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· 文献综述 ·

## 负压伤口治疗在假体乳房再造术后并发症的预防和治疗的应用现状和研究进展

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### 摘要

假体乳房再造是乳腺癌术后乳房再造方式的主流, 然而再造术后切口愈合不良、组织感染等并发症不仅增加医疗成本、影响美观, 严重者还将导致假体缺失、乳房再造失败, 极大地影响患者的生活质量。随着负压技术的进步, 闭合切口负压治疗和负压联合滴注疗法被证明在预防和治疗假体乳房再造术后并发症方面具有显著优势, 但其确切机制和使用负压技术的最佳条件及选择仍不清楚。本文从闭合切口负压治疗 (ciNPWT)、负压滴注疗法 (NPWTi-d) 的应用现状与机制研究方面进行全面而系统的综述。

### 关键词

乳腺肿瘤; 乳房成形术; 负压伤口疗法; 手术后并发症; 综述

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## Application status and research progress of negative pressure wound therapy in the prevention and treatment of complications after prosthesis-based breast reconstruction

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### Abstract

Prosthesis-based breast reconstruction is the mainstream of breast reconstruction after breast cancer surgery. However, postoperative complications such as poor incision healing and tissue infection after breast reconstruction not only increase medical costs and affect aesthetics but also lead to prosthesis loss and even breast reconstruction failure in severe cases, which significantly affect the quality of life of patients. With the progress of negative pressure technology, closed incision negative pressure therapy (ciNPWT) and negative pressure wound therapy with instillation and dwell (NPWTi-d) have been proven to have significant advantages in preventing and treating complications after prosthesis-based breast reconstruction. At the same time, the exact mechanism, the optimal conditions, and selection of negative pressure technology are still unclear. This review provides a comprehensive and systematic review of the

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application status and mechanism research of ciNPWT and NPWTi-d.

**Key words**

Breast Neoplasms; Mammoplasty; Negative-Pressure Wound Therapy; Postoperative Complications; Review

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目前, 40%以上因乳腺癌切除乳房的患者选择了乳房再造<sup>[1-2]</sup>。尽管自体皮瓣乳房再造术后患者满意度和生活质量更高<sup>[3]</sup>, 但假体乳房再造手术复杂性较低、手术时间较短、不存在皮瓣供区并发症, 已获得乳腺癌术后患者和整形外科医生的广泛认可<sup>[4-7]</sup>。2020年, 假体乳房再造手术的数量已达到乳腺癌术后乳房再造的75%<sup>[2]</sup>。然而, 约1.8%~16.9%的乳房再造患者不得不接受假体取出手术而造成植入物缺失, 严重影响患者术后的美学效果和生活质量<sup>[8-11]</sup>, 其原因可归咎于血清肿、假体周围组织感染、皮瓣坏死、伤口裂开等假体乳房再造术后并发症<sup>[8-10, 12]</sup>。

过去的几十年里, 负压伤口治疗(negative pressure wound therapy, NPWT)被广泛应用于管理创伤、皮肤或组织移植、压疮、糖尿病足等开放性伤口和外科手术闭合性切口<sup>[1, 13-18]</sup>。与常规伤口换药相比, 负压治疗在促进伤口愈合、缓解组织水肿、预防伤口感染等方面具有极大的优势<sup>[19-21]</sup>。近年来, 陆续有文献报道NPWT降低了假体乳房再造术后血清肿、伤口裂开及皮瓣坏死等并发症的发生率, 并成功挽救了因术后假体周围感染、植入物暴露等严重并发症造成的乳房再造失败。但目前缺乏综述来阐述负压治疗预防和管理假体乳房再造术后并发症的研究进展。因此本文将从负压技术如何预防和治疗并发症两大方面, 结合最新的机制研究, 对该专题进行全面的综述, 以期为临床提供防治策略和依据。

