综 述

血管内皮功能的无创检测方法、临床相关因素及应用

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摘要：血管内皮是人体重要的组织器官之一，具有重要的生理意义。采用无创检测血管内皮功能，了解其影响因素，对认识疾病的发生、发展及评估预后具有重要的意义。本文着重对无创血管内皮功能检测的方法、影响因素及其应用做一概述。
关键词：血管内皮功能；检测；影响因素；应用
中图分类号：R 363 **文献标志码：**A **文章编号：**2095-5227(2016)03-0283-03 **DOI：**10.3969/j.issn.2095-5227.2016.03.022
网络出版时间：2015-12-04 16:57:21 **网络出版地址：**http://www.cnki.net/kcms/detail/11.3275.R.20151204.1657.002.html

Influencing factors and application of noninvasive vascular endothelial function testing method

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Abstract: As part of human tissues and organs, vascular endothelial tissue has great physiological significance. Noninvasive testing of vascular endothelial function, with good understanding of its influencing factors, is extremely helpful in identifying and evaluating of the causes, development and prognosis of diseases. In this article, we review noninvasive testing methods of vascular endothelial function, its influencing factors and applications.
Keywords: vascular endothelial function; detection; influencing factors; applications

血管内皮是介于循环血液与血管平滑肌之间的生理屏障，它是人体内最大的内分泌器官，也是许多心血管激素酶激活及失活的部位。内皮通过复杂的细胞膜受体和信号转导机制感受和应答大量内部和外部刺激，从而合成和释放许多血管活性物质、凝血调节物质和生长因子等，在维持血管舒张、抑制血小板聚集及平滑肌细胞增生等方面起着关键性的作用[1]。由于其重要的解剖位置，内皮已成为血管损伤、机械冲力及心血管病危险因素(如吸烟、高胆固醇血症等)首要侵犯的靶器官。

1 无创血管内皮功能检测的方法

目前能够无创性检测血管内皮功能的方法主要有高分辨率超声检查肱动脉血流介导性舒张(FMD法)[2]、低血流介导血管收缩检测(L-FMC)[3]以及指端反应性充血前后的动脉脉搏容积变化检测(PAT法)[4]。FMD法是用袖带阻断肱动脉或股动脉血流，然后释放袖带气体而引起动脉内反应性血流增加，血流增加带来的切应力作用于血管壁，促进一氧化氮(NO)的释放，导致血管舒张，通过高频超声设备测量血管管径的变化来衡量血管内皮功能。L-FMC法通过检测血流减低或阻断状态下血管直径变化来评估内皮功能。由于FMD法和L-FMC法均需要超声仪器辅助，且可在同一检测过程中同时获得数据，故上述两种方法常合并使用。但上述两种方法均需人工操作高频超声设备，对结果的一致性有一定影响。PAT法通过测量阻断肱动脉血流前后指尖脉搏波振幅来评价内皮功能。主要检测指标包括反应性充血指数(reactive hyperemia index，RHI)及动脉增强指数(augmentation index，AI)。它完全依靠设备仪器检测，没有人为参与，具有简便易行，稳定性、重复性好的优点[5-6]。有研究提示上述方法侧重点并不相同，FMD法侧重于评价大血管内皮功能，包括外周大动脉及冠状动脉；L-FMC法主要评价大动脉内皮功能并侧重于基础静息状态下的内皮反应性；PAT法则侧重于评价微血管内皮功能[7]。

2 无创血管内皮功能检测结果的影响因素

对于普通成年人，无创血管内皮功能检测结果的影响因素主要有3方面：1)传统的心血管危险因素，主要包括人种、性别、年龄、体质量指数(body mass index，BMI)、腰围、腰臀比、空腹血糖、糖尿病、吸烟、总胆固醇、三酰甘油、高密度脂蛋白、糖化血红蛋白、心率等[4, 8-11]，即上述危险因素可能导致内皮功能的恶化。Toggweiler等[12]研究亦提示内皮功能与心血管病危险因素相关。2)精神心理因素。有研究提示工作压力及昼夜节律颠倒对内皮功能产生不利影响[13]。同时有研究指出，PAT法测定的内皮功能对急性心理应激更为敏感[14]。PAT结果同样与青少年心理状态相关[15]。3)神经系统因素。Sverrisdottir等[16]明确了内皮功能受交感神经系统影响。上述3方面影响可能与多种因素导致动脉硬化、血管内皮增生、钙化、纤维化及氧化应激、炎症、血管平滑肌增生、胶原沉积等有关[17-19]。而运动导致的交

