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· 临床研究 ·

# 富血小板纤维蛋白在位点保存中使用效果的meta分析

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**【摘要】** 目的 评价拔牙后使用富血小板纤维蛋白(platelet-rich fibrin, PRF)在位点保存中的效果。方法 检索 Pubmed、Embase、Cochrane library、知网、万方、CBM 数据库及中国、美国临床试验注册中心 2020 年 8 月 25 日前发表的有关拔牙后使用 PRF 的随机对照临床试验(randomized controlled trials, RCTs), 纳入研究的结局指标包括干槽症、水平和垂直方向牙槽骨吸收、新生骨百分比, 应用 Review Manager 5.3 版软件进行 meta 分析。结果 共检索到文献 706 篇, 经筛选后纳入 11 篇研究, 其中 8 篇定量分析, meta 分析结果显示拔牙后使用 PRF 能减少牙槽骨的吸收, 其中减少水平骨量(WMD = -0.71, 95% CI = -1.11 ~ -0.32,  $P < 0.05$ ), 颊侧垂直骨量(WMD = -1.38, 95% CI = -1.87 ~ -0.88,  $P < 0.05$ ), 舌侧垂直骨量(WMD = -0.49, 95% CI = -0.92 ~ -0.06,  $P < 0.05$ ) 的吸收, 而且提高了新生骨百分比(SMD = 1.24, 95% CI = 0.25 ~ 2.23,  $P < 0.05$ ), 但在预防术后干槽症发生(RD < 0.01, 95% CI = -0.05 ~ 0.04,  $P = 0.95$ ) 及减少牙槽窝近中(WMD = -0.11, 95% CI = -1.17 ~ 0.95,  $P = 0.84$ )、远中(WMD = -0.66, 95% CI = -1.93 ~ 0.60,  $P = 0.30$ ) 垂直方向骨吸收上差异无统计学意义。结论 拔牙后单纯使用 PRF, 可有效保存牙槽嵴水平方向及颊舌侧垂直方向的骨量。

**【关键词】** 富血小板纤维蛋白; 浓缩血小板; 牙槽窝; 牙槽骨吸收; 位点保存; 牙槽嵴保存; 临床随机对照试验; meta 分析

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**Meta-analysis of the effect of platelet-rich fibrin in alveolar ridge preservation** DONG Jingbo, LI Zhenzhen, LIU Chenxi, SHI Peikai. Department of Oral and maxillofacial surgery, Hebei Key Laboratory of Stomatology, Hebei Clinical Research Center for Oral Diseases, School and Hospital of Stomatology, Hebei Medical University, Shijiazhuang 050017, China

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**【Abstract】 Objective** To evaluate the effect of platelet-rich fibrin (PRF) on alveolar ridge preservation after tooth extraction. **Methods** Randomized controlled trials (RCTs) published before August 25, 2020 about the use of PRF after tooth extraction were searched through the PubMed, Embase, Cochrane Library, HowNet, Wanfang, CBM databases and clinical trial registration centers in China and the United States. Outcome indicators included in the studies included dry socket occurrence, alveolar bone resorption in the horizontal and vertical directions, and the percentage of new bone. Meta-analysis was conducted with Review Manager Version 5.3 software. **Results** A total of 706 studies were retrieved. After screening, 8 studies were analyzed quantitatively. Meta-analysis results showed that PRF could reduce the absorption of alveolar bone after tooth extraction, which reduced the horizontal bone mass (WMD = -0.71, 95% CI = -1.11 to -0.32,  $P < 0.05$ ) and buccal (WMD = -1.38, 95% CI = -1.87 to -0.88,  $P < 0.05$ ) and lingual sides (WMD = -0.49,