## 1 闭合切口NPWT(ciNPWT)在假体乳房再造术后并发症中的预防作用

负压伤口治疗曾被广泛应用于开放性创面<sup>[15-16]</sup>, 近20年来, ciNPWT联合泡沫敷料在保护闭合切口的作用也得到充分肯定, 多项Meta分析<sup>[22-25]</sup>报告了ciNPWT在减少关节置换术、腹部手术及血管外科手术切口并发症的作用。传统的敷料多为干燥或湿润的纱布, 然而纱布并不具备密闭性, 导致切口较易被外界污染<sup>[26-27]</sup>。ciNPWT

则取代纱布, 在闭合切口表面覆盖聚氨酯多孔海绵, 并通过负压装置对海绵敷料施加负压, 强大的负压使聚氨酯海绵和手术切口紧紧地贴合在一起, 在切口周围形成封闭的环境。与纱布相比, ciNPWT可以将切口边缘紧密固定, 促进胶原纤维合成修复切口, 并提供密闭的环境防止外部污染<sup>[28]</sup>。在假体乳房手术方面, 亦有文献报道ciNPWT减少了血清肿、皮瓣坏死、伤口破裂的发生, 以下将展开探讨。

### 1.1 ciNPWT可预防血清肿的发生

血清肿是由于术中解剖和离断淋巴管等组织导致淋巴液等浆液性液体积聚于组织腔隙而导致<sup>[29]</sup>, 在假体乳房再造术后浆液常积聚于植入物所在的腔隙(皮下平面和胸肌后平面)<sup>[30-31]</sup>。据文献<sup>[32]</sup>报道, 基于植入物的假体乳房再造术后血清肿的发生率高达20%。当前最常见的预防方法是术中严密缝合消灭死腔、放置引流管及术后加压包扎<sup>[33-34]</sup>; 也有研究<sup>[35]</sup>报道, 使用纤维蛋白胶硬化处理, 然而血清肿的发生率并无明显降低。而ciNPWT通过创造稳定、连续的负压环境有效关闭皮下间隙等组织内的腔隙, 使液体从死腔中排出<sup>[36]</sup>。Paul等<sup>[37]</sup>在基于胸肌前假体乳房再造患者的回顾性研究中观察到在23例用负压引流装置Interi的患者中无1例血清肿发生, 而未使用负压引流的23例患者血清肿发生率高达20.5%, 差异明显。Gabriel等<sup>[38]</sup>在基于665例假体乳房再造的回顾性研究中也得出相似的结论, ciNPWT组血清肿发生率为1.8%, 未使用ciNPWT组的患者血清肿发生率为5.7% ( $P=0.01$ )。Jeong等<sup>[39]</sup>不但表明ciNPWT降低了胸前假体乳房再造术后血清肿发生率(16.2% vs. 43.5%,  $P=0.020$ ), 还可缩短血清肿的存在时间(21.87 d vs. 61.70 d,  $P=0.018$ )、减少血清肿的体积(53.89 cm<sup>3</sup> vs. 189.65 cm<sup>3</sup>,  $P=0.019$ )。总之, ciNPWT可能是降低血清肿发生率的有效方法<sup>[36]</sup>。

