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## 血栓弹力图指导心脏手术输血对术后出血量的影响 meta 分析

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**[摘要]** 目的 评价血栓弹力图(thromboelastography, TEG)与常规检测指导心脏手术输血对术后出血量的影响,为治疗决策提供依据。方法 以“Thromboelastography、TEG、血栓弹力图、血栓弹力描记图”为检索词检索PubMed、Embase、The Cochrane Library、中国生物医学文献数据库和中国期刊网全文数据库建库至2015年2月关于TEG与常规检测指导心脏手术输血对术后出血量影响的随机对照试验或回顾性队列研究,对符合纳入标准的文献提取资料、评估方法学质量,并采用RevMan5.3软件进行meta分析。结果 最终纳入7篇文献共计689例患者,其中5篇为高质量研究,2篇为低质量研究。meta分析结果显示:TEG与常规检测指导心脏手术输血对术后出血量的影响差异有统计学意义[WMD = -45.67, 95% CI(-80.32, -11.03), P < 0.05]。结论 与常规检测指导心脏手术输血比较,TEG指导能明显减少患者术后出血量。

[关键词] 血栓弹力图;心脏外科手术;输血;出血;Meta分析

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### Meta-analysis of the Effect of Thrombelastography Guided Cardiac Surgery Transfusion on Postoperative Bleeding

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**[Abstract]** **Objective** To evaluate thrombelastography (TEG) and routine testing guided cardiac surgery transfusion on postoperative bleeding, and to provide evidence for the treatment strategies. **Methods** The randomized controlled trials (RCT) or retrospective cohort study (RC) about cardiac surgery transfusion guided by TEG and routine testing on postoperative bleeding were searched by Thromboelastography, TEG, and Thrombelastogram Surgery as the search term on PubMed, Embase, the Cochrane Library, Chinese Biomedical Literature Database (CBM) and China Journal Full-text Database (CNKI) from the establishment of the data base to February 2015. By extracting data and assessing methodological quality, meta-analysis was conducted using the Cochrane Collaboration RevMan 5.3 software. **Results** Seven articles and 689 patients were included. Meta-analysis indicated that there was significant difference between TEG and routine testing guided cardiac surgery transfusion on postoperative bleeding [WMD = -45.67, 95% CI(-80.32, -11.03), P < 0.05]. **Conclusion** Compared with routine testing in guiding transfusion, TEG can significantly reduce the amount of bleeding after cardiac surgery in guiding transfusion.

**[Key words]** Thromboelastography; Cardiac surgical procedure; Blood transfusion; Hemorrhage; Meta-Analysis

血栓弹力图(thromboelastography, TEG)是一种涵盖凝血和纤溶全过程的动态监测手段,能全面反映患者的凝血功能,目前已广泛应用于心脏手术、器官移植和其他出血量大的手术的出血原因判断和合理输血指导。其中,心脏手术由于采用体外循环,手术患者使用抗凝药物、存在血小板及凝血因子的活化和消耗,手术患者凝血功能受到显著干扰。异常出血是体外循环心脏手术后的严重并发症,影响患者术后恢复。由出血所致的再手术,也是心脏手术的主要并发症,一旦发生多预后不良。近年来,国外许多研究表明,应用TEG指导心脏手术输血可显著降低用血量,从而有效降低了输血带来的风险<sup>[1-7]</sup>。笔者发现虽然众多研究中均指出TEG指导手术输血能显著减少用血量,但关于术后出血量方面与常规检测指导手术输血相比却无统计学差异,且均为单一研究,缺乏高质量循证医学证据。因此,笔者检索TEG指导心脏手术输血对术后出血量影响的相关文献,采用meta分析法评价TEG指导心脏手术输血对术后出血量的影响。

## 1 资料与方法

**1.1 检索策略** 以“Thromboelastography、TEG、血栓弹力图、血栓弹力描记图”为检索词,检索PubMed、Embase、The Cochrane Library、中国生物医学文献数据库(CBM)和中国期刊网全文数据库(CNKI)建库至2015年2月的相关文献。

## 1.2 纳入标准与排除标准

**1.2.1 纳入标准:** ①试验设计为随机对照试验(RCT)或回顾性队列研究(RC);②研究内容为TEG与常规检测指导心脏手术输血对术后出血量的影响;③试验组应用TEG监测指导手术输血,对照组应用常规凝血指标检测及医师经验指导手术输血;