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95%  $CI = -0.92$  to  $-0.06$ ,  $P < 0.05$ ) and increased the percentage of new bone ( $SMD = 1.24$ , 95%  $CI = 0.25$  to  $2.23$ ,  $P < 0.05$ ). However, there was no significant difference in preventing the occurrence of dry socket ( $RD < 0.01$ , 95%  $CI = -0.05$  to  $0.04$ ,  $P = 0.95$ ) and reducing bone absorption in the vertical direction of mesial ( $WMD = -0.11$ , 95%  $CI = -1.17$  to  $0.95$ ,  $P = 0.84$ ) and distal ( $WMD = -0.66$ , 95%  $CI = -1.93$  to  $0.60$ ,  $P = 0.30$ ) alveolar ridge after tooth extraction. **Conclusion** Using PRF alone after tooth extraction can effectively preserve bone mass in the horizontal direction of the alveolar ridge and the vertical direction of the buccal and lingual sides.

**【Key words】** platelet-rich fibrin; platelet-concentrate; tooth socket; alveolar bone absorption; socket preservation; alveolar ridge preservation; randomized controlled trials; meta-analysis

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拔牙后由于束状骨的吸收,常引起牙槽骨在垂直和水平方向的吸收<sup>[1]</sup>。这种吸收是一种慢性不可逆的过程,牙槽骨宽度在拔牙后6个月内减少约50%,高度变化为0.4~3.9 mm<sup>[2]</sup>。已有研究证实位点保存技术可减缓牙槽骨吸收过程,减少牙槽骨高度和宽度的吸收<sup>[3]</sup>。近年来许多研究结果表明富血小板纤维蛋白(platelet-rich fibrin, PRF)具有良好的临床疗效,如拔除第三磨牙后软组织创面愈合良好,在上颌窦底增高术中单独应用PRF可获得理想的骨增量效果<sup>[4-6]</sup>。然而,临床医生对于PRF是否能减少拔牙后牙槽骨吸收持不同观点。本研究对PRF在位点保存中使用的效果进行meta分析,以期为临床提供参考。

## 1 资料和方法

### 1.1 文献检索

检索 Pubmed、Embase、Cochrane library、知网、万方、CBM 数据库、中国临床试验注册中心、美国临床试验注册中心。英文检索词: alveolar ridge preservation, extraction socket, tooth socket, socket preservation, platelet-rich fibrin, PRF, platelet-concentrate。中文检索词: 牙槽嵴保存, 位点保存, 牙槽窝, 富血小板纤维蛋白, PRF, 浓缩血小板。检索时间为建库至2020年8月25日。

### 1.2 纳入标准与排除标准

纳入标准: ①研究对象为拔牙患者; ②临床随机对照试验; ③干预组拔牙后牙槽窝内使用PRF, 对照组为自然愈合; ④结局指标为拔牙后干槽症, 水平骨吸收, 垂直骨吸收, 新生骨百分比, 包含其中1项或1项以上均纳入。排除标准: ①动物实验, 综述, 病例报告; ②非随机对照试验; ③PRF联

合其他骨替代材料使用; ④病例中包含第三磨牙; ⑤重度吸烟患者( $\geq 10$ 支/日)。

### 1.3 质量评价

2名评价者根据Cochrane手册5.10版推荐的“偏倚风险评估工具”<sup>[7]</sup>,对纳入的文献独立进行质量评价,任何争议都与第三人讨论解决。采用以下标准评估纳入研究的偏倚风险:随机序列生成、分配隐藏、实施者与受试者的双盲、研究结果的盲法评价、结果数据的完整性、选择性报告偏倚结果、其他偏倚。如果数据丢失或不清楚,将联系作者以获取更多数据。

### 1.4 数据提取

2名评价者根据文献的纳入与排除标准独立筛选文献,若双方观点不一致则与第三人讨论解决。提取内容为作者、发表年份、随访时间、性别、年龄、样本量、干预与对照措施、结局指标。

