

[DOI] 10.12016/j.issn.2096-1456.2021.06.010

· 综述 ·

抗凝/抗血小板治疗患者拔牙术后出血的研究进展

黄金霞, 石海涛, 潘剑

口腔疾病研究国家重点实验室 国家口腔疾病临床医学研究中心 四川大学华西口腔医院口腔颌面外科,
四川 成都(610041)

【摘要】 对接受抗凝/抗血小板治疗的患者进行拔牙手术,常因术后出血风险较高被许多口腔颌面外科门诊医生视为禁忌。多种因素与其发生术后出血相关,但目前还未达成共识。本文以近年文献为基础,对接受抗凝/抗血小板治疗患者发生拔牙术后出血的相关因素进行综述。文献复习结果表明,服用抗血小板药物的患者术后出血风险较服用抗凝药物的患者低;抗凝药物与非甾体类抗炎药、抗抑郁药选择性5-羟色胺抑制剂和5-羟色胺-去甲肾上腺素抑制剂合用,以及术前使用抗生素时,出血风险增加。此外,特定的全身疾病如糖尿病、拔牙位点感染史、较大的手术创伤等与更高的术后出血风险有一定相关性。目前普遍认为拔牙术前不停药、术后合理运用不同的止血措施是安全可行的。未来还需要更多前瞻性的对照试验,以建立不同条件下接受抗凝/抗血小板治疗的患者进行拔牙手术时的安全体系。

【关键词】 抗凝药物; 抗血小板药物; 非甾体类抗炎药; 抗抑郁药; 抗生素;
拔牙术; 术后出血; 凝血指标; 国际标准化比

【中图分类号】 R78 **【文献标志码】** A **【文章编号】** 2096-1456(2021)06-0417-05

【引用著录格式】 黄金霞,石海涛,潘剑.抗凝/抗血小板治疗患者拔牙术后出血的研究进展[J].口腔疾病防治,2021,29(6):417-421. doi: 10.12016/j.issn.2096-1456.2021.06.010.



开放科学(资源服务)标识码(OSID)

Bleeding after tooth extraction in patients receiving anticoagulation/antiplatelet therapy HUANG Jinxia, SHI Haitao, PAN Jian. State Key Laboratory of Oral Diseases & National Clinical Research Center for Oral Diseases & Department of Oral Surgery, West China Hospital of Stomatology, Sichuan University, Chengdu 610041, China
Correspondence: PAN Jian, Email: jianpancn@163.com, Tel: 86-28-85501447

【Abstract】 Tooth extraction in patients receiving anticoagulation/antiplatelet therapy is often considered contraindicated by many oral and maxillofacial surgeons because of a higher risk of postoperative bleeding. Multiple factors contribute to postoperative bleeding, but there is no consensus. Based on recent literature, this article reviews factors related to bleeding after tooth extraction in patients receiving anticoagulation/antiplatelet therapy. The literature review indicates that patients taking antiplatelet drugs have a lower postoperative bleeding risk than patients taking anticoagulant drugs. Prescription of anticoagulants together with non-steroidal anti-inflammatory drugs, selective serotonin inhibitors or serotonin-norepinephrine inhibitors increases the risk of bleeding, so does preoperative antibiotic use increase. In addition, systemic diseases such as diabetes, history of infection at the extraction site, and greater surgical trauma are associated with a higher risk of postoperative bleeding. At present, it is generally believed that it is safe and feasible to use different hemostatic measures after tooth extraction and to rationally apply different hemostatic measures after surgery. More prospective controlled trials are needed in the future to establish an assessment system for patients undergoing anticoagulation/antiplatelet therapy under different conditions during tooth extraction.

