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血小板相关指标在假体周围感染诊断中的研究进展

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摘　要

假体周围感染(Periprosthetic Joint Infection, PJI)作为关节置换术后常见的并发症之一，早期的诊断可以极大改善病人生活质量及降低治疗负担。虽然PJI的诊断近年来得到不断的完善和发展，但目前仍是一个难题，它需要血清学、组织病理学、影像学等各方面检验、检查结果进行综合判断，需要较高的检查费用且经常是有创检查；近年来，越来越多学者认为血小板相关指标对于假体周围感染有一定的早期筛查、诊断价值，并且有许多文章报道了血小板相关指标对PJI有较高的敏感性与特异性，这种血液指标的检验既简便快捷，又有数字化的检验结果，有较高的准确性，可以将其作为早期诊断PJI的参考工具。

关键词

关节假体周围感染，血小板计数，平均血小板体积，大血小板比率，关节置换手术

Advances in Platelet-Related Markers in the Diagnosis of Periprosthetic Joint Infection

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Abstract

Periprosthetic Joint Infection (PJI) is a common complication that can occur after arthroplasty.

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Early diagnosis of PJI is crucial as it can significantly improve patients' quality of life and reduce the burden of treatment. Although the diagnosis of periprosthetic joint infection (PJI) has improved in recent years, it remains a challenging problem. It requires a comprehensive assessment of serology, histopathology, imaging, and other test and examination results. This comprehensive approach often incurs high examination costs and is invasive. In recent years, an increasing number of scholars have recognized the potential of platelet-related indexes in the early screening and diagnosis of PJI. Numerous articles have reported that platelet-related indexes exhibit high sensitivity and specificity for PJI. Moreover, the blood test for these indexes is simple, quick, and provides accurate digital results. Therefore, platelet-related indexes can serve as a valuable reference tool for the early diagnosis of PJI.

Keywords

Periprosthetic Joint Infection, Platelet Count, Mean Platelet Volume, Large Platelet Ratio, Joint Replacement Surgery

1. 引言

随着近年来全球人口老龄化的发展趋势，关节置换手术作为骨性关节病的晚期根本治疗方式，其无论从数量还是术后生活质量方面都在骨科手术中越来越占据着重要的位置[1]，虽然近年来关节置换手术所使用的假体材料不断进行改进且手术技术也不断趋于成熟，但是假体周围感染(PJI)仍然是关节置换术后高发病率伴随高昂医疗费用的并发症[2]，是极具灾难性的并发症，虽然它在关节置换术后可能的病发率数值上较低，但我们全球有着庞大的老龄人口基数，其在骨科并发症中也因此占据着非常重要的地位[3]。Jämsen 等人的研究表明，糖尿病、肥胖会增加 PJI 的发生几率：体重指数正常的患者在关节置换术后发生感染的机率为 0.37% (95%CI，0.15%至 0.96%)，而病态肥胖组的感染率为 4.66% (95%CI，2.47%至 8.62%)；当患者术前血糖 < 6.9 mmol/L 时，其关节置换术后的感染率为 0.28% (95%CI，0.15%至 0.53%)，而术前血糖 ≥ 6.9 mmol/L 时，术后感染率为 3.3 (95%CI，0.96 至 11.0) [4]。也有研究表明，营养不良是增加 PJI 风险的一个因素[5]。当 PJI 发生后根本治疗方式仍然是关节翻修手术，这一术后风险和高昂的治疗费用无疑给预进行关节置换或已经行关节置换手术的患者带来巨大担忧与困扰。本病本身是一个慢性疾病，早期所表现的症状主要是非特异性的[6]，且其病情发展也仅是进行性的假体松动伴疼痛加重，这就不可避免的致使患者就医延迟，致使许多病例就医诊断时已发生不可逆转的延迟，诊断延迟是致使其预后较差的主要原因之一[7] [8] [9]，所以在关节置换手术早期诊断其发生的可能性就显得非常重要。目前国际主流的诊断标准为肌肉与骨骼感染协会(Musculoskeletal Infection Society, MSIS) 2011 年所给出的诊断共识[10]，本指南中与假体发生相通的窦道在临床上其实发生的几率是比较低的，虽然它的诊断价值很高，但是临床实用性并不高，凭借此项单独诊断的病例并不占据很大比率；本身 PJI 的致病菌可能是来自于皮肤、牙龈、泌尿道、呼吸道等位置，细菌的培养阳性率也是不尽相同的，很多的细菌的感染又可能是低毒性的，所以能够两次培养到相同致病菌的几率也是有一定困难的[11]；这就致使其余六项次要诊断在 PJI 的诊断中占据比较重要的位置，而关节液的抽取又受到自身基础疾病和解剖位置的影响，可能无法抽到所需关节液；最近，一种新的诊断 PJI 的即时检测 Synovasure™ 测试也显示了巨大的诊断

