包括性别、种族、糖尿病、高血压、化疗、相关血液 指标等。VTE 重在预防,故妇产科临床医生应该 熟悉相关高危因素、掌握规范化干预指征、发现高 危人群、尽早诊断、及时干预才可以最大限度降低 VTE 的发生率和致死率。

参考文献

- [1] Wong P, Baglin T.Epidemiology, risk factors and sequelae of venous thromboembolism [J].Phlebology, 2012, 27 (Suppl 2): 2–11.
- [2] Krivak TC, Zorn KK. Venous thromboembolism in obstetrics and gynecology [J]. Obstet Gynecol, 2007, 109(3):761–777.
- [3] Zelechowska P, Agier J, Kozlowska E, et al.Mast cells participate in chronic low- grade inflammation within adipose tissue[J].Obes Rev, 2018.doi: 10.1111/obr.12670.[Epub ahead of print].
- [4] Darvall KA, Sam RC, Silverman SH, et al. Obesity and thrombosis[J]. Eur J Vasc Endovasc Surg ,2007,33(2):223-233.
- [5] Larsen TB, Sorensen HT, Gislum M, et al. Maternal smoking, obesity, and risk of venous thromboembolism during pregnancy and the puerperium: a population-based nested case-control study[J]. Thromb Res, 2007, 120(4):505-509.
- [6] Kevane B, Donnelly J, D'Alton M, et al.Risk factors for pregnancy-associated venous thromboembolism: a review [J].J Perinat Med, 2014, 42(4):417-425.
- [7] Gunderson CC, Thomas ED, Slaughter KN, et al. The survival detriment of venous thromboembolism with epithelial ovarian cancer[J]. Gynecol Oncol, 2014, 134(1):73-77.
- [8] 徐臻,王璐,王晨阳,等.卵巢癌患者并发静脉血栓形成的危险因素及预后研究[J].中国实用妇科与产科杂志,2016,32 (11):1098-1102.
- [9] Rauh-Hain JA, Hariton E, Clemmer J, et al.Incidence and effects on mortality of venous thromboembolism in elderly women with endometrial cancer [J].Obstet Gynecol, 2015, 125 (6): 1362-1370.
- [10] Barber EL, Clarke-Pearson DL.Prevention of venous thromboembolism in gynecologic oncology surgery [J]. Gynecol Oncol, 2017, 144(2):420-427.
- [11] Bakhru A.Effect of ovarian tumor characteristics on venous thromboembolic risk[J].J Gynecol Oncol, 2013, 24(1):52–58.
- [12] Rahn DD, Mamik MM, Sanses TV, et al. Venous thromboembolism prophylaxis in gynecologic surgery: a systematic review[J]. Obstet Gynecol, 2011, 118(5):1111-1125.
- [13] Clarke-Pearson DL, Abaid LN.Prevention of venous thromboembolic events after gynecologic surgery [J].Obstet Gynecol, 2012,119(1):155-167.
- [14] 段涛.重视妊娠期抗凝药物的合理应用[J].中国实用妇科与产科杂志,2017,33(7):665-666.
- [15] 顾蔚蓉,李笑天.妊娠相关静脉血栓栓塞症防治策略及中国 实践[J].中国实用妇科与产科杂志,2017,33(6):578-584.

