The international, prospective Glanzmann Thrombasthenia Registry: treatment and outcomes in surgical intervention

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ABSTRACT

Standard treatment for Glanzmann thrombasthenia, a severe inherited bleeding disorder, is platelet transfusion. Recombinant factor VIIa is reported to be effective in Glanzmann thrombasthenia with platelet antibodies and/or refractoriness to platelet transfusions. We aimed to evaluate recombinant factor VIIa effectiveness and safety for the treatment and prevention of surgical bleeding in patients, with or without platelet antibodies and/or refractoriness, using data from the Glanzmann Thrombasthenia Registry, an international, multicenter, observational, post-marketing study of rFVIIa. Between 2007 and 2011, 96 patients were treated for 206 surgical procedures (minor 169, major 37). History of platelet antibodies was present in 43 patients, refractoriness in 23, antibodies+refractoriness in 17, while 47 had no confirmed antibodies/refractoriness. Treatments analyzed included antifibrinolytics, recombinant factor VIIa, recombinant factor VIIa+antifibrinolytics, platelets±antifibrinolytics and recombinant factor VIIa+platelets±antifibrinolytics. The most frequent treatment for minor procedures was recombinant factor VIIa+antifibrinolytics (n=65), and for major procedures, recombinant factor VIIa+platelets±antifibrinolytics (n=13). In patients without antibodies/refractoriness, recombinant factor VIIa, either alone or with antifibrinolytics, and platelets±antifibrinolytics were rated 100% effective for minor and major procedures. The effectiveness of treatment for minor procedures in patients with antibodies and refractoriness was 88.9% for recombinant factor VIIa, 100% for recombinant factor VIIa+antifibrinolytics, 66.7% for platelets±antifibrinolytics and 100% for recombinant factor VIIa+platelets±antifibrinolytics. One of four adverse events reported for surgery was considered recombinant factor VIIa-treatment-related (non-fatal thromboembolic event in an adult female receiving recombinant factor VIIa+platelets+antifibrinolytics). For all patients, regardless of platelet antibody or refractoriness status, recombinant factor VIIa, administered with or without platelets (±antifibrinolytics), provided effective hemostasis with a low frequency of adverse events in surgical procedures in Glanzmann thrombasthenia patients. This trial was registered at *clinicaltrials.gov identifier: 01476423.*

Introduction

Glanzmann thrombasthenia (GT) is an inherited, autosomal, recessive disorder of platelet function caused by quantitative or qualitative defects of the platelet membrane glycoprotein IIb/IIIa (integrin αIIbβ3) complex.[1,2] GT is rare, with an incidence of approximately 1:1 million, although this is much higher in areas where marriage between close family relatives is common.[1,3] Overall, GT is a severe bleeding disorder. Patients show signs of bleeding beginning in childhood. Bleeds are usually mucocutaneous and include easy bruising, purpura, epistaxis, gingival bleedings and menorrhagia.[2,3] Bleeding complications frequently occur after dental extraction, surgery, childbirth and trauma.

Bleeding in GT can often be treated by local hemostatic agents and antifibrinolytics (AF).[1] However, platelet transfusion is required for surgical procedures and for moderate or severe bleeds when local measures are ineffective. Repeated platelet transfusion may, however, result in the development of an allergic reaction, as well as antibodies to human leukocyte antigen (HLA) or αIIbβ3 that may render future platelet transfusion ineffective.[2,4-6]

Previously, we showed that recombinant human factor VIIa (rFVIIa) was a good alternative therapeutic agent for bleeding and surgical prophylaxis in GT.[7,8] Data from a previous international survey of 59 patients treated for 108 bleeding episodes and 34 surgical/invasive procedures[7] allowed a preliminary suggestion for a more optimal rFVIIa regimen (rFVIIa ≥80 μg/kg given at ≤2.5-h intervals for three or more doses) for the treatment of moderate/severe bleeding episodes. However, the number of evaluable surgical procedures was too small for an appropriate regimen for surgical prophylaxis to be proposed.