### 1.5 统计分析

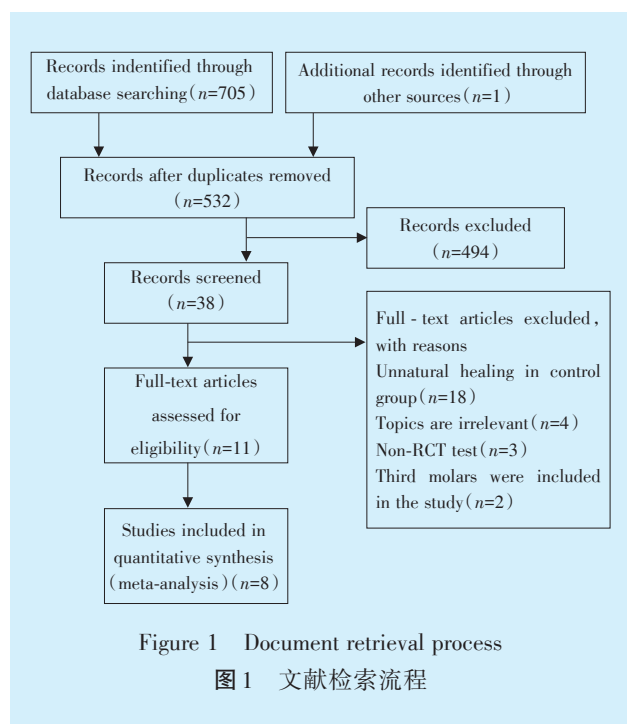
使用Review Manager 5.3软件进行meta分析。当 $P < 50\%$ ,采用固定效应模型;当 $P \geq 50\%$ 时,采用随机效应模型。风险差异(risk difference, RD)为二分类变量的效应指标,加权均数差(weighted mean difference, WMD)和标准化均数差(standardized mean difference, SMD)为连续性变量的效应指标,并计算其95%可信区间(confidence interval, CI), $P < 0.05$ 为差异有统计学意义。

## 2 结果

### 2.1 检索结果

共检索文献706篇,剔除重复文献后剩余532篇,阅读题目和摘要后初筛得到38篇。经仔细阅读全文后纳入11篇文献,其中8篇文献可行定量

分析,文献筛选流程见图1,文献纳入情况见表1。



## 2.2 质量评价

共纳入11篇随机对照临床试验<sup>[2, 8-17]</sup>,其中7篇文献提到随机序列生成的方法<sup>[8-13, 17]</sup>,如抽签,随机数字表法等,其余4篇文献提及随机<sup>[2, 14-16]</sup>,但未介绍具体方法,有2篇文献采用的是风险低的密闭信封的分配隐藏。4篇文献提及对试验结果的盲法评价<sup>[8, 10, 12, 15]</sup>,未发现有研究结局数据不完整(图2)。

## 2.3 meta分析结果

### 2.3.1 干槽症

共纳入3个研究,63位病人<sup>[8, 16, 17]</sup>。异质性检验 $I^2 = 0\%$ ( $P = 0.99$ ),采用固定效应模型进行meta分析。结果显示使用PRF对拔牙术后干槽症的发生率差异无统计学意义( $P = 0.95$ ,图3)。

### 2.3.2 水平骨吸收

9篇研究<sup>[2, 8-15]</sup>报道了牙槽骨水平骨吸收,由于测量方式,测量时间,测量点不同,最后纳入2篇研究<sup>[9, 11]</sup>,均在术后12周采用CBCT在同一测量点测量,异质性检验 $I^2 = 0\%$ ( $P = 0.58$ ),用固定效应模型进行meta分析。结果显示在拔牙后12周时,PRF组在水平方向骨吸收小于