- [16] Friedman AM, Ananth CV.Obstetrical venous thromboembolism: epidemiology and strategies for prophylaxis [J].Semin Perinatol, 2016, 40(2):81-86.
- [17] Macey MG, Bevan S, Alam S, et al.Platelet activation and endogenous thrombin potential in pre- eclampsia [J].Thromb Res, 2010, 125(3); e76-81.
- [18] Jacobsen AF, Skjeldestad FE, Sandset PM.Ante- and postnatal risk factors of venous thrombosis: a hospital-based case-control study[J].J Thromb Haemost, 2008, 6(6):905-912.
- [19] Abdul Sultan A, Grainge MJ, West J, et al.Impact of risk factors on the timing of first postpartum venous thromboembolism: a population-based cohort study from England [J].Blood, 2014,124(18):2872-2880.
- [20] Mi Y, Yan S, Lu Y, et al.Venous thromboembolism has the same risk factors as atherosclerosis; a PRISMA-compliant systemic review and meta- analysis [J].Medicine (Baltimore), 2016,95(32);e4495.
- [21] Hotoleanu C.Genetic risk factors in venous thromboembolism[J]. Adv Exp Med Biol, 2017, 906:253-272.
- [22] van Vlijmen EF, Wiewel-Verschueren S, Monster TB, et al.
 Combined oral contraceptives, thrombophilia and the risk of venous thromboembolism: a systematic review and meta-analysis[J].J Thromb Haemost, 2016, 14(7):1393-1403.
- [23] De Stefano V, Martinelli I, Rossi E, et al.The risk of recurrent venous thromboembolism in pregnancy and puerperium without antithrombotic prophylaxis [J].Br J Haematol, 2006, 135 (3):386-391.
- [24] Baratloo A, Safari S, Rouhipour A, et al.The risk of venous thromboembolism with different generation of oral contraceptives: a systematic review and meta-analysis [J]. Emergency (Tehran, Iran), 2014, 2(1):1-11.
- [25] Vinogradova Y, Coupland C, Hippisley-Cox J.Use of combined oral contraceptives and risk of venous thromboembolism: nested case-control studies using the QResearch and CPRD databases[J].BMJ,2015,350;h2135.doi;10.1136/bmj.h2135.

(2018-04-10收稿)

DOI: 10.19538/j.fk2018070104

妇科围手术期静脉血栓栓塞症的预防

瞿 红,张震宇

摘要:静脉血栓栓塞症(VTE)包括深静脉血栓形成和肺栓塞,是妇科常见的围手术期并发症,严重威胁患者生命安全。如今,VTE已逐渐引起人们的重视,VTE预防不容忽视。结合中国妇科术

作者单位:首都医科大学附属北京朝阳医院妇产科,北京 100020

通讯作者:张震宇,电子信箱:zhenyuzhang2000@163.com

后 VTE 防治经验,2017年制定了"妇科手术后深静脉血栓形成及肺栓塞预防专家共识"。文章就妇科围手术期 VTE 预防的重要性及预防措施进行详解。

关键词:静脉血栓栓塞症;深静脉血栓形成;肺栓塞:妇科手术;预防

中图分类号: R71 文献标志码: C

Prevention of venous thromboembolism in gynecological surgery. QU Hong, ZHANG Zhen-yu. Department of Obstetrics & Gynecology, Beijing Chaoyang Affiliated Hospital of Capital Medical University, Beijing 100020, China

Corresponding author: ZHANG Zhen-yu, E-mail: zhenyuzhang2000@163.com

Abstract: Venous thromboembolism (VTE), including deep vein thrombosis and pulmonary embolism, is a common perioperative complication of gynecological surgery, which threatens the life and health of patients. We have recognized the importance and necessity of the prevention of VTE and paid more attention to it. Based on our experience of prevention and treatment of VTE, we have established "The Expert Consensus on the Prevention of Deep Vein Thrombosis and Pulmonary Embolism after Gynecological Surgery". We detailedly explain the importance and measures of VTE prevention in gynecological surgery.

Keywords: venous thromboembolism; deep vein thrombosis; pulmonary embolism; gynecological surgery; prevention

VTE包括深静脉血栓形成(deep venous thrombosis, DVT)和肺栓塞(pulmonary embolism, PE),是同一种疾病在不同阶段、不同部位的两种表现形式。DVT多数发生于下肢,亦可见于上肢、肠系膜静脉或脑静脉,90%的PE继发于DVT^[1]。VTE对于外科医生而言并不陌生,是围手术期威胁患者生命安全的重要因素。西方国家已对其充分重视并建立了规范的筛查与预防体系,我国骨科和普外科也相继出台了各自专业的VTE防治指南。在妇科领域,我们通过近十年的工作逐步揭示了妇科盆腔手术后VTE的发病特点,据此制定了"妇科手术后深静脉血栓形成及肺栓塞预防专家共识",这不仅标志我国妇科术后VTE预防无据可依状态的结束,更促使术后VTE的预防工作得以全面开展。

