

出國報告（出國類別：國際會議）

無抑製劑血友病患者手術全期止血
管理的成果-161 案侵入性處置或外科
手術經驗

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派赴國家：英國

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摘要（含關鍵字）

本次參加報告的會議為世界血友病聯盟(World Federation of Hemophilia)每 2 年舉辦一次之國際會議(WFH 2018 World Congress)，主辦單位為世界血友病聯盟與地主國英國血友病協會。本人於 5 月 21 日發表，臺中榮總罕見疾病暨血友病中心整合醫療團隊國家品質標章(SNQ)認證成果：臺灣最大規模關於血友病患於手術期間凝血控制之研究，共有 161 次侵入性檢查和手術，結果顯示低出血率(1.2%)，感染率(0%)，血栓形成 (0%)，抗體發生(0%)。同時本研究對於許多種類侵入性檢查和手術提出使用凝血因子之劑量和天數可達成最佳止血效果。除此，此次國際大會指導臺中榮總埔里榮民分院黃永杰醫師，發表 moderate poster，主題為利用台灣健保資料庫，分析台灣血友病患者心理疾病(psychological disorder)的盛行率以及其危險因子，提供足夠的科學證據，進而改善台灣血友病患者的臨床照護。研究結果顯示台灣血友病患者與一般族群比較有較高的憂鬱症和焦慮症盛行率，並且 C 型肝炎病毒感染是一個重要危險因子。這個重要發現不僅學術研究上的價值，同時也有足夠的科學證據提供未來台灣血友病患者照護上更多精細嚴密的準則。

關鍵字：世界血友病聯盟，血友病，手術，心理疾病

一、 目的

參加世界血友病聯盟(World Federation of Hemophilia)每 2 年舉辦一次之國際會議(WFH 2018 World Congress)，發表臺中榮總罕見疾病暨血友病中心整合醫療團隊國家品質標章(SNQ)認證成果：臺灣最大規模關於血友病患於手術期間凝血控制之研究；另一重要工作指導臺中榮總埔里榮民分院黃永杰醫師，發表 moderate poster，主題為利用台灣健保資料庫，分析台灣血友病患者心理疾病(psychological disorder)的盛行率以及其危險因子。

二、 過程

2018 年 5 月 20 日至 2017 年 5 月 26 日參加世界血友病聯盟(World Federation of Hemophilia) 2018 年大會，2018 年 5 月 21 日發表臺中榮總罕見疾病暨血友病中心整合醫療團隊國家品質標章(SNQ)認證成果：無抑制劑血友病患者手術全期止血管理的成果經歷 161 案侵入或外科手術，2018 年 5 月 22 日發表台灣血友病患者心理疾病的盛行率以及其危險因子。

重要成果為

1. 血友病病患各種手術使用之凝血因子用量
2. 血友病病患手術發生出血併發症比率
3. 血友病病患手術發生感染併發症比率
4. 血友病病患手術發生血栓併發症比率

2018 年 5 月 23 日與台灣血友病病友團體代表，接受 Biomarin 生技藥廠討論台灣 A 型血友病基因治療的可行性。

三、 心得

本人為國際血栓和出血學會國際會員，並為亞太地區理事會成員(council member)。藉由國際會議與各國的互動，不僅讓世界各會員國對台灣血栓暨止血學術研究的重視，也提昇臺中榮總出血性疾病和血友病治療在亞太地區的地位。

四、 建議事項（包括改進作法）

會議結束後，著手臺中榮總血友病團隊大會報告內容發表於國際期刊；並且，整理大會 state of the art 預計於 2018 年 9 月 2 日台灣血栓暨止血學會舉辦 post-WFH meeting 發表，促進國內血栓暨止血學術發展。

五、 附錄

(一)海報

83 Outcome of perioperative hemostatic management in patients with hemophilia without inhibitors undergoing 161 invasive or surgical procedures

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Introduction

Perioperative management of persons with hemophilia (PWH) is challenge for surgeons and hematologists. The mortality rate was reported up to 66 % in PWH undergoing minor and major surgery in the mid 20th century.¹ A reduction of the mortality rate to 4.5 % was achieved since improvement of hemostatic controls using clotting factor concentrates (CFCs) during perioperative period.² However, dosing of CFC administration for the procedures is disagreed. World Federation of Hemophilia (WFH) devised a guideline for PWH with surgery both in CFC constraint and non-constraint countries.³

Objective

To evaluate the outcome of perioperative hemostatic management in PWH without inhibitors according the guideline of WFH.