表1 纳入研究的基本特征

Table 1 Characteristics of the included studies

Study	Year	Study type	Sex (female/male)	Age (mean)	Patients (teeth)	Test (number)	Control (number)	Duration (weeks)	Outcome indicator
Hauser <sup>[8]</sup>	2013	RCT	7/10	47	17 (17)	PRF (9)	N (8)	8	①②③
Temmerman <sup>[9]</sup>	2016	RCT	7/15	54	22 (44)	L-PRF (19)	N (21)	12	②③
Suttapreyasri <sup>[10]</sup>	2013	RCT	5/3	23	8 (20)	PRF (10)	N (10)	8	②③
Canellas <sup>[11]</sup>	2019	RCT	27/21	45	48 (48)	L-PRF (24)	N (24)	12	②③④
Clark <sup>[12]</sup>	2018	RCT	22/18	58	20 (20)	A-PRF (10)	N (10)	15	②③④
Liu <sup>[13]</sup>	2016	RCT	NR	54	34 (34)	PRF (17)	N (17)	9	②③
Girish <sup>[2]</sup>	2018	RCT	NR	43	30 (60)	PRF (30)	N (30)	24	②③
Alzaharani <sup>[14]</sup>	2017	RCT	15/9	38	24 (24)	PRF (14)	N (14)	8	②
Ivanova <sup>[15]</sup>	2019	RCT	NR	42	35 (35)	A-PRF (23)	N (12)	16	②③④
Ning <sup>[16]</sup>	2018	RCT	8/12	19	20 (40)	PRF (20)	N (20)	2	①
Marenzi <sup>[17]</sup>	2015	RCT	9/17	54	26 (108)	PRF (54)	N (54)	3	①

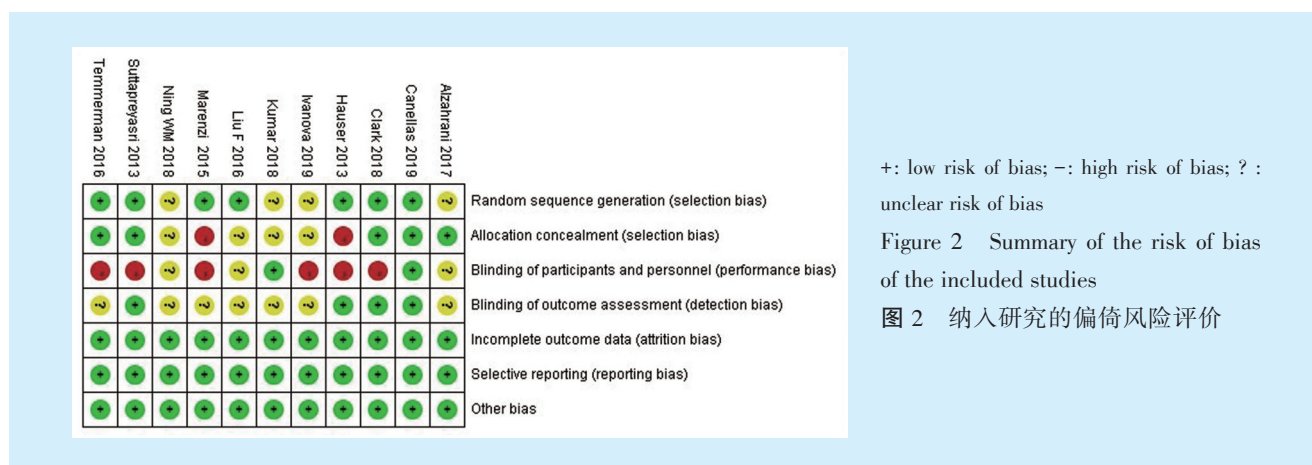
RCT: randomized controlled trial; NR: not reported; L-PRF: leukocyte and platelet-rich fibrin; A-PRF: advanced platelet-rich fibrin; N: Natural healing; ①: alveolar osteitis; ②: horizontal bone resorption; ③: vertical boneresorption; ④: the percentage of new bone tissue

自然愈合组,差异有统计学意义( $P < 0.001$ ,图4)。9篇研究中有7篇研究<sup>[2, 8, 10, 12-15]</sup>不能定量分析,其中4篇研究<sup>[8, 13-15]</sup>得到PRF组与对照组差异有统计学意义( $P < 0.05$ ),剩余3个研究<sup>[2, 10, 12]</sup>差异无统计学意义( $P > 0.05$ )。