1 预防的必要性及意义

西方国家报道,在没有采取预防措施的内外科患者中,DVT发生率高达10%~40%,而40%的妇科术后猝死归因于DVT继发的PE^[2-3]。PE,尤其是急性致命性PE—旦发生几无抢救机会。PE患者中40.9%于7d内死亡,45.4%在30d内死亡^[4]。在所有外科手术中VTE发生率高达36.5%,而其中症状性VTE仅占0.9%^[5],多数VTE患者由于不具有典型临床表现易被忽视。我们近年开展的针对未采取预防措施患者的研究发现,妇科手术后DVT的发生率为9.6%~15.6%,DVT患者中PE占46%^[6-7]。可见,妇科盆腔手术后VTE实际发生率远高于我们预期,由此带来的对患者生命健康威胁不可估量。VTE是一类可防可治的疾病,我们应当正视其危害,采取措施降低其危害,确保手术安全。

2 预防措施

- 2.1 基本预防措施(1)保证充足的有效循环血量,避免血液浓缩。(2)精细、准确、快速的外科手术操作,缩短手术时间。术后尽可能避免使用止血药物,止血药是导致血栓形成的独立危险因素^[7]。(3)对于所有患者,都鼓励术后积极早期床上活动,尽早下地活动。(4)注重宣传 VTE 预防科普知识及宣教,使患者也认识到 VTE 预防的重要性。2.2 物理预防措施 物理预防主要包括分级加压弹力袜(graduated compression stockings, GCS)、间歇性气囊加压(intermittent pneumatic compression, IPC)和足底静脉泵(venous foot pump, VFP)。
- 2.2.1 GCS GCS作为下肢 DVT的初级预防可用于预防下肢远端及无症状 DVT,使之发生率降低65%,但对于下肢近端 DVT和 PE 预防效果尚不确定^[8-9]。与无预防措施相比,GCS降低50% DVT发生率,与其他预防措施联用时可提高其预防效果,如与药物联用可降低55%下肢近端 DVT发生率^[10]。研究显示,过膝 GCS组 DVT发生率6.3%,而膝下 GCS组 DVT发生率8.8%,过膝 GCS减少了31% DVT,效果显著优于膝下 GCS,两组皮肤破损发生率差异无统计学意义^[11]。GCS在应用时应注意选择合适型号,使脚踝水平压力达到18~23 mmHg(1 mmHg=0.133 kPa),方可取得效果^[12]。
- 2.2.2 IPC IPC 对于下肢近端和远端 DVT 均有预防效果,但单独应用不能降低 PE 发生率,与药物

联合应用时可减少 57%的 PE^[13-15]。IPC 的优点在于没有出血的风险。

2.2.3 VFP VFP能够促进静脉回流,减少65% DVT,不会引起出血并发症,与药物预防联用时,可显著减少DVT形成[16-17]。VFP的预防机制与IPC相似,均可以促进纤溶蛋白活性,改善血液高凝状态从而预防血栓形成。

需要注意的是,单纯的机械预防并不能完全替代药物预防。机械预防措施应于术前开始使用,直至患者术后能够自由活动,IPC每日应用时间应不少于18 h。当患者合并以下情况时不建议采用机械预防措施[12]:(1)下肢具有开放性伤口或皮肤异常如皮炎、破损、近期接受植皮手术等。(2)下肢缺血性血管疾病。(3)下肢水肿明显者。(4)心衰、肺水肿患者。(5)安装心脏起搏器患者。(6)下肢DVT或PE者。

- 2.3 药物预防 VTE的药物预防主要包括普通肝素(low-dose unfractionated heparin,LDUH)、低分子肝素(low-molecular-weight heparin,LMWH)、维生素 K 拮抗剂华法林以及新型抗凝药物,围手术期常用的为胃肠外抗凝药物如普通肝素和低分子肝素。
- 2.3.1 普通肝素 采用LDUH可减少56%DVT和30%PE发生,但同时也增加46%的出血概率^[13]。LDUH应用方法为5000 U,皮下注射,每日2次,在应用过程中需监测活化部分凝血活酶时间(APTT)。
- 2.3.2 低分子肝素 LMWH较少引起严重出血,与无预防措施相比,可减少51% DVT和64% PE^[18]。LMWH基本采用皮下注射方式给药,每日1次,不同药物具体用量需依照说明书,由于其对凝血影响较小,应用时无需常规监测凝血。抗凝药物对于减少VTE发生均有一定效果,但也相应增加出血概率,因此,应用前应进行出血风险评估。对于合并严重肾功能不全(肌酐清除率<30 mL/min)的患者,应慎用LMWH或减量使用。
- 2.3.3 维生素 K 拮抗剂 华法林对于 DVT 和 PE 均有较好预防作用,但有引起出血的风险。如果选用华法林长期抗凝,建议在应用胃肠外抗凝药物的 24 h 内重叠应用华法林,起始剂量 2~3 mg,应用过程中监测凝血,调节国际标准化比值(INR)目标值达到 2.0~3.0。INR 达标 24 h 后应停用胃肠外抗凝药物。