潜力。然而，关节滑膜液的抽取本身就存在感染风险和一定的操作难度[12]。并且关节滑膜液并不存在单一测试，与许多测试都是相关的，比如 SF-NGAL 等指标也存在其中[13]。血液指标的获取操作简便快捷、感染风险低、结果数值化，致使血液检验指标在 PJI 的诊断中占据着重要的位置。探求一个具有单独高诊断价值的指标就显得非常重要，近年来，越来越多的学者积极探索新的血液指标尤其是血小板相关指标作为诊断 PJI 的诊断新指标[14]，甚至许多临床大夫也将其作为确诊 PJI 的一种辅助参考[15]。本综述旨在阐述各项血小板相关指标对假体周围感染的诊断建议的最新信息。

2. 血小板计数(Platelet Count, PLT)与 PJI

血小板及其相关指标对于 PJI 的诊断价值，近几年来也是国内外学者研究的热门。血小板作为人体三大血细胞之一，本身就是一种原始的免疫细胞，对于外界病原体的侵入具有一定的免疫应答的能力[16]，例如，血小板为免疫细胞制造许多化学引诱剂，在其表面具有细菌和病毒产物的受体，释放抗微生物活性物质并杀死各种病原体[17]。在癌症化疗期间，低血小板计数可能预示着较为严重的感染发生可能[18]，这无疑给我们诊断 PJI 时提供了一定的参考；并且血小板越来越被认为是一种免疫调节剂，Kirschenbaum 等人[19]报道，血小板增强了感染性休克患者血浆中暴露的正常中性粒细胞的聚集和内皮细胞粘附。此外，血小板富含促炎药物，能释放高活性微粒[20] [21]。血小板也可能在呈现抗原和对抗感染[22]的过程中发挥关键的作用。Greig 等人[23]通过小鼠模型研究表明，血小板的减少会致使小鼠的细菌负荷增加，是 PJI 的一个潜在危险因素。Cao 等人[14]也通过回顾性病例对照研究发现 PJI 患者血小板值显著升高，并且得出了“与红细胞沉降率和 C 反应蛋白相比，血小板显示出更高的准确性”这一令人振奋的结论。Xu 等人的研究表明[24]，虽然血小板计数(platelet count, PLT)的 AUC (ROC 曲线下面积)小于红细胞沉降率(erythrocyte sedimentation rate, ESR)、C 反应蛋白(C-reactive protein, CRP)和血浆纤维蛋白原的 AUC，但血小板计数可能是诊断 PJI 有用的标志物，敏感性为 57.5%，特异性为 83.1%。术前常规测量血小板计数，方便、快速。血小板计数可能是在关节置换术前筛查 PJI 的很有前途的生物标志物。