### 2.3.3 垂直方向骨吸收

共有8篇研究结局指标包括了牙槽骨垂直方向上的骨吸收<sup>[2, 8-13, 15]</sup>,由于测量方式,测量时间,测量点不同,最后纳入4篇研

究<sup>[8-11]</sup>,其中颊舌侧采用CBCT测量,近远中采用根尖片测量,颊侧异质性检验 $I^2 = 0\%$ ( $P = 0.74$ ),舌侧异质性检验 $I^2 = 0\%$ ( $P = 0.70$ )采用固定效应模型进行meta分析。近中异质性检验 $I^2 = 91\%$ ( $P = 0.001$ ),远中异质性检验 $I^2 = 97\%$ ( $P < 0.001$ ),采用随机效应模型进行meta分析。结果显示,PRF组牙槽骨颊舌侧垂直方向骨吸收小于自然愈合组,差异有统计学意义( $P < 0.05$ ,图5);近远中垂直方



+: low risk of bias; -: high risk of bias; ? : unclear risk of bias

Figure 2 Summary of the risk of bias of the included studies

图2 纳入研究的偏倚风险评价

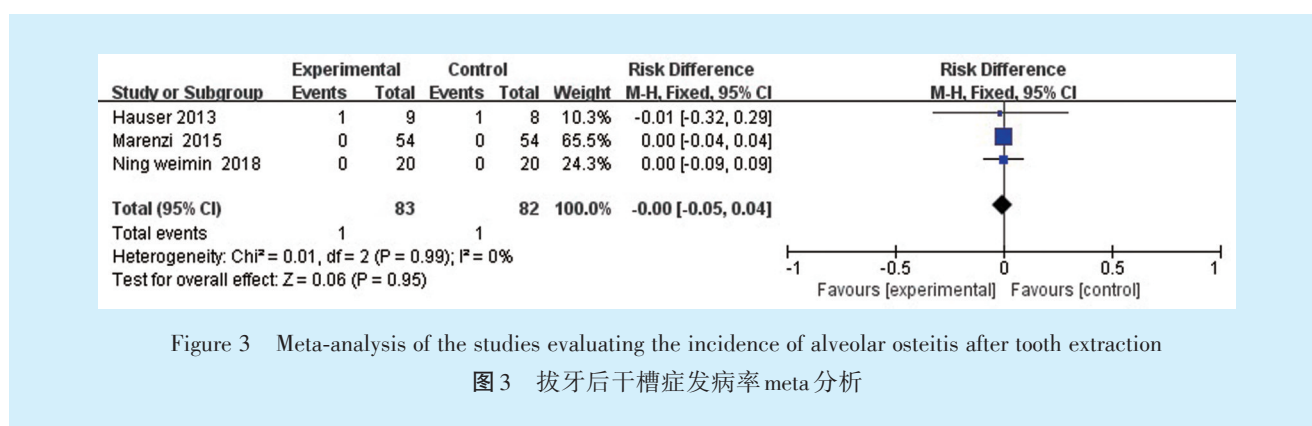


Figure 3 Meta-analysis of the studies evaluating the incidence of alveolar osteitis after tooth extraction