### 1.2 ciNPWT可预防术区愈合不良

相比关节置换等其他假体植入手术, 乳腺导管并非完全无菌, 乳房手术切口裂开和皮瓣坏死

等愈合不良的情况可能会为细菌定植提供潜在的入口<sup>[40-42]</sup>,因此预防假体乳房再造术后伤口裂开和皮瓣坏死能降低术区细菌污染的风险。

早先 Gabriel 等<sup>[38]</sup>使用 ciNPWT 管理 25 例两阶段扩张器/假体乳房再造术后切口的数据表明,伤口裂开发生率为 12%,皮瓣坏死发生率仅 4%,总体并发症发生率远低于假体乳房再造术后总体并发症发生率(50%)<sup>[3]</sup>,但此研究为单一队列回顾性研究。Gabriel 等<sup>[38]</sup>又进一步在 665 例假体乳房再造的研究数据上表明,ciNPWT 组伤口破裂发生率远低于不使用 ciNPWT 的对照组(2.4% vs. 5.4%,  $P=0.0178$ ),组织坏死(5.1% vs. 9.3%,  $P=0.007$ )和计划外手术(2.4% vs. 5.4%,  $P=0.049$ )的发生率也远低于对照组。Irwin 等<sup>[43]</sup>在 307 例即刻胸肌前平面假体乳房再造的队列中也得到类似的结果,ciNPWT 组裂开较少(0.8% vs. 5.5%,  $P=0.01$ )且无 1 例植入物移除,而仅采用标准敷料的对照组假体移除率高达 3.9%,差异显著( $P<0.05$ )。Ferrando 等<sup>[44]</sup>的研究则极具代表性:相比仅使用标准辅料护理的对照组(22 例),ciNPWT 组(25 例)存在显著差异的危险因素( $P=0.04$ ),如乳房肥大、抽烟史、放疗史、手术史和是否使用脱细胞真皮基质等,但 ciNPWT 组的组织坏死(4% vs. 32%,  $P=0.02$ )和总体并发症(4% vs. 45%,  $P=0.001$ )发生率明显低于对照组,术后结果也存在显著的统计学差异。

目前有两种 ciNPWT 设备用于乳腺手术的闭合切口,分别是 PICO™和 PREVENA™,两者分别能在闭合切口上产生 -80 mmHg (1 mmHg=0.133 kPa)和 -125 mmHg 的负压<sup>[45]</sup>。ciNPWT 促进手术切口愈合的机制包括:(1)负压可使紧密贴合在切口的泡沫敷料压缩 80%,以此对抗切口裂开的侧向张力并将其降低约 50%<sup>[15,46]</sup>;(2)泡沫敷料和切口保护膜为切口提供密闭稳定的环境,防止细菌定植,保持伤口湿润和温暖<sup>[1,47]</sup>;(3)负压导致细胞间液的流动,对细胞产生剪切力等机械作用力,抑制细胞凋亡、上调细胞信号分子以促进细胞增殖、血管和肉芽组织的形成<sup>[15,48]</sup>;(4)清除细胞外液、减轻组织水肿,并去除有害物质如肿瘤坏死因子  $\alpha$  和基质金属蛋白酶<sup>[48-50]</sup>。当前对于 ciNPWT 能否改善切口周围组织灌注还有争论。既往负压治疗能改善伤口血流灌注的认识似乎深入人心<sup>[51-52]</sup>,但 Kairinos 等<sup>[53]</sup>评估了关于“负压治疗改善伤口血流

灌注”的研究后发现,所有研究的测量工具都是激光多普勒;根据流体连续性方程,负压导致切口周围组织受压迫,进一步使血管直径缩小,血流流经狭窄的血管时速度会增加,而这将使激光多普勒误将其记录为组织灌注增加,但事实上组织灌注可能是减少的<sup>[53-55]</sup>。合理的解释可能是,负压压迫组织造成相对缺血的状态,刺激低氧诱导因子 1 $\alpha$  的表达,从而诱导血管内皮生长因子和血管生成素的水平升高,有助于诱导血管生成并形成肉芽组织<sup>[56-57]</sup>。然而,负压过大易造成组织完全缺氧、坏死,机体不同处的皮肤和组织所能承受的压力也不同<sup>[15,58]</sup>;目前 ciNPWT 对于假体乳房再造手术闭合切口的最佳负压水平尚无明确结论。

