常指肱动脉脉压,其研究较多。弗雷明汉(Framingham)研究显示随年龄增长收缩压呈逐渐上升趋势,而舒张压在早期上升,至 60 岁以后下降,导致脉压在早期上升较缓,后期加速上升^[9]。此外脉压与高体质量指数、空腹血糖、甘油三酯和低高密度脂蛋白及吸烟史相关,种族和性别不同其脉压也存在细微的差异,女性脉压在绝经前较男性增大缓慢,但在绝经后脉压增加明显,推测可能和体内雌激素分泌减少有关,雌激素可能是脉压保护性因素^[10-11]。另有研究发

现,在高血压人群中脉压增高受血糖、吸烟等多种因素综合影响,且女性脉压增大高于男性^[12]。YOON等^[13]通过对人群检测生化指标及血压发现,与脉压正常组比较,脉压增大组脉压随年龄、体质质量指数、腰围、收缩压、血清总胆固醇、甘油三酯、空腹血糖、血尿素氮、肌酐、红细胞、白细胞、转铁蛋白饱和度和血清铁增加而增大,提示脉压与年龄、体质质量指数、腰围、收缩压、总胆固醇、甘油三酯、空腹血糖、血尿素氮、肌酐、红细胞、白细胞、红细胞比容、总铁结合力、血红蛋白、血清铁和高密度脂蛋白C均相关,但因影响素较大无法确定主要因素,待后续研究进一步证实。研究发现在体质(体质质量指数<22 kg/m²)较轻的女性中,大量饮酒与脉压呈正相关,而在控制了普通和腹型肥胖,男性脉压与静息心率升高[(75.9±12.7)次/min]存在关联,但并未阐述呈何关系,提示超重男性的脉压与静息心率相关^[14-15]。此外,在继发性高血压患者中,无论保持卧位或是站立位,血浆醛固酮浓度>12 ng/dL时与脉压>51 mmHg (1 mmHg=0.133 kPa)相关,这表明较高的血浆醛固酮浓度可能是高血压患者脉压增大,且提示血浆醛固酮浓度是动脉弹性降低的危险因素^[16]。目前B型脑利钠肽已普遍用于心力衰竭的诊断,具有重要的诊断价值。在基因研究层次上,B型脑利钠肽水平主要由利钠肽前体B基因决定,其基因型分为GG、GT、TT三型。研究发现,利钠肽前体B基因GG型的脉压大于GT+TT基因型,提示脉压可能与利钠肽前体B基因相关^[17]。

中心脉压由主动脉根部血压计算得来,主要反应心脏大血管变化。影响其变化的有心率、每搏输出量^[18]、左室射血分数及大动脉弹性等。另外,中心脉压增大与其尿微量白蛋白及高胆固醇血症密切相关^[19-20]。近年来研究发现,血清碱性磷酸酶水平与24 h平均脉压、中心脉压均相关,血清碱性磷酸酶每增加2.27倍,外周肱动脉脉压增加3.04 mmHg,中心脉压增加4.02 mmHg^[21]。由此可见,中心脉压除与心脏大血管变化相关外,还与微量白蛋白尿及高胆固醇血症血清碱性磷酸酶有关。

3 脉压与靶器官损害

3.1 脉压与脑卒中及认知功能 心脑血管疾病一直是高血压最严重并发症,作为高血压防治的关键。近年来大量研究发现,无论是否存在高血压,脉压增大多伴有靶器官损害。LIU等^[22]和SELVARAJ等^[23]研究发现,脉压是脑卒中的独立危险因素,并且脉压增加10 mmHg与卒中风险呈正相关,且脉压>60 mmHg时风险性增加。因此,脉压作为脑卒中的危险因素引起诸多研究学者关注。脉压不仅与脑卒中发病相关,与复发也关系密切,在既往脑卒中患者诊疗过程中,脉压控制不良者,脑卒中再发率大大提高^[24]。CHANG等^[25]和

SU等^[26]通过对672例自发性脑出血患者的研究发现,脑出血与外周脉压增大相关,且证明脉压增大是脑出血高死亡率的独立危险因子,与长期卒中结局显著相关,尤其在60岁以上患卒中人群更为显著。

脉压可反映人群认知功能,研究发现,脉压能显示脑血管硬化程度,随着脑血管硬度严重程度的增加,脉压水平增加11.7 mmHg^[27]。通过检测动态脉压发现,较高的日间和夜间动态脉压测量与较差的认知相关^[28],其可能机制是脉压增大通过降低舒张指数而使脑神经纤维供血不足,从而使神经细胞功能缺失恶化,导致认知功能受损^[9-29]。