3. 血小板与平均血小板体积之比(Platelets Count to Mean Platelet Volume, PVR)与 PJI

目前在 PJI 的诊断方面国内外主流的研究方向是将血小板参数之间的指标进行联合评判，尤其是血小板计数与平均血小板的比值，其相比于单独的血小板参数更具有临床价值。因为他已经在许多的领域展现出很高的诊断价值，PVR 升高已被证明是预测重度脓毒症患者结直肠癌发病[25]和死亡率的有用血液学标志物[26]，并且此项指标在心血管病理学中越来越受到关注[27] [28]。Paziuk 等人[15]首次将 PVR 应用在假体周围感染的领域之中，证明了 PVR 在预测 PJI 中具有较高的潜力，Tirumala [27]等人研究表明 PVR 的灵敏性与特异性可与红细胞沉降率媲美，但也有研究表明 PVR 对于 PJI 的诊断相关性有较差的表现，但是他们的研究具有本地区域性，所以这种差异可能与地区、人群具有相关性。Shang 等人[29]的研究表明，此种差异可能与手术位置差异有关，其研究表现出不同诊断指标的诊断价值因研究的位置不同(如髋、膝关节)而发生变化。。更有研究表明，血小板与血清学指标联合后会显著提升其诊断 PJI 的敏感性及特异性，Sahin 等人[30]的研究结果表明，PJI 组患者血小板与平均血小板体积(PVR)之比的均值明显高于对照组无菌松动组，且这种差异是有明显统计学意义的。但是，作为一种新兴指标，也存在研究出现了相反的结果，Huang 等人[31]的研究表明，PVR 在 PJI 诊断中的敏感性低于 ESR，且 PVR 在 PJI 诊断中的特异性与 CRP 和 ESR 相似。虽然得出了相反的结论，但是 Huang 等人的纳入研究患者明显要少于 Paziuk 等人的研究，所以我们怀疑，可能需要更大规模的高质量研究来补充 PVR 对于 PJI 的诊断价值。

4. 其他血小板指标与 PJI

对于假体周围感染的诊断，血小板的一些其他指标也逐渐被挖掘出来，比如代表血小板数量、大小和活性的血小板相关指标，如血小板密度(plateletcrit, PCT)和血小板分布宽度(platelet distribution width, PDW)，被认为是血小板活化的标志物，在局部炎症患者中通常升高[32]。也有报道提示，PCT 水平的增加与重症监护病房患者的感染和医院死亡率相关[33] [34]。但是目前来说，对假体周围感染的诊断更多的是停留在血小板与 PVR 这两项指标上面，PCT 和 PDW 并不是当前研究热度，所能检索到的研究也是屈指可数，仅有部分文献对其进行了相关的研究，Qiao 等人[35]的研究提示，PCT 的诊断价值仅为中等，PDW 表现较差，ROC 曲线的曲线下面积分别为 0.726 和 0.677 相较于血小板和 PVR 这些指标(ROC 曲线下面积分别为 0.750 和 0.750)，没有明显的诊断优势。Shang 等人评估了 PCT 诊断 PJI 的可能性，虽然 PCT 的 ROC 曲线下面积在血小板相关标志物中最低(ROC 曲线下面积分别为：PCT，0.706；PVR，0.718；PLT，0.727)，但其敏感性优于血小板和 PVR (敏感性：PCT，68.4%；PVR，62%；PLT，65.8%)。研究表明，PCT 和 PDW 目前对于 PJI 的诊断价值可能并不像 PLT 和 PVR 那样令人兴奋，但是鉴于目前仅能检索到较少的文献，并且其联合诊断价值、其与血小板的比值是否会像平均血小板体积一样有着诊断 PJI 的不凡潜力尚需更谨慎丰富的研究来补充。

5. 结局与展望

血小板及其相关指标与 PJI 是具有一定相关性的，尤其是血小板计数和血小板与平均血小板体积的比值这两项指标，当然，目前没有充分证据表明它可以取代血沉及 C 反应蛋白在 PJI 诊断中的地位，但是它对于诊断有潜在假体感染风险的患者是非常有价值的，尤其是存在于其联合诊断价值，血小板计数和 PVR 联合血清学及滑液参数其诊断的灵敏性与特异性也会相比于 MSIS 所列出的仅联合 C 反应蛋白与红细胞沉降率都表现出更高的临床价值，所以说，血小板相关指标对于 PJI 的诊断是值得研究和期待的，但是其更为确切的诊断能力还需要更为广泛的前瞻性研究数据来支持。

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