The Glanzmann Thrombasthenia Registry (GTR)[8] was an observational, international registry established following the approval of rFVIIa in Europe in 2004. This article describes the effectiveness and safety reported for the various hemostatic agents examined in surgical procedures in GT patients, with or without antibodies and/or refractoriness, in the GTR.

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Methods

The Glanzmann Thrombasthenia Registry

The GTR was a post-marketing, observational, international registry with the primary objective of collecting and evaluating data on the effectiveness and safety of rFVIIa in patients with GT for treatment and prevention (surgical prophylaxis) of bleeding.[8] Data were also collected on the use of other systemic hemostatic agents. Treatment was based on local clinical practice rather than a set protocol. Data entry into the GTR was between 10th May 2007 and 16th December 2011.

Ethics

This study was conducted in accordance with the Declaration of Helsinki and Guidelines for Good Pharmacoepidemiology Practices. Each participating center complied with local regulations. Where required, ethical and/or regulatory approval was obtained before data entry into the registry. Signed informed consent to participate in the GTR was obtained from all patients (or parents/legal guardians for minors).

Inclusion and exclusion criteria

The GTR included patients (males and females of any age) with congenital GT defined as patients with lifelong bleeding tendency characterized by impaired or absent platelet aggregation to physiological stimuli, and prolonged bleeding time or prolonged platelet function analyzer closure time.

Optional diagnosis criteria were impaired clot retraction, quantitative or qualitative evaluation of glycoprotein IIb/IIIa receptors including flow cytometry and identification of gene defects. Platelet refractoriness (refractoriness) and the presence of platelet antibodies (AB) were coded initially and assessed periodically as deemed important by the investigator. Patients with acquired thrombasthenic states caused by autoimmune disorders or medications were excluded.

Definitions

1. Surgical procedures were categorized *post hoc* as major or minor (Table 1).

2. Treatment was categorized into five treatment groups: 1) rFVIIa alone; 2) rFVIIa with AF (rFVIIa+AF); 3) platelets alone or with AF (P±AF); 4) combined use of rFVIIa and platelets with or without AF (rFVIIa+P±AF); and 5) AF alone (AF). AF were usually given during the pre-, intra- and post-operative periods. The history of AB and/or refractoriness was categorized as follows: no AB/refractoriness, AB+refractoriness, refractoriness only or AB only. However, as tests for AB may not have been available at all centers, AB may also have been present in some cases in the refractoriness-only group.