【Key words】 anticoagulants; antiplatelet drugs; nonsteroidal anti-inflammatory drugs; antidepressants; antibi-

【收稿日期】 2020-03-02; **【修回日期】** 2020-12-09

【基金项目】 四川省学术技术带头人培养基金(2017-A);四川省干部保健科研课题(川干研2019-901);四川大学华西口腔医院探索与研发项目(LCYJ2019-1)

【作者简介】 黄金霞,医师,硕士研究生,Email: huangjinxia@sina.com

【通信作者】 潘剑,教授,博士,Email: jianpancn@qq.com, Tel: 86-28-85501447

otics; tooth extraction; postoperative hemorrhage; coagulation markers; international normalized ratio

J Prev Treat Stomatol Dis, 2021, 29(6): 417-422.

【Competing interests】 The authors declare no competing interests.

This study was supported by the grants from Sichuan Academic and Technical Leader Training Foundation (No. 2017-A); Sichuan Cadres Health Care Project (No. 2019-901); Research and Develop Program, West China Hospital of Stomatology Sichuan University (No. LCYJ2019-1).

心血管疾病是全球高发病,并且是导致死亡的主要原因之一^[1]。有相当大一部分患者因患心房颤动、机械心脏瓣膜置换术、冠状动脉支架植入或静脉血栓栓塞症,需要长期接受抗凝/抗血小板治疗以预防血栓形成^[2]。这些患者相较于正常患者术后出血的发生率较高^[3],此类患者出现严重出血并发症在早期已有研究报道^[4]。除了抗凝/抗血小板药物抑制凝血的药理作用外,还有药物种类、患者是否服用抗生素等其他因素被报道与出现拔牙术后出血相关^[5-6]。对于这类患者,熟悉拔牙术后出血的危险因素很有必要。本文就接受抗凝/抗血小板治疗的患者拔牙术后出血的危险因素进行综述,为临床操作提供参考。

1 药物因素

1.1 药物种类

抗血小板药物和抗凝药物种类较多,依据作用靶点不同,抗血小板药物可分为影响花生四烯酸代谢药物、P2Y₁₂受体拮抗剂、血小板膜糖蛋白IIb/IIIa受体拮抗剂和磷酸二酯酶抑制剂;抗凝药物分为维生素K拮抗剂(vitamin K antagonists, VKAs)、肝素及低分子量肝素、凝血酶抑制剂和凝血Xa因子抑制剂^[7]。新型的凝血酶抑制剂(达比加群)和凝血Xa因子抑制剂(利伐沙班、阿哌沙班和依度沙班)作用靶点不是维生素K,也被合称为非维生素拮抗剂类口服抗凝药物(non-vitamin K antagonist oral anticoagulants, NOACs),它们被认为相较于华法林(VKAs类抗凝药物)有更低的出血风险^[8]。有研究证实服用华法林的患者较服用NOACs的患者出现更多拔牙术后出血事件,但是这一差异经多元分析后不具有统计学意义。另外也有研究结果显示服用VKAs类药物和NOACs类药物术后出血发生率差异无统计学意义^[9]。以上研究结果的分歧可能是患者基础条件、拔除牙的数目、手术操作、出血评价指标等的不同而造成的。

就文献报道来看,服用抗血小板药物的患者术后出血的发生率较低^[10],甚至有报道表明服用阿司匹林(影响花生四烯酸代谢的抗血小板药物)的患者拔牙术后出血发生率与正常患者没有统计学差异^[11]。在Grobe等^[12]的临床研究中,接受抗血小板治疗的患者拔牙术后出血发生率(1.4%)比另一项研究中接受抗凝治疗(抗凝药物为一种维生素K拮抗剂——苯丙羟基香豆素)治疗的患者低(7.4%)。其他研究也有类似结果(抗血小板治疗1.8%,华法林8.6%)^[10]。可以看出,服用抗血小板药物的患者术后出血风险较服用抗凝药物的患者低。值得注意的是,对服用抗血小板药物的患者,双联疗法患者拔牙术后出血的发生率比单药高,虽然这一差异没有统计学意义^[13]。此外,当同时服用抗血小板药物和抗凝血药物时,出血事件包括拔牙术后出血的发生率增加^[6]。

