

心脏瓣膜置换术后非外科性出血的相关因素分析及术后精准输血的相关进展

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【摘要】 心脏瓣膜置换术是心外科最常见的手术,而非外科性出血又是其术后最常见的并发症。导致患者术后非外科性出血的原因众多,可概括为疾病本身、体外循环人工装置及术中特殊要求这 3 个方面,具体包含肝功能异常、体外循环前放血稀释、体外循环管道、氧合器及血泵,低温、血液稀释、鱼精蛋白与肝素的中和等。目前对于术后出血大部分医院还是以出血量和凝血试验结果为依据进行输血,少数医院已经开始利用血栓弹力图进行精准输血,但仍属于探索研究阶段,目前尚无统一标准。本篇综述将以致心脏瓣膜置换术后非外科性出血的相关因素及术后精准输血和减少输血的理念为重点进行论述,以期预防再次开胸止血的发生。

【关键词】 血液凝固障碍; 体外循环; 心脏瓣膜疾病

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Analysis of factors related to non-surgical hemorrhage and related progress of precise blood transfusion after cardiac valve replacement surgery

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【Abstract】 Cardiac valve replacement is the most common surgical procedure in cardiac surgery, which often results in non-surgical bleeding. There are many factors that cause non-surgical bleeding after cardiac surgery, which can be summed up as the disease itself, the artificial device of cardiopulmonary bypass and the special requirements during the operation, including the abnormality of liver function, extracorporeal circulation conduits, oxygenators and blood pumps, hypothermia, hemodilution, neutralization between protamine and heparin. At present, most hospitals still use the results of blood loss and coagulation test as the reference for blood transfusion. Only a few hospitals have used thromboelastogram to guide blood transfusion, which is still in the exploratory stage, so far there is no unified reference standard. This review will focus on the related factors leading to non-surgical bleeding and the concept of accurate blood transfusion and reducing blood transfusion after heart valve replacement in order to prevent the occurrence of rethoracotomy to hemostasis.

【Key words】 Blood coagulation disorders; Cardiopulmonary bypass; Heart valve diseases

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自 1960 年心脏瓣膜置换术 (Cardiac valve replacement, CVR) 开创以来,每年达到 CVR 指针的患者占成人心脏病手术的首位,而其术后最常见的并发症即是非外科性出血^[1]。有报道称 2% ~ 5% 的患者因非外科性出血需再次开胸止血,显著增加了术后病死率及并发症发生率,而导致非外科性出血的主要原因即疾病本身、体外循环人工装置和术中特殊要求^[2]。目前对于非外科性出血的处理仍然是输血,而在我国绝大部分医院仍以术中出血量及凝血试验结果作为参考依据。但凝血试验本身在指导患者术后输血方面

是有限的^[3-4]。本文将对心脏瓣膜病本身、体外循环人工装置及体外循环术中特殊要求等导致 CVR 术后非外科性出血的相关因素进行深入分析,强化术后精准输血及减少输血理念的重要性,以加快对血栓弹力图 (Thromboelastography, TEG) 指导术后输血的完善,进而降低心脏术后二次开胸止血的发生率。现综述如下。

1 心脏瓣膜置换术后非外科性出血的相关因素

1.1 疾病本身

临床上心脏瓣膜病患者多有肝功能受损的情况,

进而对凝血因子的生成造成影响,若患者肝功能受损严重导致门静脉高压则可导致脾脏功能亢进,进而对血小板造成损害。此外患者长期的缺血缺氧状态导致体内红细胞增多,但凝血物质并未相应增加,术前为达到体外循环血液稀释的标准,常需放血行等比稀释,导致凝血物质的进一步减少。

1.2 体外循环人工装置

1.2.1 管道 体外循环管道主要起运输血液的作用,由生物高分子材料组成,因其与血液的生物相容性不佳。当血液与体外循环管道内表面广泛接触时可造成凝血因子及血小板的过度消耗。究其原因主要是体外循环可诱发全身炎症反应综合征,进而激活凝血系统产生抗凝物质^[5-6]。再者血液接触体外循环管道后也可直接导致细胞因子的释放和体液级联反应系统的激活,进而激活凝血、纤溶系统导致患者凝血功能紊乱^[7]。