Methods

In this consecutive case study, patient data of all moderate and severe hemophilia patients undergoing invasive or surgical procedures at one hemophilia comprehensive care center between the period of 2011 and 2016 were evaluated retrospectively. PWH who have been diagnosed with an inherited or acquired hemostatic defect other than hemophilia, a present or past history of inhibitors, cirrhosis or low platelet count were excluded. The peak level of clotting factor before major procedure was targeted to 100 IU dL⁻¹ and 80 IU dL⁻¹ for HA and HB patients, respectively except for 120 IU dL⁻¹ before total joint replacement; it was 80 IU dL⁻¹ before minor surgery. The dosing of recombinant CFC administration after surgery was based on the WFH guideline to maintain the desired trough level. The duration of recombinant CFC administration was extended to 21 to 28 days after procedures in some types of major surgery, ex. spinal surgery, total joint replacement, intestine resection. The hemostatic response to surgery with clotting factor were reviewed using a four-point scale (i.e. excellent, good, fair, poor/none) via patients' operation note, consistent with the WFH guidelines.

Results

A total of 80 HA and 9 HB patients undergoing invasive or surgical procedure were enrolled. Among enrolled PWH, 70 (87.5 %) HA and 5 (55.5 %) HB patients were severe type. Twelve (15.0 %) of the HA patients were on prophylactic therapy, and all were below 18 years old. Of HB patients, only one (11.1 %) was on prophylactic therapy (Table 1). The time of drainage removal were according the standards of surgical care. Three patients with total joint replacements received transfusions of red blood cells during the operation, but otherwise blood component transfusion was not needed in all the other procedures during perioperative period. No thromboprophylactic therapy was used during perioperative period except for patients who underwent cardiac catheterization receiving half of standard dose of heparin. None of PWH was found with thromboembolic events after the procedures. In addition, none developed inhibitors of coagulation factors during more than 3 months of follow-up after the procedures. Three complication was noticed; two ones were delayed bleeding after surgery noticed (Figure 1A and B). Adjunctive therapy with antifibrinolytic agents was used in 4 of patients with major procedure, including one total joint replacement and 3 ureter stone removal, and all patients with dental management.

Contact Information

¹Craddock et al. *Ann Surg* 1948; ²Rudowski et al. *Ann R Coll Surg Engl* 1981; ³Srivastava et al. *Haemophilia* 2013

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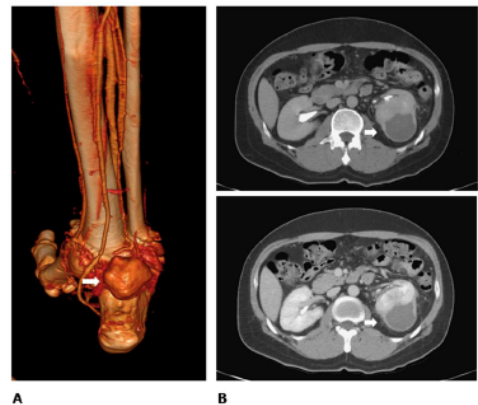
Table 1