1.2 药物管理

对于抗凝/抗血小板患者拔牙前是否停药存在较多争议:拔牙前暂时停药抗凝药物、服药后一定时间再行操作和无需停药在不同的研究中都有报道^[14-16]。笔者回顾了相关文献,证据表明对服用VKAs类和NOACs类药物的患者,术前停药与否并不会改变术后出血事件的发生率^[10,17]。而对于继续服用抗血小板药物行拔牙术的患者,有研究发现其术后出血的发生率甚至与正常患者没有统计学差异^[10]。事实上,随着近年研究的深入,目前普遍认为拔牙手术是低出血风险手术^[18],对于服用NOACs、VKAs类抗凝药物和抗血小板药物的患者,拔牙术前都无需停药^[13,19]。尽管如此,有研究认为由于NOACs类药物半衰期短,起效快,手术距离最近一次服药的时间间隔是一项风险因素,间隔时间短时术后出血风险高,因此建议避开血药浓度峰值^[20]。由此可以看出,在患者的凝血指标国际标准化比值(international normalized ratio, INR)控制在一定治疗范围内并保证合理止血措施的情况下,不停药进行拔牙手术是安全可行的。

1.3 药物合用

抗生素和止痛药是口腔门诊中常用的药物。研究报道术前使用抗生素是拔牙术后出血的危险因素之一,但该文中并未提及具体的抗生素种类^[6],曾有病案报告报道过老年患者(>75岁)合用NOACs药物和克拉霉素、红霉素或甲硝唑时出现其他部位严重出血事件^[21],甲硝唑也被报道与华法林合用时发生严重出血事件^[22]。非甾体类抗炎药(nonsteroidal anti-inflammatory drugs, NSAIDs)、抗抑郁药选择性5-羟色胺抑制剂(selective serotonin inhibitors, SSRIs)和5-羟色胺-去甲肾上腺素抑制剂(serotonin-norepinephrine reuptake inhibitors, SNRIs)由于影响血小板活性,与抗凝药物合用时会增加出血风险^[21]。口腔拔牙术后常用止痛药布洛芬和双氯芬酸钠都属于NSAIDs类药物,按前述观点与抗凝药物合用会增加出血风险;而抗凝药物利伐沙班被报道与阿片类药物合用会增加术后出血风险^[23]。因此,在术后开具处方时应谨慎,笔者在临床上对长期服用激素、糖尿病、肾移植、慢性肾炎和免疫系统缺陷的患者会预防性服用抗生素以及术后开具抗生素;一般的患者术前不使用抗生素,术后抗生素处方会依据拔牙创伤而定,如翻瓣去骨拔除阻生牙则嘱其口服3~5 d抗生素,简单正畸牙拔除则不开具抗生素处方。对抗凝/抗血小板患者,会优先选择扑热息痛,并嘱其冰敷缓解肿痛,效果不佳时再用布洛芬等。

其他一些心血管用药如胺碘酮(抗心律失常药物)、阿托伐他汀和辛伐他汀(降血脂药)、比索洛尔和氨氯地平(降压药);抗癫痫药物如丙戊酸钠、氟西汀;抗真菌药物如氟康唑等可与抗凝药物相互作用增加出血风险^[21]。但这些多数是病案报道,且不是针对拔牙后的研究,是否会增加拔牙术后出血的风险则需要进一步分析,但值得引起临床注意。

2 患者因素

2.1 凝血指标

口腔外科门诊中一般都运用凝血指标INR作为是否行拔牙手术的重要指证,围绕拔牙术的INR安全范围,学者们作出大量探索,但这一标准在不同的研究中有较大差异:在 $INR < 4.0$ 、 < 3.5 ,在 $2.0 \sim 3.0$ 或 < 2.5 时安全完成拔牙术均有报道^[2, 9, 10, 24]。Bajkin等^[25]研究发现, $INR > 3.5$ 的患者行翻瓣手术时的术后出血发生率(18.2%, 2/11)较