图3 拔牙后干槽症发病率meta分析

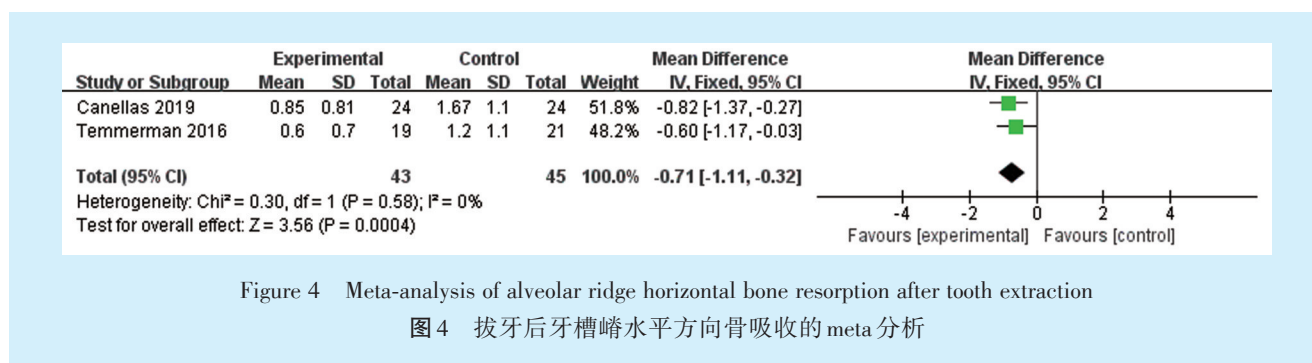


Figure 4 Meta-analysis of alveolar ridge horizontal bone resorption after tooth extraction

图4 拔牙后牙槽嵴水平方向骨吸收的meta分析

向骨吸收差异无统计学意义 ( $P > 0.05$ , 图6)。8篇研究中有4篇研究<sup>[2, 12, 13, 15]</sup>不能定量分析, 其中3篇研究<sup>[2, 12, 15]</sup>得到PRF组与对照组差异有统计学意义 ( $P < 0.05$ ), 只有1个研究<sup>[13]</sup>差异无统计学意义。

2.3.4 新生骨百分比 共纳入3篇研究<sup>[11, 12, 15]</sup>, Meta分析结果显示: 异质性检验  $I^2 = 79%$  ( $P = 0.009$ ), 用随机效应模型。结果显示, 拔牙后12~16周PRF组的拔牙窝新生骨百分比大于自然愈合组, 差异有统计学意义 ( $P = 0.01$ , 图7)。

#### 2.4 发表偏倚

由于各个结局指标的纳入研究数量较少, 不足10篇, 未能绘制漏斗图评估发表偏倚。

### 3 讨论

PRF含有许多浓缩生长因子以及良好的三维纤维蛋白空间结构, 这种三维网状结构便于营养物质和氧气弥散至细胞周围, 有利于诱导细胞的移动和增殖等愈合过程<sup>[18]</sup>。近年来PRF及其衍生物已成功运用到口腔领域。Pan等<sup>[19]</sup>做过关于PRF位点保存的meta分析, 但其干预组并非单纯使用PRF, 对照组也纳入了非自然愈合的研究。Lin等<sup>[20]</sup>在meta分析中纳入标准包括了随机对照临床试验和对照临床试验, 而本文仅纳入了随机对照临床试验。此外, 一系列研究<sup>[21-23]</sup>已证实许多因素可能会影响牙槽骨的吸收, 比如吸烟、不同牙