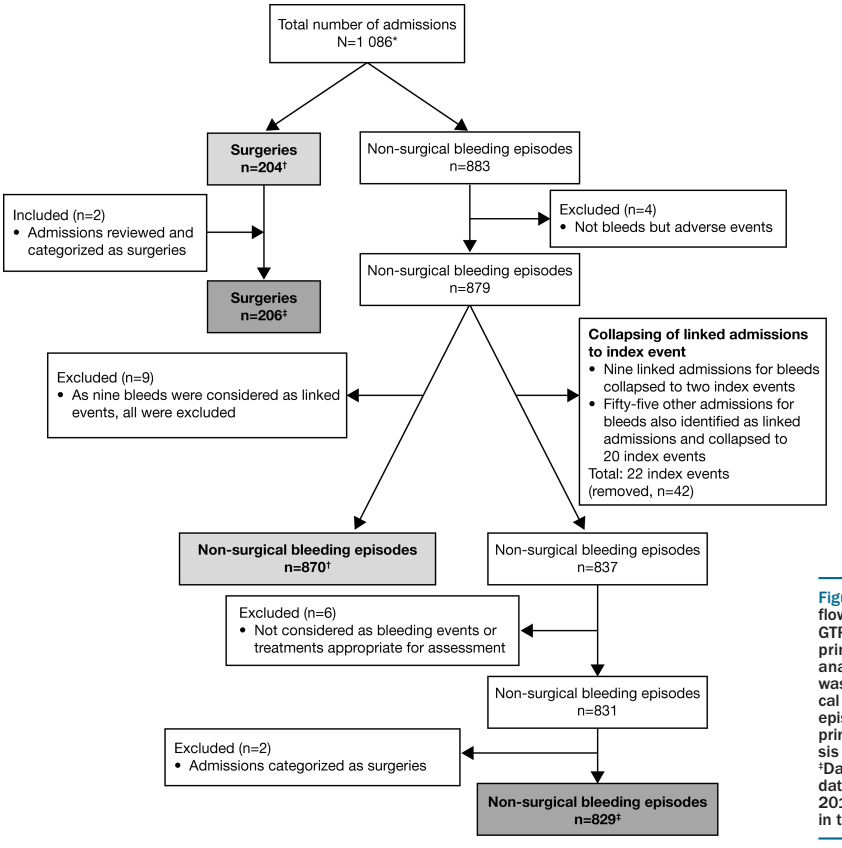

Figure 1. Chart depicting the flow of admissions into the GTR and the data used for primary and secondary analysis. *One admission was considered both a surgical procedure and a bleeding episode. †Data used for the primary effectiveness analysis (performed in 2012). ‡Data used for the secondary data analysis (performed in 2014). All data were included in the safety analysis.

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3. Definitions used for treatment effectiveness, past or present refractoriness to platelet transfusions and post-surgical bleeding are summarized in Table 1.

4. Safety assessments included frequency of adverse events (AEs) and serious AEs (SAEs) during and after treatment.

Statistical methods

The analysis of treatment effectiveness was based on all treatment-allocated patients for whom the effectiveness end point was known. All patients and treatment episodes were included in the safety analysis. All evaluations were summarized with numerical variables (mean, standard deviation, median, maximum and minimum), while categorical variables were summarized as numbers and percentages. No formal statistical comparisons were performed.

Results

Recruitment into the GTR and effectiveness and safety datasets

Data were collected from 1086 admissions (883 for bleeding and 204 for surgery; one admission was considered as both); 218 patients with GT were enrolled from 45 sites in 15 countries from Europe, Africa, Asia and North America (Figure 1). All 1086 admissions were included in the safety analysis. However, for the effectiveness evaluations, review of the data showed that four admissions were AEs and not treatments for bleeds and hence were excluded from the evaluations (Figure 1). In addition, it was found that on several occasions multiple admissions contained information on the same bleeding episode; in these instances, the admissions were collapsed and one designated as the index event. In total, 64 admissions for bleeds were considered to be linked events and were collapsed into 22 index events. Lastly, as two admissions previously considered as bleeding episodes were in fact minor surgeries, these were transferred for analysis of the surgical procedures (Figure 1). In total, the *post hoc* secondary effectiveness analysis was performed using data from 829 admissions for non-surgical bleeding, and 206 surgical admissions (Figure 1).

Clinical and demographic characteristics of the GTR population undergoing surgical procedures and types of procedures

The clinical and demographic characteristics of patients entered into the GTR who underwent surgery are provided in Table 2. Of 206 invasive procedures reported in 96 patients, 169 (in 78 patients) were minor and 37 (in 29 patients) were major. The majority of surgical procedures (78.6%) (Table 2) were performed in adults aged 18 years of age or over (29 major, 133 minor). Only 21.4% of procedures (8 major and 36 minor) were performed in children under 18 years of age (Table 2).

Minor procedures: treatment and outcome

Among the 169 minor surgical procedures performed, the most common was dental (n=134, 79.3%), followed by endoscopy (n=11, 6.5%) and nasal procedures (n=8, 4.7%). Most of the minor procedures were treated with rFVIIa, either alone (56/169; 33.1%) or with AF (65/169; 38.5%) (Table 3). Data on the number of minor procedures rated as "effective" (see definition in Table 1) for the different treatment modalities (overall and stratified according

Table 1. ***Post hoc*** **definitions of surgical category, and definitions of treatment effectiveness, platelet refractoriness and post-surgical bleeding.**