## 2 NPWT 联合滴注疗法(NPWTi-d)在假体乳房再造术后严重感染中的治疗作用

ciNPWT 对乳房再造术后假体周围感染似乎有预防作用<sup>[38,43-44]</sup>,但对于抗生素难治性严重假体周围感染的治疗则无能为力<sup>[59-60]</sup>。近年来,NPWTi-d 在假体周围感染的治疗上颇有成效。相比 ciNPWT,两者的差别在于:(1)ciNPWT 使用聚氨酯敷料覆盖于闭合切口表面,而 NPWTi-d 则将聚氨酯泡沫敷料充填假体所在的腔隙;(2)NPWTi-d 间歇性地滴注溶液浸润伤口床、充分灌洗伤口后再被间歇性施加的负压移除,充分地清除伤口腔内碎屑、抑制细菌生物膜形成<sup>[61-62]</sup>,ciNPWT 则不具备这种功能和优势;(3)ciNPWT 只能提供持续的负压,而 NPWTi-d 则可提供间断的负压,间断负压能更迅速地促进组织愈合<sup>[63]</sup>。

Phillios 等<sup>[64]</sup>在猪真皮上研究滴注对生物膜的影响发现与覆盖含有抗菌溶液的敷料相比,滴注抗菌溶液可显著减少创面生物膜细菌数量。Yang 等<sup>[65]</sup>的随机对照研究证明,NPWTi-d 组创面生物膜细菌数量平均减少了 48%,而未使用负压滴注疗法的细菌数量平均增加了 14%。Kim 等<sup>[66]</sup>的多中心临床试验也得出相似结论:与接受传统 NPWT 治疗的清创术后患者相比,接受 NPWTi-d 治疗的患者创面组织细菌数量显著减少(-0.18 Log<sub>10</sub> CFU/g vs. 0.6 Log<sub>10</sub> CFU/g,  $P=0.02$ )。在临床实践中,临床医生可掌控 NPWTi-d 滴注溶液的种类以及负压抽吸与溶液滴注的交替时间<sup>[62,67]</sup>。NPWTi-d 使用的滴注溶液种类包括生理盐水、抗生素溶液、次氯酸盐溶



液、聚维酮碘和聚己胺加甜菜碱<sup>[68]</sup>，但除 Antognoli 等<sup>[61]</sup>使用 0.1% 聚己胺+0.1% 甜菜碱作为滴注溶液，目前有关假体乳房再造的文献中使用的滴注溶液均是生理盐水；Kim 等<sup>[69]</sup>的随机对照试验证明，滴注生理盐水与滴注 0.1% 聚己胺加 0.1% 甜菜碱在住院时间、切口愈合、复诊次数方面无明显差异，但生理盐水组的患者需要负压滴注治疗的时间更短 [ (5.73 ± 3.75) d vs. (7.73 ± 5.49) d,  $P < 0.05$  ]，提示生理盐水和其他消毒液一样有效。Faust 等<sup>[68]</sup>关于使用 NPWTi-d 的经验也支持滴注溶液首选生理盐水；目前滴注负压伤口疗法的专家共识普遍认为生理盐水是最合适的滴注溶液<sup>[62, 67, 70]</sup>。

目前使用 NPWTi-d 管理乳房再造术后严重假体周围感染的文献中所设置的滴注时间均为 10~20 min<sup>[62, 70]</sup>，但负压的持续时间则从 45 min 至 4 h 不等，对于溶液滴注和负压持续的最佳时间尚无相关研究和明确结论<sup>[68]</sup>，需要大量基础实验和临床随机对照试验进一步研究。

间断负压被证明能更好地促进组织愈合。Lessing 等<sup>[15]</sup>使用持续负压和间断负压对猪模型的创面进行为期 7 d 的对比研究发现，与持续负压相比，间断负压治疗可使创面肉芽组织增加 43%。另一方面，负压的压迫使组织处于相对缺氧状态，促进释放血管舒张因子一氧化氮，在滴注期（负压停止期）使血管舒张导致组织反应性充血、血流灌注增加<sup>[58, 71-72]</sup>。此外在美学上，长期连续负压会造成假体腔隙容积减小，而间断给予负压可减少假体腔隙容积损失，避免乳房皮肤松弛<sup>[61]</sup>，从而提高术后患者对乳房的满意度。