2.3.4 磺达肝癸钠 Xa因子抑制剂磺达肝癸钠相较于LMWH可减少48%DVT,但对于PE的预防两者差异无统计学意义[13]。用法为2.5 mg皮下注射,每日1次。

对于药物预防时限,建议于术后6~12 h开始使用,应用前均应评估出血风险,良性疾病为术后7~10 d或至可以自由活动,恶性肿瘤至术后4周[19]。以下情况不建议采用药物预防[12]:(1)患者合并活动性出血或凝血功能障碍。(2)合并活动性消化道溃疡。(3)严重的肝肾功能异常。(4)肝素或磺达肝癸钠过敏者。(5)既往曾有肝素诱导的血小板减少症(heparin-induced thrombocytopenia, HIT)。

3 基于风险分级的预防

减少 VTE 的危害重在预防, 预防措施应个体化, 基于风险分级的预防措施更为有效, 尤其是高危和极高危的患者。目前国际广泛使用的 VTE 风险评估模型是 Caprini 评分系统^[20]。但由于种族、疾病分布特点以及医疗技术水平等方面的差异, 应建立适于我国女性患者的盆腔术后 DVT 风险评估系统。

3.1 明确患者风险及其所处风险分级 风险评估基于各种导致 DVT形成的危险因素,主要包括患者自身因素和手术相关因素两方面,可归结为3个要点:静脉血管壁损伤、血流停滞或缓慢及血液高凝状态。根据我国研究提出妇科术后 DVT形成的6个高危因素:年龄≥50岁、高血压、静脉曲张、手术时间≥3 h、术后卧床时间≥48 h以及开腹手术。每个因素赋值1分,依据积分将患者分为4个风险等级,建立妇科 Caprini 评分系统(G-Caprini) 「19」。见表1。

表1 妇科术后 DVT 危险度分级(G-Caprini)

低危 0 0.43 中危 1 3.31 高危 2 5.36 极高危 ≥3 28.31	危险分级	分值(分)	术后DVT发生率(%)
高危 2 5.36	低危	0	0.43
1,7,5	中危	1	3.31
极高危 ≥3 28.31	高危	2	5.36
	极高危	≥3	28.31

3.2 个体化预防 根据 G-Caprini 确定患者所处 风险等级,采取相应预防措施:(1)低危患者术后 尽早下地活动。(2)中危患者术后采取药物或机械

预防。(3)高危患者术后无大出血风险者,采取药物预防(LMWH或 LDUH);术后出血风险高者,先机械预防(IPC为佳),待评估出血风险降低后改为药物预防。(4)极高危患者术后无大出血风险者,采取机械与药物联合预防;术后出血风险高者,先机械预防(IPC为佳),待出血风险降低后改为机械与药物联合预防。

4 预防中应注意的问题

(1)要取得良好预防效果,需重视围手术期VTE筛查。对具有前述6个高危因素其中任一者应在术前排除DVT后实施手术,术后2~7d进行筛查。(2)DVT筛查首选无创的下肢加压超声,确诊DVT者应除外PE,首选CT肺血管造影(computed tomographic pulmonary angiography, CTPA)。(3)术后出现可疑PE症状者亦应行相关检查排除PE,并及时采取相应预防措施。(4)恶性肿瘤术后推荐药物预防持续4周。(5)不推荐将下腔静脉滤器作为围手术期VTE常规预防措施。

妇科手术后VTE具有较高发生率,后果严重,但是一类可防、可治的疾病,需要引起我们充分重视,做好术前、术后筛查与预防,将危害降至最低。而VTE所致孕产妇死亡仍缺乏充足资料。我们应继续深入探索,研究妇产科领域VTE的特点、诊断及预防策略,丰富证据,完善预防体系。