	Definition
Major surgery	• A body cavity was entered, or • A mesenchymal barrier (e.g. pleura, peritoneum or dura) was crossed, or • A facial plane was opened, or • An organ was removed, or • Normal anatomy was operatively altered
Minor surgery	• Any invasive operative procedure in which only skin, mucous membranes or superficial connective tissue were manipulated
Effectiveness end point	
• Effective	• Normal hemostasis
• Partially effective	• Mild bleeding tendency
• Ineffective	• Excessive bleeding tendency
Platelet refractoriness*	• Bleeding during surgery despite an adequate amount† of platelet infusion and/or • Persistence of bleeding despite an adequate amount† of platelet infusion and/or • Re-bleeding within 24 h despite an adequate amount† of platelet infusion
Post-surgical bleeding	• Bleeding after effective outcome of the initial prophylactic treatment for the surgical procedures, occurring up to 7 days after the last hemostatic treatment‡

**Past or present. †An adequate amount is determined by the treating clinician. ‡Bleeding occurring beyond seven days after the last hemostatic treatment was considered a new bleeding episode unrelated to the surgical procedure or its prophylactic regimen.*

Table 2. **Clinical and demographic characteristics of the GTR population having surgical procedures.**

Variables n (%)	Patients (n=96)	Procedures (n=206)
Female	52 (54.2)	114 (55.3)
Age distribution on admission*		
Age <12 years	21 (21.9)	34 (16.5)
Age 12-17 years	6 (6.3)	10 (4.9)
Age ≥18 years	69 (71.9)	162 (78.6)
GT disease type		
Type 1	48 (50.0)	114 (55.3)
Type 2	6 (6.3)	14 (6.8)
Variant	1 (1.0)	2 (1.0)
Unknown	41 (42.7)	76 (36.9)
No AB/refractoriness	47 (49.0)	89 (43.2)
Presence of AB	43 (44.8)	104 (50.5)
Anti-αIIbβ3	35 (36.5)	87 (42.2)
Anti-human leukocyte antigen	16 (16.7)	45 (21.8)
Other	7 (7.3)	18 (8.7)
Refractoriness	23 (24.0)	57 (27.7)
AB+refractoriness	17 (17.7)	44 (21.4)

**For all patients, mean ± standard deviation: 28 ± 17 (range 1-80). For all procedures, mean ± standard deviation: 27 ± 14 (range 1-80). AB: platelet antibodies; αIIbβ3: glycoprotein IIb/IIIa; GT: Glanzmann thrombasthenia; refractoriness: platelet refractoriness.*

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to the status of platelet antibodies and platelet refractoriness) are shown in Table 3.

Use of rFVIIa

Data on rFVIIa use were available for 133 minor procedures treated with rFVIIa, rFVIIa+AF or rFVIIa+P±AF. For all minor procedures, median rFVIIa use was 100 μg/kg (range 3.6-300 μg/kg), with very similar median values (range 90-117 μg/kg) for the different patient groups (*Online Supplementary Table S1*). The median dosage interval was most commonly 2 h across groups, with a median of 2.0-3.0 doses used. The median cumulative rFVIIa dose range and duration of treatment used for minor surgeries were found to be more variable across the groups (*Online Supplementary Table S2*).

Use of platelets

Platelets±AF were used in 26 minor procedures, with 80.8% of treatments overall being rated effective (Table 3). This treatment was rated partially effective in one of three procedures in the AB+refractoriness group and four of 12 in the AB-only group. For the 13 minor procedures treated with rFVIIa+P±AF, 84.6% of procedures were rated effective overall (Table 3).

Ineffective treatments

Only three of the 169 minor procedures were rated "ineffective." Two were in the AB-only group (rFVIIa+AF and rFVIIa+P±AF) and one in the no AB/refractoriness group (AF only). Post-surgical bleeding (as defined in Table 1) was reported following rFVIIa treatment for two minor dental procedures at two and three days after the last dose of rFVIIa; both were successfully treated with additional rFVIIa.

Major procedures: treatment and outcome

Among the 37 major surgical procedures performed, the most common were gastrointestinal and orthopedic (n=9, 24.3% each). Major procedures were treated most frequently with rFVIIa+P±AF (n=13, 35.1%). Most of the major procedures were in the no AB/refractoriness group (n=25, 67.6%), followed by nine (24.3%) in the AB-only group, with only one (2.7%) and two (5.4%) major procedures in the AB+refractoriness and refractoriness-only groups, respectively. Effectiveness ratings for the different treatment modalities for major procedures (overall and stratified according to the status of platelet antibodies and platelet refractoriness) are shown in Table 3.