Hemophilia A	n	Age at procedure (years)	Severe hemophilia n (%)	Clotting factor use		Adequacy of transfusion (%)	Complication (n)
				Onset (days)	Total amount (IU)		
major procedure	47						
total joint replacement	9	33 (35.46)	9 (100%)	26 (25-28)	1290 (111-1376)	E (85), G (1)	postoperative bleeding (1)
total hip	1	32	1 (100%)		26		126
total knee	1	33	1 (100%)		21		99
ligament reconstruction	3	12 (40.00)	2 (66.7%)	21 (17-23)	760 (740-813)	E	retinal detachment (1)
internal fixation	2	24 (48.47)	1 (50%)	20 (18-21)	955 (798-1121)	E	
cutting bone internal	1	30	1 (100%)		14		723
ureter stone removal	3	31 (66.67)	3 (100%)	14	888 (703-880)	E (25), G (1)	renal thrombosis (1)
prostate adenoid resection	1	40 (66.67)	1 (100%)	14	341 (178-826)	E	
cholesterol extraction	2	10 (1-12)	2 (100%)	14	862 (718-846)	E	
hemorrhoid ligation	1	10	1 (100%)		10		52
hemorrhoid	1	45 (43.40)	1 (100%)	18 (8-21)	488 (412-805)	E	
soft tissue tumor resection	1	34	1 (100%)	10	371	G	
deep wound with closure	8	48 (48.00)	4 (50%)	7 (5-9)	313 (130-305)	E	
teeth extraction with traction cord (stage)	12	39 (10.56)	4 (33%)	7 (7-9)	548 (315-351)	E	
minor procedure	80						
arthroscopy with biopsy	6	37 (32.50)	5 (83.3%)	3 (3-5)	261 (227-209)	E	
ankle/foot internal	3	30 (21.00)	3 (100%)	3	181 (178-209)	E	
TAE	1	39 (57.42)	1 (100%)	4 (3-5)	289 (225-286)	E	
radiotherapy ablation	3	49 (66.42)	3 (100%)	4 (3-5)	276 (156-260)	E	
cholesterol extraction	4	12 (30.77)	4 (100%)	4 (3-5)	254 (226-265)	E	
cardiac catheterization	2	9 (9-10)	2 (100%)	3	241 (214-207)	E	
abdominal surgery	80	41 (37.56)	60 (75%)	11 (1-2)	31 (45-100)	E	
internal fixation tumor of bone	1	30	1 (100%)	7	289	G	
bone cancer biopsy	1	46	1 (100%)	3	289	E	
ESWL	1	31	1 (100%)	3	259	E	
Hemophilia B	9						
major procedure	8						
gastroscopy internal	1	21	1 (100%)	14	85	E	
hemorrhoid ligation	1	48	1 (100%)	10	79	G	
CARD side fixation	1	30	1 (100%)	14	79	E	
teeth extraction with traction	5	31 (21.42)	1 (20%)	5 (5-7)	396 (244-451)	E	
minor procedure	8						
arthroscopy with biopsy	2	40 (21.40)	1 (50%)	3	242 (209-205)	E	
gastroscopy internal	6	32 (60.00)	6 (100%)	1 (1-2)	80 (72-117)	E	

Note: we reported as excellent (E), good (G), fair (F), poor (P), none (N).

*Adapted from Craddock et al. in the guideline of World Federation of Hemophilia, E, excellent; G, good; CARD, Cardiac Catheterization; ESWL, Extracorporeal shock wave lithotripsy; TAE, Transcatheter Aortic Valve Replacement.

Figure 1



Conclusions

To date, there is little evidence to test whether the recommended levels of clotting factor is adequate. In addition, the current guideline for recommended level and duration of CFC use is simply classified into two categories, major and minor surgery. The current guideline for recommended level and duration of CFC use is simply classified into two categories, major and minor surgery. However, surgery types in PWH, as well as general population are diverse. Therefore, it is not clear for different procedures of CFC dose per infusion, the number of infusions and duration required to maintain hemostasis during the perioperative period, and anticipated complication. The study highlights a lower rate of bleeding, infection, thromboembolic event and inhibitor development during the perioperative period. It provides recommended dose and duration of CFC administration for several major and minor surgeries to achieve excellent hemostatic control. However, specific treatment guidelines for different invasive or surgical procedures are needed to be devised based on large cohort or case series studies.

(二)大會照片剪影



附註:

最上排中:王建得醫師發表臺中榮總罕見疾病暨血友病中心整合醫療團隊國家品質標章(SNQ)認證成果

最下排左:與台灣血友病病友團體代表，接受 Biomarin 生技藥廠討論台灣 A 型血友病基因治療的可行性。

最下排右: 指導臺中榮總埔里榮民分院黃永杰醫師，發表 moderate poster。