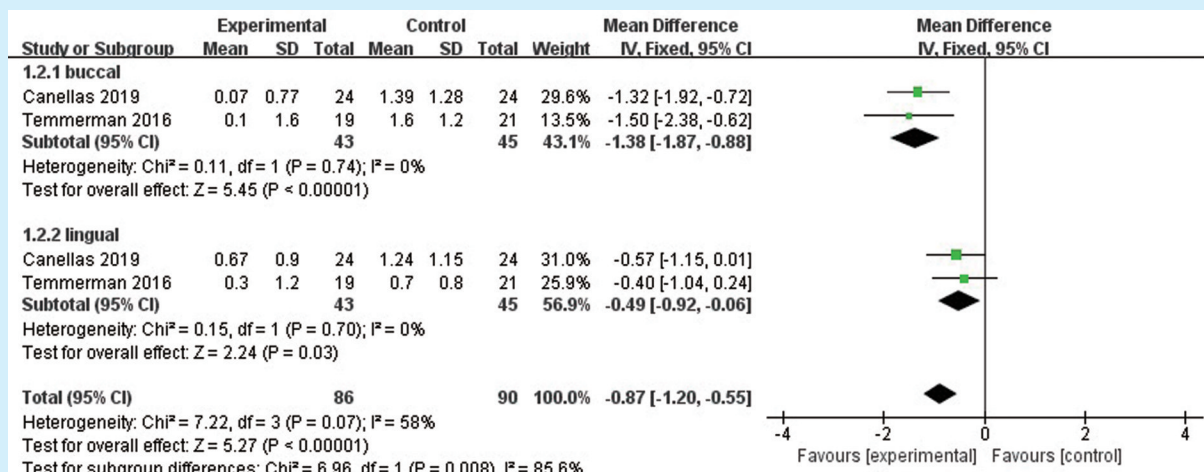


Figure 5 Meta-analysis of vertical bone resorption in the lingual and buccal alveolar ridges after tooth extraction  
图5 拔牙后牙槽嵴颊侧、舌侧垂直方向骨吸收的meta分析

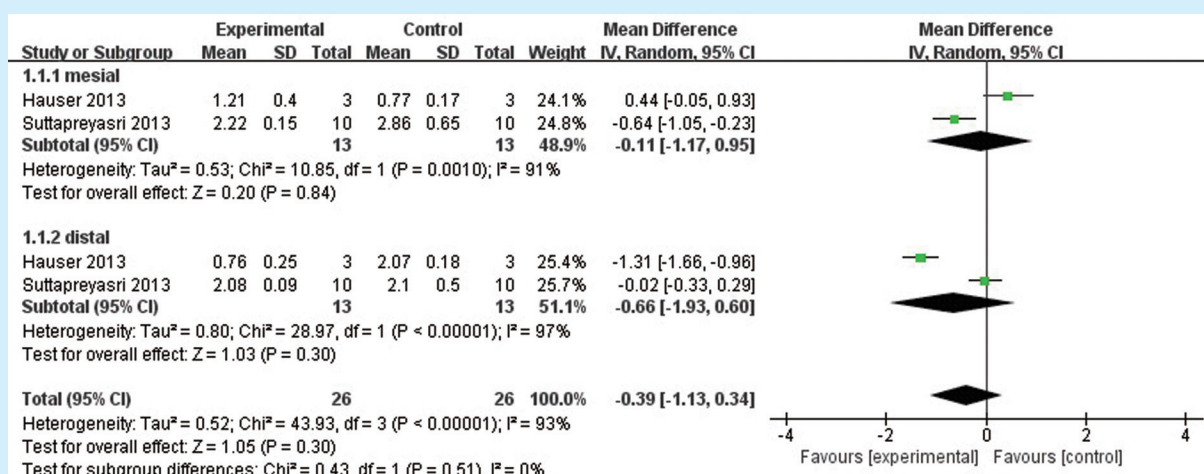


Figure 6 Meta-analysis of vertical bone resorption in the mesial and distal alveolar ridges after tooth extraction  
图6 拔牙后牙槽嵴近中、远中垂直方向骨吸收的meta分析

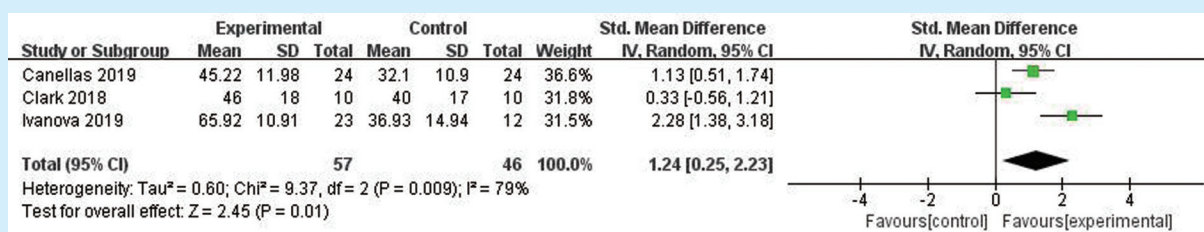


Figure 7 Meta-analysis of the percentage of new bone tissue after tooth extraction  
图7 拔牙后新生骨组织百分比的meta分析