Use of rFVIIa

Data on rFVIIa use were available for analysis in 25 major procedures treated with rFVIIa, rFVIIa+AF or rFVIIa+P±AF. For all major procedures, the median rFVIIa dose was 90 μg/kg (interquartile range 90-92, range 25-240), with relatively similar median values ranging from 90-142 μg/kg reported for the different patient groups (*Online Supplementary Table S1*). The dosage interval was 2-6 h across the groups (median 3 h) with wider variation in the number of doses (median 2.0-14.5) (*Online Supplementary Table S1*). Information on the cumulative rFVIIa dose is provided in *Online Supplementary Table S2*.

Use of platelets

The effectiveness outcome for cases treated with platelets (P±AF, rFVIIa+P±AF) was available in 19 major surgical procedures (Table 3). Of these, all seven major procedures treated with P±AF, and eight of 12 treated with rFVIIa+P±AF, were effective, with three treated with rFVIIa+P±AF partially effective.

Ineffective treatment

Only one (in the no AB/refractoriness group, treated with rFVIIa+P±AF) of the 37 major procedures was rated "ineffective." No post-surgical bleeding (as defined in Table 2) was reported following rFVIIa and/or platelet treatment for major procedures.

Safety outcome

Forty-six AEs in 18 patients were reported in the registry, of which 15 were SAEs. In a total of 15 AEs (in 9 patients) the treatment included rFVIIa. Seven SAEs in the GTR were entries for AEs only, all unrelated to rFVIIa

Table 3. Treatments rated "effective" (see Table 1 for definition) stratified according to surgical category and to the history of platelet antibodies and/or platelet refractoriness.

Patient groups/surgical category	rFVIIa number effective/total number (%)	rFVIIa+AF number effective/total number (%)	P±AF number effective/total number (%)	rFVIIa+P±AF number effective/total number (%)	AF number effective/total number (%)	Overall number effective/total number (%)
A. Minor procedures (n=169)*						
No AB/refractoriness (n=64)	24/24 (100.0)	17/17 (100.0)	11/11 (100.0)	4/4 (100.0)	4/8 (50.0)	60/64 (93.8)
AB+refractoriness (n=43)	16/18 (88.9)	19/19 (100.0)	2/3 (66.7)	3/3 (100.0)	0/0 (–)	40/43 (93.0)
Refractoriness only (n=11)	4/4 (100.0)	3/5 (60.0)	0/0 (–)	1/2 (50.0)	0/0 (–)	8/11 (72.7)
AB only (n=50)	9/10 (90.0)	19/23 (82.6)	8/12 (66.7)	3/4 (75.0)	1/1 (100.0)	40/50 (80.0)
All minor procedures (n=168)	53/56 (94.6)	58/64 (90.6)	21/26 (80.8)	11/13 (84.6)	5/9 (55.6)	148/168 (88.1)
B. Major procedures (n=37)†						
No AB/refractoriness (n=24)	4/4 (100.0)	3/3 (100.0)	5/5 (100.0)	6/9 (66.7)	3/3 (100.0)	21/24 (87.5)
AB+refractoriness (n=1)	0/0 (–)	0/0 (–)	1/1 (100.0)	0/0 (–)	0/0 (–)	1/1 (100.0)
Refractoriness only (n=2)	0/0 (–)	0/0 (–)	0/0 (–)	1/2 (50.0)	0/0 (–)	1/2 (50.0)
AB only (n=8)	2/2 (100.0)	2/4 (50.0)	1/1 (100.0)	1/1 (100.0)	0/0 (–)	6/8 (75.0)
All major procedures (n=35)	6/6 (100.0)	5/7 (71.4)	7/7 (100.0)	8/12 (66.7)	3/3 (100.0)	29/35 (82.9)

**Effectiveness outcome was missing for one minor surgical procedure treated with rFVIIa±AF in a patient from the AB-only group. †Effectiveness data were missing for two major surgical procedures, one treated with AF from the no AB/refractoriness group and one procedure treated with rFVIIa±P±AF from a patient in the AB-only group. AB: platelet antibodies; AF: antifibrinolytic agent(s); P: platelets; refractoriness: platelet refractoriness; rFVIIa: recombinant factor VIIa.*

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treatment, and were as follows: six SAEs in one patient (angina, alternation of clinical status, hyperthermia, face and eyelid edema, and staphylococcus infection), and one SAE in a second patient (viral meningitis). Table 4 summarizes the AEs reported in treated patients.