收稿日期：2015-09-04
基金项目：国家自然科学基金项目 (30872731)
Supported by the National Science Foundation of China(30872731)
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感神经兴奋，推测可能是通过提高NOS及SOD等酶的活性而改善内皮功能[16]。

3 无创血管内皮功能检测的应用

由于血管内皮功能被证实与多种因素相关，并互为因果。所以血管内皮功能已经成为多种病理生理过程以及疾病的发生、发展、预后评价中重要的指标，是基础与临床之间的重要桥梁。无创血管内皮功能检测由于其便捷性及稳定性，目前已用于多方面的监测及评估。

3.1 健康人群内皮功能的监测 血管内皮功能的变化，往往意味着血管机械功能、生理功能、内分泌功能甚至神经功能的变化。对于大规模健康人群，与健康状况具有良好相关性的无创血管内皮检测得到了广泛的应用。如应用PAT法监测大气污染以及吸二手烟对内皮功能的损害，并进一步明确了改善大气条件及控制吸烟可使之逆转[20-21]。Li等[22]明确进食高脂肪食物后损害内皮功能，黑巧克力可改善轻度高血压肥胖患者的内皮功能[23]。对于非成年人，PAT同样可以用于其血管功能的评价[24]。青年人食用能量饮料后可使RHI降低[25]。食用橄榄油可增加RHI指数[26]。肥胖并胰岛素抵抗的青少年出现内皮功能损害[27]。

3.2 患病人群疾病的认识及评估 心血管疾病与内皮功能具有多种共同的影响因素，如性别、年龄、BMI、腰围、腰臀比、空腹血糖、糖尿病、吸烟、总胆固醇、三酰甘油、高密度脂蛋白、糖化血红蛋白等，故血管内皮功能可能为危险因素和疾病之间的重要中间因素，即诸多心血管危险因素导致了血管内皮功能受损，从而进一步影响疾病的进程。相反，疾病可导致血管内皮功能受损，从而出现多种病理过程。目前已有多项研究采用血管内皮功能评估疾病的发生、发展及预后。有研究指出，RHI是糖尿病患者冠状动脉粥样硬化的独立预测因子[28]。Kurose等[29]发现肥胖患者改善生活方式后，其内皮功能好转。代谢综合征患者改善生活方式后也可使内皮功能好转[30]。PAT可以对稳定心绞痛患者进行危险分层，并帮助识别血管剩留风险[31]。冠心病患者若内皮功能受损，则更易因精神紧张出现心肌缺血[32]。PAT亦可预测冠心病患者运动后的心肌缺血[33]。对于高危冠心病患者，其心血管事件亦与内皮功能相关[30]。舒张性心衰患者的内皮功能存在异常[34]，PAT检测可以预测舒张性心衰患者预后[35]。并有研究提示，FMD及PAT是心血管事件和全因死亡的独立预测因子[36-37]。血管内皮功能检测可用于非心脏手术的危险分层[38]。

3.3 疾病治疗或干预措施的评估 治疗或干预措施可能通过改善血管内皮功能而对疾病产生影响。可应用无创内皮功能检测评估经桡动脉介入术后患者的血管功能[39]。血管内皮功能可反映氯吡格雷对血小板的抑制程度[40]。内皮功能的改善，意味着充血性心衰患者心脏再同步化治疗有效[41]。而内皮功能差，可能与单纯右心起搏治疗的合并症相关[42]。通过内皮功能的监测，可知急性心梗患者应坚持适当的伸展运动[43]。对于老年心衰患者，由内皮功能的改善程度可知辅助蹬车运动较传统运动更好[44]。

4 结语

综上所述，无创血管内皮功能的检测方式本身具有一定的稳定性及一致性，可操作性较强。此方法检测的内皮功能已证实与多种因素相关，并可进一步与疾病建立联系。通过了解机体在各因素作用下血管内皮功能变化，可以评估疾病的发生、发展及预后。可以预见，无创检测血管内皮功能，将更多参与到研究以及临床诊疗之中。

尽管目前无创检测血管内皮功能的研究较多，但其仍处于初级阶段。对血管内皮功能变化的机制、影响因素以及作用方式等缺乏系统、全面的阐述。与疾病建立的联系仍较零散，缺乏大规模、大样本临床研究。虽然检测的一致性较好，但仍无法准确检测特定人群，如上臂血管畸形、狭窄，血压偏低等；操作水平以及环境因素也可能对结果产生较大影响。现仍缺乏高龄老年人群的研究数据。需要在今后的研究中逐渐完善。

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