参考文献

- [1] Goldhaber SZ, Bounameaux H.Pulmonary embolism and deep vein thrombosis[J].Lancet, 2012, 379(9828): 1835–1846.
- [2] Geerts WH, Pineo GF, Heit JA, et al. Prevention of venous thromboembolism: the seventh ACCP Conference on antithrombotic and thromblytic therapy [J]. Chest, 2004, 126: 338S-400S.
- [3] Davis JD.Prevention, diagnosis, and treatment of venous thromboembolic complications of gynecologic surgery [J]. Am J Obstet Gynecol, 2001, 184(4):759-775.
- [4] Heit JA, Silverstein MD, Mohr DN, et al. Predictors of survival after deep vein thrombosis and pulmonary embolism- a population-based cohort study [J]. Arch Int Med, 1999, 159:445-453.
- [5] Leizorovicz A, SMART Venography Study Steering Committee. Epidemiology of post- operative venous thromboembolism in Asian patients: results of the SMART venography study [J]. Haematologica, 2007, 92(9):1194-1200.
- [6] Qu H, Li Z, Zhai Z, et al. Predicting of venous thromboembolism for patients undergoing gynecological surgery [J]. Medicine, 2015, 94(39); e1653.

- [7] 刘玉珍,张震宇,郭淑丽,等.妇科盆腔手术后下肢深静脉血栓形成的临床研究[J].中华妇产科杂志,2006,41(2):107-110
- [8] Gould MK, Garcia DA, Wren SM, et al. Prevention of VTE in nonorthopedic surgical patients; antithrombotic therapy and prevention of thrombosis, 9th ed; American College of Chest Physicians Evidence-Based Clinical Practice Guidelines [J]. Chest, 2012,141(2 Suppl); e227S-e277S.
- [9] Geetts WH, Heit JA, Clagett GP, et al.Prevention of venous thromboembolism[J].Chest, 2001, 119:132s-175s.
- [10] Sachdeva A, Dalton M, Amaragiri SV, et al. Elastic compression stockings for prevention of deep vein thrombosis [J]. Cochrane Database Syst Rev, 2010, (7): CD001484.
- [11] Dennis M, Cranswick G, Deary A, et al.The CLOTS (Clots in Legs Or sTockings after Stroke) Trial Collaboration. Thighlength versus below-knee stockings for deep venous thrombosis prophylaxis after stroke: a randomized trial [J]. Ann Intern Med, 2010, 153(9):553-562.
- [12] 中华医学会外科学分会.中国普通外科围手术期血栓预防与管理指南[J].中华外科杂志,2016,54(5):321-327.
- [13] Autar R.NICE guidelines on reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in patients undergoing surgery [J].J Orthopaedic Nursing, 2007,11(3-4):169-176.
- [14] Urbankova J, Quiroz R, Kucher N, et al.Intermittent pneumatic compression and deep vein thrombosis prevention: a metaanalysis in postoperative patients [J]. Thromb Haemost, 2005, 94(6):1181-1185.
- [15] 张舰,桑翠琴,赵娜,等.妇科盆腔手术后下肢深静脉血栓的 预防[J].现代妇产科进展,2014,23(9):695-699.
- [16] Roderick P, Ferris G, Wilson K, et al. Towards evidence—based guidelines for the prevention of venous thromboembolism systematic reviews of mechanical methods oral anticoagulation dextran and regional anaesthesia as thromboprophylaxis [J]. Health Technol Assess, 2005, 9(49); iii-iv, ix-x, 1-78.
- [17] Giannoni MF, Ciatti R, Capoccia L, et al. Total knee replacement prevention of deep-vein thrombosis using pharmacological (low-molecular-weight heparin) and mechanical (intermittent foot sole pump system) combined prophylaxis: preliminary results[J].Int Angiol, 2006, 25(3):316-321.
- [18] Zufferey P, Laporte S, Quenet S, et al. Optimal low-molecular-weight heparin regimen in major orthopaedic surgery: a meta-analysis of randomised trials [J]. Thromb Haemost, 2003, 90 (4):654-661.
- [19] 郎景和,王辰,瞿红,等.妇科盆腔手术后深静脉血栓形成及 肺栓塞预防专家共识[J].中华妇产科杂志,2017,52(10):
- [20] Caprini JA. Risk assessment as a guide to thrombosis prophylaxis[J].Curr Opin Pulm Med, 2010, 16(5):448-452.

(2018-04-10收稿)