3.2 脉压与心脏疾病 大量研究发现脉压与心脏疾病关系密切。在弗雷明汉研究中,诊所脉压预测冠心病风险方面更优于收缩压,卧位测得脉压差异与冠状动脉缺血独立相关^[30-32]。FANG等^[33]和KIM等^[34]报道,在55岁以上的男性中脉压在50 mmHg基础上每增加10 mmHg,心血管疾病特异性死亡率增加2.5倍,而女性外周脉压和缺血性冠状动脉粥样硬化性心脏病之间的关联较男性更显著。此外年龄性脉压增大与心血管事件发生有关,研究发现在年龄>50岁人群中,脉压大于70 mmHg较脉压低于50 mmHg患冠状动脉性疾病的风脸增至3倍,而在年龄<50岁人群中却无此变化^[30]。心血管事件与脉压是独立正相关的,其在性别差异较大,男性对脉压的敏感性更显著,但因是在60岁前,在不同种族、地区及年龄(>45岁)时差异却并不明显,可能年龄相关的脉压增大还受种族与地区影响。GU等^[35]通过对13个国家研究发现,年龄<60岁的受试者脉压都没有增加心血管风险分层,对于年龄≥60岁的患者,较高的脉压提高了血管风险。最近的研究表明,在老年人群中,脉搏压力放大,作为重要的指标对心血管病的预后和死亡风险起到了重要的预测作用^[36]。GLASSER等^[37]将周围脉压分<45 mmHg、45~54.9 mmHg、55~64.9 mmHg、≥65 mmHg四组,并研究脉压与冠心病发生风险,结果显示与脉压<45 mmHg者比较,45~54.9 mmHg、55~64.9 mmHg、≥65 mmHg的冠心病事件风险比分别为:3.82,3.08和4.73,提示脉压≥65 mmHg与冠心病事件风险性较大,但亦可看出脉压正常组患病风险亦略高于脉压偏高组。脉压可能参与心脏重构过程,有研究表明,增加脉压被认为是左心室肥厚发生过程中的一个危险因素,并且可能增加左心室肥厚发展的风险^[35]。脉压增大时可预测心血管事件,在减h同样与心血管事件相关。研究报道心力衰竭早期变化也与脉压变化相关,脉压低于45 mmHg或高于75 mmHg的患者与保留射血分数的心力衰竭(HFpEF)预后密切相关,在脉压≤40 mmHg时,可以预测晚期心力衰竭患者的死亡风险^[38-39]。BORRELL等^[40]研究发现脉压与美国成年人心脏疾病特异

性死亡风险有关,但并未明确支持脉压增大或是减小。在妊娠中晚期脉压增大心血管风险逐步增加,在产后脉压及心血管风险急剧下降,这可能与妊娠期内分泌孕激素及雌激素相关,产后孕激素水平下降,而雌激素上升,提示雌激素是可能脉压的保护性因素,但孕激素对脉压影响的尚不能明确^[41]。

中心脉压主要与心脏及大血管损害事件相关,特别是对于年龄在 65 岁以下的年轻患者,中心脉压增大可增加心血管疾病风险^[42]。研究发现,中心脉压 50 mmHg 是心脑血管事件(如中风,心肌梗塞或充血性心力衰竭)的危险因素,与心血管病死亡率、全因死亡率相关,对重复冠状动脉支架植入术患者死亡率的预后具有重要意义。进一步研究发现中心脉压>60 mmHg 和心脏血管血栓形成有关,且各自独立促进心血管疾病风险增加^[43~45]。与外周脉压相比,中心脉压尤其像 24 h 平均血压一样,24 h 内测量的平均中心脉压可提高高血压患者的低心血管风险的预测能力,对患者发生心血管事件预测范围更大、可靠^[46]。此外,中心脉压增大还可作为心脏压力的负荷指标,与心脏靶器官损伤显著相关^[47]。

3.3 脉压与肾脏损害 脉压增大通过加快动脉硬化速度,能使肾脏小动脉发生变化,影响并降低肾脏的功能^[48]。KOSE 等^[49]在脉压≥65 mmHg 的人群中比较血尿素氮、血肌酐、肾小球滤过率基线值和 12 个月后的值,发现该人群 12 个月后的血尿素氮显着增加,血肌酐和肾小球滤过率显着下降,提示脉压≥65 mmHg 是肾小球滤过率下降的显著预测因子。另外,有学者^[16,50]研究发现,肱-踝脉搏波传导速度与颈-股脉搏波传导速度均与肾功能下降相关,但在控制年龄、低密度脂蛋白及总胆固醇的影响因素后,颈-股脉搏波传导速度、肱-踝脉搏波传导速度与肾功能下降的相关性不及脉压,颈-股脉搏波传导速度、肱-踝脉搏波传导速度与肾功能下降之间受其他因素影响,脉压增大可加快动脉硬化速度,但动脉硬并不是肾脏功能受损的主要原因,可能与血流灌注不足有关。