INR范围在 $2.0 \sim 3.5$ 的患者高(5.0%, 3/60),提示INR值较高患者术后出血的风险更大;但也有研究认为术后出血与INR值之间并无联系^[10]。样本量以及研究纳入的患者的INR值所处的范围可能是造成以上分歧的原因。

活化部分凝血活酶时间(activated partial thromboplastin time, APTT)和凝血酶原时间(prothrombin time, PT)也是常用的凝血指标。Mau-privez等^[20]认为 $APTT > 1.8$ 时出血风险增加。Hasegawa等^[6]分析了发生术后出血患者的值,发现术后出血的患者INR值(2.1 ± 0.7)高于未发生的患者(1.9 ± 0.5),据此认为INR升高也是术后出血危险因素之一;另一项研究也有类似的结果,在该项试验中,出血患者的INR(2.6 ± 0.6)也高于未出血组(2.1 ± 0.4)^[26]。

另外,有研究报道患者自述凝血指标正常,但即刻检查后发现患者自述与真实情况并不相符,指出有必要获取术前即刻凝血指标,以便更准确评估术前风险^[27]。

2.2 其他风险因素

对于口服抗凝药物的患者,当伴有一些全身疾病如肝脏疾病、糖尿病、肾功能不全时,其发生拔牙术后的出血概率提高^[28]。Hasegawa等^[6]却认为伴发的系统疾病、吸烟酗酒等不是拔牙术后出血的危险因素。手术部位毗邻肿瘤的患者有更高的出血风险,需要特别关注^[2]。Iwabuchi等^[26]经多元分析后得出年龄、拔牙位点急性感染史是接受抗凝治疗患者发生拔牙术后出血的危险因素。除此之外, Morimoto等^[29]发现拟拔除牙手术时如果伴有急性炎症,则发生拔牙术后出血的风险增加。

3 手术因素

3.1 手术操作

下牙槽神经阻滞麻醉被认为是术后出血的危险因素之一^[26],而上牙槽后神经和眶下神经阻滞麻醉由于其解剖毗邻静脉丛,有较高刺破血管导致出血的风险,因此在麻醉方式的选择上应优先考虑浸润麻醉。手术时间的选择应该避开抗凝药物的血药浓度峰值,即距上次服药至少4~5 h后(对NOACs类药物而言)^[30]。由于炎症、拔牙的手术方式(直接拔除和手术拔除)和一次拔除牙的数目与术后出血相关^[6, 29],因此拔牙前应该先控制牙周卫生,术中应该尽量使用微创拔牙器械,缩短操

作时间,控制一次拔牙的数目,以降低术后出血的发生。但也有研究^[31]发现拔牙数目和术后出血并发症并无联系。笔者的经验是条件允许时优先选择浸润麻醉,使用微创拔牙的方法,一次手术中只拔除同侧患牙,总数不超过3颗。

3.2 术后措施

关于术后止血的方法多种多样,最为普遍的是棉球局部加压和缝合^[20],但也有研究认为缝合对止血的作用有限,反而会带来更多的创伤^[19]。氨甲环酸被认为是有效的止血剂,可通过漱口液、浸泡缝线、加入明胶海绵等方式发挥止血效果^[32],明胶海绵的运用也较为普遍^[33]。合理运用以上止血措施,能够避免绝大多数的术后出血。

其他止血措施还包括氧化纤维素棉卷加压、抗纤维蛋白溶解药物、丙烯酸酯夹板、硫酸钙、纤维凝胶、氨基己酸、冰敷、停戴活动义齿、蓝紫光照射、电凝止血等^[32,34]。此外,一些新型材料如Hemcon Dental Dressing(以壳聚糖为基质的生物止血材料)、Feraclum Gel(一种新型凝胶)也被报道可以获得良好的止血效果^[35-36]。