④研究对象为具有潜在大量输血的心脏手术患者;⑤观察指标为手术开始至术后24 h内出血量;⑥提供或有足够数据信息可行meta分析。

**1.2.2 排除标准:** ①排除综述、个案报道、动物实验、实验室研究、重复发表的文献;②排除研究对象为急诊手术、患有血液系统疾病、肝功能不全及近期服用抗凝药物患者的文献;③排除信息提供不完整的文献。

**1.3 文献筛选和质量评价** 由两名研究者按照入选标准对纳入研究的文献独立进行质量评价和资料提取,然后交叉核对,如有分歧通过讨论解决,讨论未达成一致的由第3位研究者协助解决。本研究采用改良Jadad量表对文献进行评价。方法学质量评价:①随机序列产生恰当为2分,不清楚为1分,不恰当为0分;②分配隐藏恰当为2分,不清楚为1分,不恰当为0分;③盲法恰当为2分,不清楚为1分,不恰当为0分;④描述了撤出与退出为1分,未描述为0分。总计分为1~7分,1~3分为低质量研究,4~7分为高质量研究。

**1.4 统计学方法** 采用RevMan5.3软件对所提取的数据进行分析。各研究间异质性检验采用 $I^2$ 检验,若 $P > 0.1$ 和 $I^2 < 50\%$ ,则表明各研究间无异质性,采用固定效应模型合并效应量进行meta分析;反之,则表明各研究间具有异质性,采用随机效应模型合并效应量进行meta分析。计量资料采用加权均方差作为效应量,以各效应量及其95%可信区间(CI)表示结果。采用漏斗图分析研究结果是否存在发表偏倚。

## 2 结果

**2.1 检索结果** 最初从PubMed、Embase、The Cochrane Library、CBM和CNKI中分别检索出文献371



可引起血管内皮细胞异常激活致凝血功能受损<sup>[10]</sup>;缝合及分流器等操作激活组织因子;外科创伤致大量炎性介质释放<sup>[11]</sup>。④其他:血液稀释、纤溶系统激活<sup>[1]</sup>、底物消耗等。TEG 是一种涵盖凝血和纤溶全过程的动态监测手段,能全面反映患者凝血及血小板功能,其参数包括 R 值、K 值、 $\alpha$  角及 MA 值。R 值即血样开始检测到初始血凝块形成所需时间,当凝血因子缺乏和(或)抗凝剂存在时 R 值延长,高凝状态时缩短;K 值即凝血形成时间, $\alpha$  角即血凝块形成速率,主要与纤维蛋白原相关;MA 即最大振幅,主要取决于血小板的质和量,可直接反映血小板功能。因此,TEG 可有效监测凝血过程并反映血小板功能,尤其适用于体外循环易发生凝血功能紊乱的心脏手术<sup>[12]</sup>。

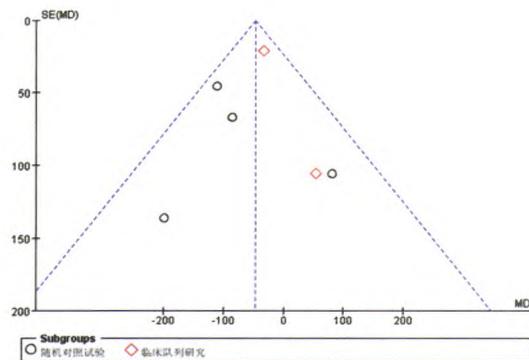


图 2 血栓弹力图与常规检测指导

#### 心脏手术输血对术后出血量影响纳入文献的 meta 漏斗图

那么如何正确评估心脏手术患者围术期凝血功能并合理成分输血关系到患者生命。Cosmi 等<sup>[13]</sup>在围术期分别应用活化部分凝血活酶时间(APTT)、凝血酶原时间(PT)等常规检测手段及 TEG 对患者血液凝集状态进行评估,并对术中出血情况进行监测,结果发现,相比常规检测手段,TEG 能更好地预测术中出血风险。若根据结果予以干预,便可降低术中出血风险,并减少手术输血量。因此认为,TEG 检测有良好的术前评估价值。Andrew 等<sup>[5]</sup>分别根据 TEG 及 APTT、PT、纤维蛋白原等检测结果制定输血方案,结果发现试验组术中用血量比对照组减少 58.8%,有效降低了输血带来的风险。因此,相对于常规检测方法,TEG 显示出明显的优势。