假体乳房再造术后感染的发生率为 4.8%~35.4%<sup>[73]</sup>，是术后假体缺失最主要的原因<sup>[8, 74]</sup>。移除假体曾是治疗抗生素难治性假体周围组织感染的首选方法，待控制感染数月后再延期行乳房再造，包括植入新的乳房假体，或行自体皮瓣乳房再造<sup>[75]</sup>。然而，二次乳房再造后皮肤紧缩、包膜挛缩、疤痕等并发症严重影响美观，降低患者满意度<sup>[75-76]</sup>；此外，由于患者遭受了数月之久假体缺失的心理打击，58%~66.7% 的患者在假体被移除后放弃延期乳房再造<sup>[77]</sup>。基于 NPWTi-d 上述特点和优势，负压联合滴注疗法治疗假体周围感染应用广泛，极大缩短再次植入假体的时间，成功避免假体缺失，改善了美学问题和患者生活质量。Meybodi 等<sup>[78]</sup>最早将 NPWTi-d 用于治疗乳房再造术

后严重假体周围感染，5 例严重假体感染在平均 12 d 内被治愈并重新植入假体，从而避免假体缺失。Cheong 等<sup>[79]</sup>使用 NPWTi-d 在 1 周之内成功控制 5 例假体周围严重组织感染，并重新植入新的假体完成乳房再造。Djohan 等<sup>[80]</sup>使用 NPWTi-d 管理 9 例假体周围组织感染的患者并均在 1 周内重新植入假体，除 1 例患者蜂窝织炎复发不得不改为自体皮瓣再造乳房，其余 8 例患者均成功避免假体缺失。Knackstedt 等<sup>[81]</sup>首次对假体周围感染的患者进行了长达 1 年的随访，14 例接受 NPWTi-d 治疗的假体周围感染病例中有 10 例成功保留了假体并且没有感染复发；类似地，Meybodi 等<sup>[82]</sup>基于此前的研究，对 30 例因乳房假体周围严重感染接受 NPWTi-d 的患者进行平均 40 个月的随访，25 例（约 83%）成功地植入了新的乳房假体且没有感染复发。Haque 等<sup>[83]</sup>则首次对 40 例患者开展回顾性对照研究：相比未接受 NPWTi-d 的对照组，NPWTi-d 组能够更早行再次植入假体 [ (10.3 ± 2.77) d vs. (247.45 ± 111.28) d,  $P < 0.001$  ]，且患者对乳房满意度的 Breast-Q 评分较高 (55.00 ± 14.93 vs. 39.69 ± 19.99,  $P < 0.05$ )。此外，NPWTi-d 组均成功保留假体、无一再次入院，而对照组入院次数远高于 NPWTi-d 组。Antognoli 等<sup>[61]</sup>开展的包含 25 例患者的回顾性队列研究也发现，16 例接受 NPWTi-d 的患者中有 15 例患者成功控制感染、避免假体缺失（成功率达 94%），相比未接受负压滴注疗法的患者其再次住院次数 [ (4 ± 1) 次 vs. (2 ± 1) 次,  $P = 0.002$  ] 和就诊次数 [ (24 ± 9) 次 vs. (11 ± 5) 次,  $P = 0.02$  ] 均明显减少，每例患者的总住院费用平均减少了 58 275 美元，极大节约了医疗成本。

### 3 小结与展望

综上所述，负压伤口治疗可以在假体乳房再造术后发挥积极作用，ciNPWT 能促进切口愈合，预防假体乳房再造术后伤口并发症尤其是血清肿、伤口破裂以及皮瓣或组织坏死；NPWTi-d 可作为重要手段治疗假体周围严重组织感染、减少术后假体缺失，提升患者的满意度和生活质量，并能节约医疗成本。未来仍需大量基础实验和临床随机对照研究关注负压治疗技术在假体乳房再造术后促进组织愈合、预防和治疗并发症的确切机制，明确不同临床情景下负压治疗的最佳参数如负压

大小、滴注液种类和负压持续时间,以期提高乳腺癌患者在接受假体乳房再造术后的生活质量。

利益冲突:所有作者均声明不存在利益冲突。

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