4 小结

随着人口老龄化进程的发展和医疗水平的进步,有越来越多的人群需长期服用抗凝/抗血小板药物,这类人群在进行侵入性手术时有较高的术后出血风险。但是临床上,这些患者的基本状况如年龄、基础疾病、所用药物、用法用量等不尽相同,所需拔除的牙齿的难易程度、牙周情况等也相差较大,哪些因素会增加术后出血的风险尚未达成共识。众多学者对术后出血的风险因素进行了探索,但由于实验方法和样本量等的差异,各研究结果也不尽相同。笔者建议抗凝/抗血小板患者首先需按时至内科复诊,确定其生理指标处于治疗范围内再行拔牙术;在拔牙之前应掌握患者全身状况及用药情况,通过加强口腔卫生指导等方式以控制口腔炎症,充分沟通以消除患者的顾虑和术后出血的恐惧心理,拔牙过程中做到微创操作,充分止血以及建立随访机制,将风险降到最低。当然,后续还需要更细化、更大量样本的临床试验来建立一个具体而完善的安全体系,从而指导临床医生如何准确预判特定患者的术后出血风险以及正确规避和处理术后出血。

【Author contributions】 Huang JX, Shi HT wrote and revised the article, Pan J guided the writing of the article. All authors read and approved the final manuscript as submitted.

参考文献

- [1] Schmidt MI, Duncan BB, Azevedo EG, et al. Chronic non-communicable diseases in Brazil: burden and current challenges[J]. *Lancet*, 2011, 377(9781): 1949-1961. doi: 10.1016/S0140-6736(11)60135-9.
- [2] Baron TH, Kamath PS, McBane RD. Management of antithrombotic therapy in patients undergoing invasive procedures[J]. *N Engl J Med*, 2013, 368(22): 2113-2124. doi: 10.1056/NEJMra1206531.
- [3] Hanken H, Grobe A, Heiland M, et al. Postoperative bleeding risk for oral surgery under continued rivaroxaban anticoagulant therapy [J]. *Clin Oral Investig*, 2016, 20(6): 1279-1282. doi: 10.1007/s00784-015-1627-9.
- [4] Ziffer AM, Scopp IW, Beck J, et al. Profound bleeding after dental extractions during dicumarol therapy[J]. *N Engl J Med*, 1957, 256(8): 351-353. doi: 10.1056/NEJM195702212560806.
- [5] Yoshikawa H, Yoshida M, Yasaka M, et al. Safety of tooth extraction in patients receiving direct oral anticoagulant treatment *versus* warfarin: a prospective observation study[J]. *Int J Oral Maxillofac Surg*, 2019, 48(8): 1102-1108. doi: 10.1016/j.ijom.2019.01.013.
- [6] Hasegawa T, Yanamoto S, Tachibana A, et al. The risk factors associated with postoperative hemorrhage after tooth extraction: a multi-center retrospective study of patients receiving oral anti-thrombotic therapy[J]. *Oral Maxillofac Surg*, 2017, 21(4): 397-404. doi: 10.1007/s10006-017-0645-y.
- [7] Mega JL, Simon T. Pharmacology of antithrombotic drugs: an assessment of oral antiplatelet and anticoagulant treatments[J]. *Lancet*, 2015, 386(9990): 281-291. doi: 10.1016/S0140-6736(15)60243-4.
- [8] Bennaghmouch N, de Veer A, Bode K, et al. Efficacy and safety of the use of non-vitamin K antagonist oral anticoagulants in patients with nonvalvular atrial fibrillation and concomitant aspirin therapy: a meta-analysis of randomized trials[J]. *Circulation*, 2018, 137(11): 1117-1129. doi: 10.1161/CIRCULATIONAHA.117.028513.
- [9] Berton F, Constantinides F, Rizzo R, et al. Should we fear direct oral anticoagulants more than vitamin K antagonists in simple single tooth extraction? A prospective comparative study[J]. *Clin Oral Investig*, 2019, 23(8): 3183-3192. doi: 10.1007/s00784-018-2739-9.
- [10] Lu SY, Lin LH, Hsue SS. Management of dental extractions in patients on warfarin and antiplatelet therapy[J]. *J Formos Med Assoc*, 2018, 117(11): 979-986. doi: 10.1016/j.jfma.2018.08.019.
- [11] Hanken H, Tieck F, Kluwe L, et al. Lack of evidence for increased postoperative bleeding risk for dental osteotomy with continued aspirin therapy[J]. *Oral Surg Oral Med Oral Pathol Oral Radiol*, 2015, 119(1): 17-19. doi: 10.1016/j.oooo.2014.08.016.
- [12] Grobe A, Fraederich M, Smeets R, et al. Postoperative bleeding risk for oral surgery under continued clopidogrel antiplatelet therapy[J]. *Biomed Res Int*, 2015: 823651. doi: 10.1155/2015/823651.
- [13] Lu SY, Tsai CY, Lin LH, et al. Dental extraction without stopping single or dual antiplatelet therapy: results of a retrospective cohort study[J]. *Int J Oral Maxillofac Surg*, 2016, 45(10): 1293-1298. doi: 10.1016/j.ijom.2016.02.010.