For surgery (Table 4), two SAEs and two non-serious AEs were reported in 4 rFVIIa-treated patients. One thrombotic event (deep vein thrombosis) developed in an adult female with platelet refractoriness treated with rFVIIa+P+AF after an emergency laparotomy (ovarian cyst and hematoma with bilateral ureteral compression; major surgery); the event was non-fatal and judged by the investigator to be probably or possibly related to rFVIIa. The second SAE was rectorrhagia in an adult male who underwent a colonoscopy (minor surgery) and received rFVIIa+AF, and was considered unlikely to be related to rFVIIa, and the patient recovered. The two non-serious AEs were one allergic reaction attributed to platelet transfusion in an adult male without platelet refractoriness or antibodies treated with rFVIIa+P+AF (minor surgery), and one pyrexia in a male child without platelet antibodies or refractoriness treated with rFVIIa+P+AF (major surgery); both were considered unlikely to be related to rFVIIa and the patients recovered completely.

Discussion

The GTR data reported here come from the largest observational study on GT patients and include information on the management of invasive procedures; the shortcomings of the previous survey[7] are addressed in that the use of hemostatic agents other than rFVIIa is now included.

Use of rFVIIa

In general, rFVIIa, either alone or with AF, was used more frequently than platelets (P±AF), not only in patients with antibodies and/or refractoriness, but also in patients without either. The GTR results further indicate that rFVIIa has a good safety profile in GT patients.

Assessment of rFVIIa dosage and dose schedule in this large registry suggests that in minor procedures, rFVIIa dosage of 90-140 μg/kg given at approximately 2-h intervals for two or more doses (until effective hemostasis), with the first dose given immediately pre-operatively could be used. This is similar to the regimen we previously suggested for bleeding episodes (rFVIIa ≥80 μg/kg at intervals of 2.5-h or less for three or more doses),[7] and is also similar to standard rFVIIa dosing in patients with congenital hemophilia A or B with inhibitors.

In major procedures, a rFVIIa dosage of 90 μg/kg was used most frequently. The median dose interval as a group was slightly longer (3 h), likely related to the tendency for dosing intervals to lengthen over time when duration of treatment is longer. For major procedures, rFVIIa at 90 μg/kg or more at intervals of 2.5-h or less should be used, at least at the beginning. The subsequent number of doses required would have to be determined by the clinical situation and dosing should be continued until hemostasis is assured.

Use of platelets

As expected, platelet transfusion was effective in covering surgical procedures in patients without platelet antibodies and refractoriness, and less effective in patients with platelet antibodies and/or platelet refractoriness. Of interest is that some of the procedures in the AB-only group had a successful outcome with P±AF, and was also successful in three out of four procedures in the AB+refractoriness group (Table 4). A possible explanation of this finding is that some patients with a history of AB and/or refractoriness were no longer refractory, or that antibodies were no longer present, at the time of surgery. It may also be due to patients with HLA antibodies only being given HLA-matched platelets; but even if HLA-unmatched platelets are given, previous data suggest that more than 50% of patients may not manifest refractoriness to platelet transfusion.[9-11] These observations suggest that even in patients with a history of AB and/or refractoriness, treatment with platelets may be attempted when other agents are ineffective or not available.[7] Successful platelet transfusion following removal of platelet antibodies by plasmapheresis[12,13] or immunoadsorption[14] has also been reported.