1.2.2 氧合器和血泵 血泵是体外循环中促进血液流动的动力装置,而氧合器是血液在体外进行气体交换的装置。血泵运转时形成的负压使其对流过它的血液细胞产生剪切力的作用,从而破坏血液中的有形成分^[8]。同时也能影响血液中血管假性血友病因子的结构,使其增加对血小板表面糖蛋白受体 GP II b、GP III a 和 GPIIb α 的亲合力,进而活化血小板^[9]。有研究表明血小板功能和数量的改变是体外循环造成 CVR 术后非外科性出血的主要原因^[10]。此外血液有形成分的破坏必将导致体外循环血液中酸性物质的增多而降低凝血因子的活性。有文献指出当血液 pH 值从 7.4 降到 7.0 时,凝血因子 VII a 及 VII a/TF 复合物的活性将显著降低,同时因子 Xa/Va 激活凝血酶原的速率将明显下降^[11]。

1.3 体外循环术中特殊要求

1.3.1 低温 低温是体外循环术中心脏停跳后各组织器官特别是脑组织的保护措施,其可降低患者基础代谢率及耗氧量,从而达到保护患者各脏器的作用,同时也减少了体外循环灌注量,增加了体外循环的安全性。但也显著降低了凝血酶活性及血小板功能。研究表明当体温低于 36 °C 后,随着体温的降低,凝血酶生成率下降,凝血时间延长^[12-13]。对血小板而言,低温主要影响其聚集功能,但影响程度有限,因为复温后血小板的聚集功能可部分恢复^[14]。

1.3.2 血液稀释 体外循环需通过预充相应的液体来排出体外循环机中的气体,同时预冲液进入人体后会造成患者血液的稀释,降低血液黏度,减少凝血物质的消耗,减轻术中炎症反应,但同时也降低了凝血因子与抗凝血因子的浓度。研究表明凝血因子的水平只需

达正常的 20% ~ 30% 即可满足基本凝血需求,术后纤维蛋白原只需术前的 50% 便可止血^[15-16]。但也有研究表明因抗凝血酶的活性较凝血酶更易受到血液稀释的影响而导致患者凝血功能紊乱^[17]。

1.3.3 肝素与鱼精蛋白 体外循环术中需全身肝素化以防止血液在管道中凝集,而停循环后又需用鱼精蛋白来中和肝素。肝素主要与抗凝血酶-III 结合形成肝素-抗凝血酶-III 复合物以降低 Xa 因子活性,而鱼精蛋白的作用主要是从其复合物中置换出肝素,阻止抗凝血酶-III 构象改变。但鱼精蛋白中和肝素的用量不易把控,用量过少则肝素中和不全。过多则可通过干扰凝血激酶的活性导致渗血增多^[18]。

2 术后精准输血

随着科技和医学的发展,体外循环有了很大的改进,如高分子生物材料的生物相容性及抗凝特性的提高,血泵及氧合器的更新换代等,均降低了体外循环对 CVR 患者凝血功能的影响,但其程度有限,CVR 术后仍需通过输血来改善患者凝血功能。但至今还没有统一有效的预测心脏术后输血需求的检测方法^[19]。长期以来,我国临床医师主要依据术中出血量及传统的凝血检测结果进行输血,但常规凝血试验只是检测凝血瀑布级联反应中的一部分,即内源性或外源性凝血途径,或纤维蛋白溶解部分的情况,所以凝血试验本身在指导患者术后输血方面是有限的^[3-4]。

TEG 检测的是凝血全貌,了解的是血液凝固的动态变化情况,并且 TEG 能够较快的显示检测结果,这也是其在临床上广受关注的原因之一。早在 1999 年 Shore-Lesserson 等^[20]就证实 TEG 可应用于心脏术后的输血。2013 年 Bolliger 和 Tanaka^[21]也表明在指导输血方面 TEG 明显减少了输血量。更有文献表明如果患者凝血试验结果异常而 TEG 结果正常时,可考虑暂不予输注血制品^[22-23]。现今临床上通过 TEG 的各项指标来指导输血,已经取得了很大的进步。具体是以凝血时间 R 值作为输注新鲜冰冻血浆的依据,以最大血块强度 MA 值(反映正在形成的血凝块的最大强度或硬度及血栓形成的稳定性)来决定是否输注血小板、以血块形成速率 K 值(指从 R 时间结束到振幅达到 20 mm 所用的血凝块形成时间)和 Angle 值(是指从血凝块形成点到描记图最大曲线弧度作切线与水平线的夹角)来判断是否输注冷沉淀。但具体输血方案尚未统一,几篇文献的输血方案均不同^[24-26]。