- [14] Kearon C, Hirsh J. Management of anticoagulation before and after elective surgery[J]. *N Engl J Med*, 1997, 336(21): 1506-1511. doi: 10.1056/NEJM199705223362107.
- [15] Scopp IW, Fredrics H. Dental extractions in patients undergoing anticoagulant therapy[J]. *Oral Surg Oral Med Oral Pathol*, 1958, 11(5): 470-474. doi: [https://doi.org/10.1016/0030-4220\(58\)90090-2](https://doi.org/10.1016/0030-4220(58)90090-2).
- [16] Precht C, Demirel Y, Assaf AT, et al. Perioperative management in patients with undergoing direct oral anticoagulant therapy in oral surgery--a multicentric questionnaire survey[J]. *In Vivo*, 2019, 33(3): 855-862. doi: 10.21873/in vivo.11550.
- [17] Ahmed I, Younis M, Shah AA. Extraction in patients on oral anti-coagulant therapy with and without stopping the drug: a comparative study[J]. *J Maxillofac Oral Surg*, 2019, 18(4): 555-558. doi: 10.1007/s12663-019-01205-0.
- [18] Steffel J, Verhamme P, Potpara TS, et al. The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation[J]. *Eur Heart J*, 2018, 39(16): 1330-1393. doi: 10.1093/eurheartj/ehy136.
- [19] Yang S, Shi Q, Liu J, et al. Should oral anticoagulant therapy be continued during dental extraction? A meta-analysis[J]. *BMC Oral Health*, 2016, 16(1): 81. doi: 10.1186/s12903-016-0278-9.
- [20] Mauprivez C, Khonsari RH, Razouk O, et al. Management of dental extraction in patients undergoing anticoagulant oral direct treatment: a pilot study[J]. *Oral Surg Oral Med Oral Pathol Oral Radiol*, 2016, 122(5): e146-e155. doi: 10.1016/j.oooo.2016.06.003.
- [21] Stöllerberger C. Drug interactions with new oral anticoagulants in elderly patients[J]. *Expert Rev Clin Pharmacol*, 2017, 10(11): 1191-1202. doi: 10.1080/17512433.2017.1370369.
- [22] Nutescu E, Chuatrisorn I, Hellenbart E. Drug and dietary interactions of warfarin and novel oral anticoagulants: an update[J]. *J Thromb Thrombolysis*, 2011, 31(3): 326-343. doi: 10.1007/s11239-011-0561-1.
- [23] Constantinides F, Rizzo R, Pascasio L, et al. Managing patients taking novel oral anticoagulants (NOAs) in dentistry: a discussion paper on clinical implications[J]. *BMC Oral Health*, 2016, 16: 5. doi: 10.1186/s12903-016-0170-7. doi: 10.1186/s12903-016-0170-7.
- [24] Hamzah NA, Graf HL, Meyer AL, et al. Haemostasis in oral surgical procedures involving patients with a ventricular assist device [J]. *Int J Oral Maxillofac Surg*, 2020, 49(10): 1355 - 1359. doi: 10.1016/j.ijom.2019.07.009.
- [25] Bajkin BV, Vujkov SB, Milekic BR, et al. Risk factors for bleeding after oral surgery in patients who continued using oral anticoagulant therapy[J]. *J Am Dent Assoc*, 2015, 146(6): 375-381. doi: 10.1016/j.adaj.2015.01.017.