快速准确诊断术后凝血异常对有效治疗至关重要。TEG 能有效评估术后出血的原因,为正确治疗提供指导。如患者术后明显出血,而 TEG 各参数正常,常提示出血是由手术原因引起<sup>[14]</sup>。如鱼精蛋白中和肝素后,TEG R 值仍明显小于非肝素酶中和的 R 值,且全血活化凝血时间未恢复术前水平,说明出

血是由于肝素拮抗不完全引起,应补充鱼精蛋白<sup>[15]</sup>,但需考虑鱼精蛋白有逆转肝素抗凝作用的效果,故应谨慎进行<sup>[16]</sup>。如 MA 较术前明显降低,且血小板计数明显低于术前水平,则提示血小板功能不足。如 R 值明显延长,同时  $\alpha$  降低,K 值增大,说明凝血因子缺乏。如 CL30 明显下降,则提示纤溶亢进<sup>[17]</sup>。Koster 等<sup>[18]</sup>报道,使用改良的多通道 TEG 应用于体外循环后凝血功能异常的鉴别诊断,并根据结果正确指导治疗,可显著减少并发症和再次手术发生率。本研究发现,与常规检测指导手术输血比较,TEG 指导能显著减少患者术后出血量,可能原因为 TEG 指导围术期成分输血仅需 15 min 即可得出报告,能动态、及时地反映机体凝血状态<sup>[19]</sup>。

但本研究最终纳入的研究篇数偏少,总样本量偏小,虽然漏斗图分析提示研究结果不存在发表性偏倚,但纳入的文献质量各有差异以及很有可能漏检部分灰色文献,因而可能存在实施和结果测量偏倚,从而影响研究结果。所以需要不断累积新的RCT 研究以提高结论的可靠性。目前国内外 TEG 与常规检测指导心脏手术输血对术后出血量影响的研究结论不一,国内 TEG 开展使用不久,临床研究偏少且大都是回顾性研究,尚无规范的 RCT 研究,国外也仅有 5 篇<sup>[1-5]</sup>。今后该方面研究需从以下方面改进:①努力开展前瞻性、多中心 RCT 研究;②扩大样本量;③要有正确的随机分配、隐蔽分组方案及退出和失访等方面的控制以增加 RCT 研究质量;④除关注出血及输血方面指标外还应考虑机体其他器官并发症及输血不良反应方面的情况。

国内外尚未见关于 TEG 与常规检测指导心脏手术输血对术后出血量比较的 meta 分析报道。本研究的意义在于率先运用循证医学方法研究 TEG 与常规检测指导心脏手术输血对术后出血量的影响,对国内 TEG 的开展运用提供理论依据。本研究不足为文献篇数较少,且仅关注了术后出血量一项指标,下一步我们将持续关注 TEG 指导心脏手术输血的 RCT,不断纳入更多优质的 RCT 研究,运用循证医学证据对除术后出血外的输血方面指标及机体其他器官并发症、输血不良反应和病死率等方面进行综合评价,帮助临床医师做出更合理的临床决策,从而为心脏手术输血指导提供更多、更有效的选择。

本院心外科尚未将 TEG 普及于心脏手术输血指导,一般多应用于心脏瓣膜手术,余手术多以常规检测和临床经验判断来监测评估患者凝血功能和指导输血。目前国内临幊上较为常用的检测项目有凝血全套、弥漫性血管内凝血全套、凝血因子含量测

定、凝血酶 - 抗凝血酶Ⅲ复合物、血浆纤溶酶 - 抗纤溶酶复合物等, 在一定程度上均存在敏感性、特异性不足的问题。而在国外 TEG 已经用于心脏各项手术<sup>[20]</sup>, 且在评估凝血功能和输血指导下比常规检测更占优势<sup>[1-7]</sup>, 不但减少了用血量, 降低了输血风险, 节约了医疗资源, 而且也减少了异常出血及出血再次手术等并发症。欧洲心胸外科协会指南将 TEG 列为心脏手术中抗凝和抗血小板治疗的 B 类推荐, 指出 TEG 可指导术后输血<sup>[21]</sup>。由于国内此仪器引进和应用时间较短, 目前临床还未普遍使用, 但随着研究的深入, 在不远的将来会有更多的患者从这项检查中受益。

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