Table 4. Summary of adverse events reported in treated patients in the GTR*

	Treatment including rFVIIa		Hemostatic treatment not including rFVIIa		Total	
	Patients, n	Adverse events	Patients, n	Adverse events	Patients, n	Adverse events
Surgical bleeding						
All, n.	4	4	–	–	4	4
Serious adverse events, n.	2	2	–	–	2	2
Non-serious adverse events, n.	2	2	–	–	2	2
Non-surgical bleeding						
All, n.	5	11	10	24	13	35
Serious adverse events, n.	2	5	1	1	2	6
Non-serious adverse events, n.	4	6	10	23	13	29
Total†						
All, n.	9	15	10	24	17	39
Serious adverse events, n.	4	7	1	1	4	8
Non-serious adverse events, n.	6	8	10	23	15	31

**A total of 46 AEs in 18 patients were reported in GTR; seven AEs were reported in 2 patients and were not associated with any bleeding episode or hemostatic treatment. †As patients may have had both surgical and non-surgical bleeding, and/or serious and non-serious adverse events, some patients have been included in the patient counts more than once. AE: adverse event.*

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Combined use of platelets and rFVIIa

One of the questions raised previously is whether combined use of platelets and rFVIIa (rFVIIa+P±AF) has an advantage over rFVIIa (alone or with AF) or P±AF.[7] Interestingly, rFVIIa+P±AF was less effective than rFVIIa and rFVIIa+AF. It is possible that rFVIIa+P±AF was used in patients with more difficult or challenging clinical situations; additional hemostatic agent(s) might have been added to the regimen when effectiveness was in doubt while using another hemostatic agent(s). In support of this supposition, two (one minor, one major) of the four treatment failures were in the rFVIIa+P±AF treatment group.

Use of AF without platelets or rFVIIa

The successful use of AF without platelets or rFVIIa was reported in a small number of procedures, and may be due to AF treatment being started with the intention to use other systemic hemostatic agent(s) should hemostasis not be achieved, but that these agents were subsequently considered not to be needed. The less controlled data collection process compared with actual clinical trials makes it inherently difficult to interpret or directly compare effectiveness between treatments. We do suggest, however, that AF should not be recommended as sole therapy, particularly for major procedures, without the backup availability of rFVIIa or platelet concentrates.

Safety

One potential concern regarding the use of rFVIIa in GT patients is whether rFVIIa is thrombogenic. The data reported here suggest that all of the systemic hemostatic agents used were safe for surgical procedures in GT patients. Of the 206 procedures performed in 96 patients, only one thromboembolic event was reported; this is in contrast to the higher thromboembolism rate, particularly arterial thrombosis, attributed to rFVIIa when used off-label in patients without a hemostatic defect.[15-17]

Limitations

The major limitation of the study reported here is that data were not obtained with defined treatment protocol(s) in a randomized manner, and treatment effectiveness and safety were not assessed at multiple consistent, predefined time points. Furthermore, due to the common use of multiple agents in GT, and delays in obtaining platelets, it is particularly difficult to ascribe effectiveness to any one or more products. In addition, as the coding of history of refractoriness or antibodies was performed at first admission and when the investigator was considered appropriate, the lack of documentation of specific antibody testing or refractoriness at the time of a particular episode limits the analysis (particularly of use of platelet-based regimens).

Formal clinical trials are unfortunately hindered by the rarity of GT. The data reported here represent the largest dataset available in the literature, including those in other databases.[7,18,19] Furthermore, these registry data represent real-life clinical practices and the standards of care at the participating sites. Narrative information, as provided in the GTR, often provides additional useful insights that might differ from the coding of effectiveness at an earlier time point after surgery.

Conclusions

The number of surgical procedures performed in GT patients reported here represents the largest experience so far available in the literature. In general, both rFVIIa and platelets were observed to be effective, and rFVIIa was safe for both minor and major procedures in patients with or without antibodies and/or refractoriness.

The dosage and schedule required for surgery was very similar to the optimal regimen reported for bleeds in previous studies, being 90-140 μg/kg at intervals of 2.5 h or less for two or more doses for minor surgery, and more doses for major surgery, until hemostasis is achieved.[7,20,21] The frequent use of this agent in GT patients without platelet antibodies or refractoriness suggests some investigators used this as the first-line treatment for their GT patients.

GTR Participating Investigators

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Authorship and Disclosures

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[no notes on this page]