CVR 术后应用 TEG 指导输血可个体化、精准化,使输血更加安全有效。但 TEG 也有一定的局限性,正常情况下,凝血以血小板黏附于受损的血管壁为起

始,但 TEG 无法检测这种血小板和血管内皮的相互作用。典型例子即 VwF 因子缺乏的患者,其血凝块功能可以正常,但因血小板与血管内皮之间黏附性差,导致血凝块不能黏附到受损的血管壁而造成出血^[27]。此外 TEG 因测试的技术方面和激活剂的种类、浓度与质量的不同导致其指导临床输血的参考值还备受争议^[28-33]。但根据 2011 年 Afshari 等^[34]对心脏外科患者进行了一项大型回顾性研究,并对出血患者进行了一项 Meta 分析,均未表明 TEG 对术后并发症的发生率和病死率有关,即从安全性的角度说明了 TEG 指导术后输血的可行性。

虽然术后精准输血取得了很大的进步,但对血制品的需求仍然很大。2011 年邓硕曾和纪宏文^[35]在对《心脏手术血液保护指南》的解读中指出我国自 2007 年以来心脏手术输血率超过 70%,对血液的供应已经造成了巨大的压力。2016 年美国一项研究表明心脏手术消耗了近 20% 的异体血^[36]。目前全球的血液供应都很紧张,况且输注异体血的并发症较多,例如输血相关肺损伤,循环超载,急性呼吸窘迫综合征,免疫调节和病原体的传播等^[37-40]。甚至有研究表明输血已成为心脏术后并发症发生率及病死率的独立危险因素^[41]。故而从精准输血到减少输血的过度迫在眉睫。

有研究表明纤维蛋白原浓缩物和凝血酶原复合物浓缩剂的使用可显著改善患者凝血功能及减少异体血的输注量^[42-44]。因为纤维蛋白原可以通过连接血小板糖蛋白 II b/III a 受体促进血小板聚集,增加纤维蛋白凝块的硬度^[45-46]。而凝血酶原复合物可以通过改善凝血酶的生成来纠正凝血时间的延长^[42]。

3 总结与展望

通过对 CVR 术后非外科性出血相关因素的深入研究,目前,对心脏术后非外科性出血的处理已取得了较大的进步。首先是体外循环装置的改进,使其对患者的血液保护作用有了很大的提高;同时指导手段也从传统的凝血试验变为了 TEG。就目前对 TEG 指导输血的报道而言,基本达到了个体化及精准化输血,但其参考标准仍然存在很大争议。根据对临床实践中的观察及探索发现体外循环术后凝血因子的损害较重,且 TEG 指标 R 值的可靠性远较其他指标低,故而在此希望有更多关于体外循环对凝血因子损害的研究,以加快对 TEG 指导术后输血的完善,进而降低心脏手术后二次开胸止血的发生率。

利益冲突 所有作者均声明不存在利益冲突

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聚醚醚酮及其复合材料在创伤骨科内置物中的研究进展

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【摘要】 聚醚醚酮有力学性能优良、生物相容性佳、耐腐蚀、抗疲劳、耐高温、可透 X 线等诸多优点。近年来,越来越多的研究探索聚醚醚酮及其复合材料应用于骨科内置物,其有望代替钛合金成为骨科置入物的主要材料,但在用于骨折固定的钢板螺钉系统和髓内钉中应用仍相对较少且不成熟。本文将对近年来聚醚醚酮及其复合材料应用于创伤骨科内置物的研究进展作一回顾与总结。

【关键词】 生物相容性材料; 内固定器; 骨板; 骨螺丝

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Research progress of polyether ether ketone and its composites in Orthopedic trauma implants

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【Abstract】 Polyether ether ketone exhibits considerable advantages, such as excellent mechanical properties, good bio-compatibility, corrosion resistance, fatigue resistance, high temperature resistance and X-ray transmission. In recent years, substantial researches have been reported to explore the applications of polyether ether ketone and its composites in orthopedic implants development, which is expected to replace titanium alloy as the main material. However, the application of polyether ether ketone in plate-screw system and intramedullary nail used in fracture fixation is still scarce, and yet not well-rounded. This article reviews and summarizes recent research progress of polyether ether ketone and its composites used in orthopaedic trauma implants.

【Key words】 Biocompatible materials; Internal fixators; Bone plates; Bone screws

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聚醚醚酮是一种全芳族半结晶热塑性工程塑料,这种聚合物由主链结构中含有酮键和两个醚键的重复单元组成,属于特种高分子材料。它具有力学性能优良、耐腐蚀、抗疲劳、耐高温、无毒、质轻、蠕变量低、惰性高、可透 X 线等诸多优点。聚醚醚酮因为其出

色的力学性能,可与不同材料进行复合弥补劣势、加强优势,在骨科置入物方面具有潜在的广泛应用前景。目前,聚醚醚酮应用于颈椎和腰椎融合器已较为成熟^[1-3]。聚醚醚酮还可用于髓关节置换术中的髓臼杯^[4]。但其在创伤骨科钢板螺钉和髓内钉系统的