位的牙齿、全身因素等。为了减少吸烟对本研究的影响,在制定纳入标准时将重度吸烟患者(10支/日)排除,而且第三磨牙在拔除过程中常会在分牙、去骨时产热,也会对牙槽骨的愈合产生影响,

故将包含第三磨牙的研究排除。

### 3.1 术后干槽症发生率

本研究结果表明,拔牙术后是否使用PRF对术后干槽症无影响,这与Del Fabbro等<sup>[24]</sup>的结果一

致。虽然 PRF 中含有大量的白细胞,特别是在白细胞-富血小板纤维蛋白(leukocyte and platelet rich fibrin, L-PRF)中,但是 PRF 中白细胞的作用效果尚无确定性结论。有学者认为白细胞作为机体防御系统的重要组成部分,可以抗菌,防止创口感染<sup>[25]</sup>。也有学者认为白细胞可引起炎症反应,加重术后症状<sup>[26]</sup>。需要注意的是干槽症在常规拔牙术后的发生率较低(1%~4%)<sup>[27]</sup>,而且本文纳入的样本量过少,对于本研究的结果应慎重解释。

### 3.2 水平和垂直牙槽骨的吸收

在牙槽骨水平方向上,meta 分析结果显示 PRF 组与自然愈合组差异具有统计学意义。这与 Lin 等<sup>[20]</sup>的系统性综述结果并不一致,其水平方向骨吸收纳入 2 篇研究,结果显示 PRF 组水平方向骨吸收小于对照组,但未达到统计学差异,其中 1 篇研究是非随机对照临床试验,本文并未纳入<sup>[28]</sup>。拔牙后的牙槽骨的高度会发生明显的吸收,特别是颊舌侧方向。查阅以往文献,尚未有 meta 分析评价 PRF 在保存牙槽窝颊舌侧骨量上是否有效。Avila-Ortiz 等<sup>[29]</sup>使用骨替代材料进行位点保存的 meta 分析中,在保存颊舌侧骨量及远中骨量上得到了与本文相同的结果,近远中方向与颊舌侧方向结果不同,可能与拔牙窝邻牙存在与否、测量工具的不同有关。

### 3.3 新生骨百分比

PRF 可在 7~14 d 内缓慢释放生长因子,而且有学者在体外研究证明 PRF 可促进骨髓间充质干细胞的成骨能力<sup>[30-31]</sup>。本文结果表明在术后 12~16 周时,PRF 组的新生骨百分比高于自然愈合组,然而存在较大的异质性,原因可能是研究之间测量时间不同。

### 3.4 局限性

PRF、改良型富血小板纤维蛋白(advanced platelet-rich fibrin, A-PRF)、L-PRF 采用了不同离心方法制备而成,尽管现有文献未能证明其在牙槽嵴保存方面的差异,但相关文献报道 A-PRF, L-PRF 含有更多的白细胞与生长因子<sup>[32-33]</sup>,这可能造成一定的异质性,此外拔牙的手术过程、患者是否吸烟、是否翻瓣等也有可能产生一定的异质性。本研究纳入了 8 篇研究进行定量分析,但由于测量方法、时间、测量点的不同,每个 meta 分析中只纳入了 2 到 3 篇研究,对 meta 分析的结果应当谨慎解释。

本研究表明拔牙后使用 PRF 可有效保存牙槽

嵴水平及颊舌侧方向的骨量,对术后减少干槽症发生率及近远中垂直方向骨吸收无明显效果,但鉴于本研究纳入的试验过少,仍需纳入更多更高质量的随机对照试验研究。

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