

卵圆孔未闭相关疾病的诊治进展

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【摘要】 卵圆孔未闭是一种常见的先天性心脏病, 且与多种疾病包括隐源性脑卒中、先兆性偏头痛、减压病、低氧血症等相关。该文介绍卵圆孔未闭相关疾病的诊疗状况。

【关键词】 卵圆孔未闭; 隐源性卒中; 先兆性偏头痛; 减压病; 低氧血症

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卵圆孔是房间隔中原发隔与继发隔之间的一个通道, 在胎儿血液循环中, 来自胎盘的含氧血液可通过此孔道从右心房流入动脉循环, 供养胎儿的身体发育。胎儿出生以后, 胎盘血液循环终止, 肺循环开始建立, 卵圆孔关闭。若 3 岁之后此通道仍未闭合称为卵圆孔未闭 (PFO)。PFO 在直径、长度以及与周围结构的关系方面具有较大的异质性, 孔径较大、右向左分流 (RLS) 量大、合并房间隔膨出瘤、长欧式瓣或希阿里氏网的 PFO 的致病性较高^[1]。高危 PFO 与隐源性卒中、先兆性偏头痛、减压病、低氧血症等疾病显著相关。

1 隐源性卒中

隐源性卒中是临床上诊断评估不充分、经过充分评估仍未发现病因或多种病因并存但无法确定病因的一种卒中分型^[2]。在隐源性卒中人群中, PFO 的发生率高达 40%^[3], 可能机制包括静脉系统血栓穿过 PFO 至脑血管形成栓塞、PFO 内形成原位血栓、房性心律失常。反常性栓塞风险 (RoPE) 评分是目前临床评估 PFO 相关卒中的工具^[4], 但由于存在缺少 PFO 解剖特点等缺陷, 只能将该评分工具作为参考。

多项随机对照试验表明, 相较于内科药物治疗, 封堵术可显著降低 PFO 合并卒中复发的风险^[5-8]。1 项荟萃分析显示, 在隐源性卒中合并 PFO 患者中, 封堵术在减少卒中和短暂性脑缺血复发方面优于药物治疗^[9]。1 项纳入 1 565 例患者的荟萃分析发现, 与抗血小板治疗相比, 接受抗凝治疗

的患者在预防卒中复发中无临床净获益, 但对于 RoPE 评分较高的患者, 抗凝治疗可显著降低卒中复发风险^[10]。抗凝治疗优于抗血小板治疗, 且不增加出血风险^[11]。

2 先兆性偏头痛

研究发现, 先兆性偏头痛与 PFO 显著相关^[12-13], 可能机制包括: (1) 引起偏头痛的代谢物和血管活性物质如 5 羟色胺和缓激肽等绕过肺过滤器, 直接通过 RLS 引起偏头痛^[14]; (2) 体循环中的微栓子通过 PFO 直接进入动脉系统, 导致微栓塞, 触发低灌注^[15], 同时微栓塞引起血氧饱和度降低, 引发皮质扩散抑制, 导致偏头痛^[16]; (3) 遗传因素^[17]。

PFO 封堵术治疗偏头痛未显示显著优越性^[18-20]。但 PFO 封堵术可以停止或减少先兆偏头痛患者的发作次数和持续时间^[21]。中重度的 RLS 对偏头痛的临床特征有显著影响, 经皮 PFO 封堵术能显著缓解偏头痛症状^[22]。1 项纳入患 PFO 相关隐源性卒中和偏头痛的成年患者的研究发现, 相较于单独抗血小板治疗, PFO 封堵术联合抗血小板治疗无法减少偏头痛发作的年平均次数^[23]。P2Y₁₂ 血小板抑制剂可能减轻 PFO 患者的偏头痛症状, 表明偏头痛的发病机制可能与血小板的活化有关^[24], 因此, 术后抗血小板药物应作为评价 PFO 封堵疗效的重要混杂因素。

3 减压病

减压病是指在外界压力骤减之后, 体内溶解的气体游离, 形成血管泡和血管外泡, 从而引发一系列病理生理的过程, 其中损害发生在神经系统的为神经减压病。减压病的易感人群以潜水员多见。当潜水员快速上升时, 氮气溶解在血液中, 可通过 RSL 进入动脉血液, 导致各种急性临床症状, 严重者有致残或死亡。在有 RSL 的潜水员中, 减压病

更常见。分流量大的 PFO 是潜水员发生减压病的主要危险因素^[25]。PFO 封堵术可能是治疗 PFO 伴减压病的有效方法^[26]。1 项比较 PFO 封堵和保守治疗的研究表明,直径较大 PFO 或减压病严重的患者可能受益于 PFO 封堵术^[27]。但有研究提示,即使成功闭合 PFO,减压病也可能复发^[28]。目前尚无足够的证据表明 PFO 封堵术是减压病的首要预防措施,尚需大量随机对照试验来评估 PFO 封堵术治疗减压病的疗效。

4 低氧血症

平卧呼吸 - 直立性低氧血症综合征 (POS) 是一种罕见且临床上易被漏诊的疾病,以直立位时的体位性呼吸困难和动脉饱和度降低 (SaO_2 或 $\text{SpO}_2 < 90\%$ 或 $\text{PaO}_2 < 60 \text{ mmHg}$) 为特征,一般发生于成年患者,当患者仰卧时动脉血氧饱和度正常,而直立时血氧饱和度突然下降。POS 的可能病因包括心内分流、肺水平分流和通气 - 灌注不匹配。高海拔肺水肿 (HAPE) 也与 PFO 相关,PFO 在 HAPE 易感的登山运动员中发生率较高,在高海拔地区,具有较大 PFO 的 HAPE 易感者低氧血症更严重^[29]。阻塞性睡眠呼吸暂停低通气综合征 (OSAHS) 与 PFO 相互作用,可加重原有疾病的发生发展。李肖楠等^[30]对 OSAHS 合并 PFO 患者的研究发现,PFO 通过多种机制改变 OSAHS 患者的睡眠结构,可加重 OSAHS 患者的睡眠障碍程度。

关于封堵 PFO 对 POS 潜在益处的数据尚不足,排除肺部疾病导致的严重缺氧以及严重的临床症状后,可以考虑 PFO 封堵术。PFO 封堵可以解决体位性呼吸困难和低氧血症,是治疗 POS 的有效方法^[31]。对于 PFO 合并高海拔肺水肿及 OSAHS 患者,封堵术可使患者获益,但慢性重度肺动脉高压患者不适用^[32]。

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