- [26] Iwabuchi H, Imai Y, Asanami S, et al. Evaluation of postextraction bleeding incidence to compare patients receiving and not receiving warfarin therapy: a cross-sectional, multicentre, observational study[J]. *BMJ Open*, 2014, 4(12): e005777. doi: 10.1136/bmjopen-2014-005777.
- [27] Brennan MT, Hong C, Furney SL, et al. Utility of an international normalized ratio testing device in a hospital-based dental practice [J]. *J Am Dent Assoc*, 2008, 139(6): 697-703. doi: 10.14219/jada.archive.2008.0251.
- [28] Cocero N, Mozzati M, Ambrogio M, et al. Bleeding rate during oral surgery of oral anticoagulant therapy patients with associated systemic pathologic entities: a prospective study of more than 500 extractions[J]. *J Oral Maxillofac Surg*, 2014, 72(5): 858 - 867. doi: 10.1016/j.joms.2013.12.026.
- [29] Morimoto Y, Niwa H, Minematsu K. Risk factors affecting postoperative hemorrhage after tooth extraction in patients receiving oral antithrombotic therapy[J]. *J Oral Maxillofac Surg*, 2011, 69(6): 1550-1556. doi: 10.1016/j.joms.2010.10.018.
- [30] Patel JP, Woolcombe SA, Patel RK, et al. Managing direct oral anticoagulants in patients undergoing dentoalveolar surgery[J]. *Br Dent J*, 2017, 222(4): 245-249. doi: 10.1038/sj.bdj.2017.165.
- [31] Kämmerer PW, Frerich B, Liese J, et al. Oral surgery during therapy with anticoagulants-a systematic review[J]. *Clin Oral Investig*, 2015, 19(2): 171-180. doi: 10.1007/s00784-014-1366-3.
- [32] Ockerman A, Miclotte I, Vanhaverbeke M, et al. Local haemostatic measures after tooth removal in patients on antithrombotic therapy: a systematic review[J]. *Clin Oral Investig*, 2019, 23(4): 1695-1708. doi: 10.1007/s00784-018-2576-x.
- [33] Lababidi E, Breik O, Savage J, et al. Assessing an oral surgery specific protocol for patients on direct oral anticoagulants: a retrospective controlled cohort study[J]. *Int J Oral Maxillofac Surg*, 2018, 47(7): 940-946. doi: 10.1016/j.ijom.2018.03.009.
- [34] Okamoto T, Ishikawa I, Kumasaka A, et al. Blue-violet light-emitting diode irradiation in combination with hemostatic gelatin sponge (spongel) application ameliorates immediate socket bleeding in patients taking warfarin[J]. *Oral Surg Oral Med Oral Pathol Oral Radiol*, 2014, 117(2): 170 - 177. doi: 10.1016/j.oooo.2013.09.009.
- [35] Kumar KR, Kumar J, Sarvagna J, et al. Hemostasis and post-operative care of oral surgical wounds by hemcon dental dressing in patients on oral anticoagulant therapy: a split mouth randomized controlled clinical trial[J]. *J Clin Diagn Res*, 2016, 10(9): ZC37 - ZC40. doi: 10.7860/JCDR/2016/17275.8462.
- [36] Rai S, Rattan V. Efficacy of feracrylum as topical hemostatic agent in therapeutically anticoagulated patients undergoing dental extraction: a comparative study[J]. *J Maxillofac Oral Surg*, 2019, 18(4): 579-583. doi: 10.1007/s12663-018-1156-6.

(编辑 张琳)



官网



公众号