3.4 脉压与动脉硬化 动脉硬化一直被认为是心血管疾病和脑血管疾病的共同基础^[7],与心脑血管及肾脏一样,脉压与外周动脉疾病、颈动脉血管损伤均有不同程度相关^[51~52]。对外周动脉性疾病临床常用踝-肱指数及脉搏波传导速度评估,KORHONEN 等^[53]对受试者测量外周动脉脉压及踝-肱指数,并将外周脉压分≥65 mmHg 及<65 mmHg 两组。其结果显示,脉压<65 mmHg 组脉压值与踝-肱指数呈负相关,而脉压≥65 mmHg 组其与踝-肱指数呈正相关,提示脉压与外周动脉疾病相关。研究显示颈动脉内中膜厚度和脉搏波传导速度的相关性较弱,而二者均与脉压显著相关,提示脉压与二者关系密切,分析其可能原因,颈动脉内中膜增厚是通过影响血流通过的速度及对血管壁的压力改变,增大脉压,而脉搏波传导速度则

是影响血管壁弹性来影响脉压,血管壁弹性分可逆的血管壁收缩和不可逆转的纤维化和钙化影响,假使是可逆的血管壁收缩,动脉内中膜厚度不受影响,在此种情况下,动脉内中膜厚度与脉搏波传导速度关系较弱,但最终是改变血流及血压,两者均表现脉压增大^[54]。与脉压相同的还有脉压指数,脉压指数与颈动脉中膜厚度呈正相关,脉压指数多考虑收缩压因素,对单纯收缩压增大者考虑非动脉硬化性因素存在^[55]。在韩国老年男性和女性(年龄>60 岁)的研究中发现脉压和代谢综合征之间存在正相关,且与主动脉 PWV 及颈内动脉中膜厚度相关^[56],而脉压>60 mmHg 与中国女性 2 型糖尿病发病有关,特别是 52~59 岁的女性^[57]。FUJITA 等^[58]在隐匿性高血压及白大衣高血压患者中发现,24 h 平均脉压在除外年龄、性别、糖尿病病程、体质质量指数、吸烟、总胆固醇等的影响因素外,与动脉硬化独立相关,提示 24 h 平均脉压增大者存在动脉硬化可能。家庭血压显示,清晨脉压显示了与 2 型糖尿病患者的动脉僵硬度相关,清晨收缩压增加,导致清晨脉压增大,且家庭脉压小于 54.6 mmHg 时可防止动脉硬化的发展,为控制动脉硬化提供可靠参考^[59]。近年来动态动脉硬化指数在评估动脉硬化上受到大多学者喜爱,24 h 动态动脉硬化指数。动态动脉硬化指数和脉压同是心血管疾病和死亡率结果的独立预测因子,都能提供新发疾病的风险预测,但脉压似乎比动脉僵硬指数具有更大的临床研究价值^[60]。此外,研究发现颈-股脉搏波传导速度作为动脉硬化的金标准是对男性低脉压增幅的预测因子,而对控制协变量后的女性则无此作用,颈-股脉搏波传导速度成为 58 岁以上女性脉压扩增的决定因素,可能反映了性激素对大血管壁弹性的保护作用^[61~62]。

研究发现中心动脉脉压可能与颈动脉内膜增厚和心肌肥厚有关^[61]。众所周知,颈-股脉搏波传导速度是反应主动脉弹性的指标,肱-踝脉搏波传导速度主要反应外周动脉弹性及外周动脉疾病,而研究发现肱-踝脉搏波传导速度也可以成为中心动脉硬化的良好标志,且发现肱-踝脉搏波传导速度和中心脉压增大之间的相关性很大,提示外周动脉疾病时可能同时存在中心动脉硬化性疾病^[63]。近年多用脉搏波速度和增强指数反应动脉硬化,研究报道脉搏波速度和增强指数与中心脉压之间有强相关联性,随动脉僵硬度增加,主动脉储存压力增大,脉搏波速度和增强指数相应增大,脉压随之增大^[64]。BRAND 等^[65]通过对 136 例患下肢缺血者研究发现,当中心脉压增大时,颈-股脉搏波传导速度明显减小,提示中心脉压与颈-股脉搏波传导速度比值增大可能是外周动脉疾病的新指标。

4 总结

综上所述,周围脉压与中心脉压的影响因素不完全相同。目前所知外周脉压可能与年龄、性别、种族、

静息心率、血糖、吸烟、饮酒、体质质量指数、腰围、血清总胆固醇、甘油三酯、高密度脂蛋白C、血尿素氮、血肌酐、红细胞、白细胞、红细胞比容、总铁结合力、血红蛋白、血清铁和血浆醛固酮浓度等多重因素有关，其中年龄和性别是脉压增大的重要因素，在女性老年患者脉压增大明显；而中心脉压除受年龄、性别、身高、体质质量、体质质量指数的影响外，还与尿微量白蛋白、血清碱性磷酸酶生化指标及心脏每搏输出量、心脏左室射血分数和大动脉弹性有关。脉压的变化能预示多靶器官损害，尤其是脑、心、肾及动脉，且外周脉压主要与脑卒中及肾脏损害有关；而中心脉压主要反应中心动脉功能也心脏靶器官损害有关；在认知功能、动脉硬化上外周脉压与中心脉压各有利弊，说法不一，有待进一步研究。

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