OBSERVATIONAL STUDY OF COSTS AND APPROPRIATENESS OF USE OF HEMOSTATIC DEVICES AND DRUGS IN DIFFERENT TYPES OF BLEEDING.

Filoso Immacolata[1], Iacolare Maria Rosaria.[2], Monti Ida [3], Tortora Attilio[4], Contiello Claudio[5], De Luca Assunta[5], Scarano Anna [5], Gerbi Giovanni[6], Mignano Gaetano[6], Falconio Lucio Marcello[7]

[1] *Director of Hospital Pharmacy;* [2] *Pharmacist Manager involved in the procurement of Implantable Medical Devices;*
[3] *Pharmacist Manager involved in the procurement of Medicines and Pharmaceuticals;* [4] *Pharmacist with a scholarship;*
[5] *Professional Nurse ;* [6] *Healthcare Operator (OSS);*
[7] *Pharmacist Manager involved in the procurement of Medical Devices and Medical Supplies.*

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ABSTRACT

Introduction:
Bleedings can result from insufficient blood coagulation and represent a relevant clinical aspect in medical practice. In most cases, these are genetically determined disorders that persist throughout a person's life, leading to a significant financial burden on the National Health System and affecting the patient's quality of life.
On the other hand, the bleeding phenomenon can be influenced in its potential complications by various factors such as pharmacological therapies, autoantibodies, clinical situations, lifestyle, and other factors related to possible genetic predispositions. These undesirable effects pose a diagnostic and therapeutic challenge that often presents characteristics of urgency and severity due to disruptions in the patient's hemostatic balance.
Pharmacological therapy with anticoagulants, whether they are heparin-based or NOACs, can affect the duration and quantity of bleeding. Therefore, it is essential to always inform the surgeon and the general practitioner before any procedure if the patient is on these medications. The replacement or discontinuation of these drugs should only be carried out under medical guidance, even if it's for preparing for minor or major surgical interventions. Stopping bleeding is an essential medical procedure, both in the operating room and in outpatient settings. The choice of hemostatic drug or device to use is based on the type of bleeding to be treated and can be a lifesaver for the patient, expediting the recovery process. Making the most appropriate choice promptly can lead to significant economic savings, making it an effective and efficient practice without wasteful decisions.
Materials and Methods:
The study is observational and multicentric, spanning over 36 months, with data collected from a cohort of 75,000 patients treated at the departments and clinics of the San Giuliano Hospital within the territory of ASL Napoli 2 Nord in the northern area of the Campania capital. The degree of bleeding from the lesions was classified based on a scale validated by the FDA, dividing the phenomenon into grades ranging from 0 to 4. Grade 0 refers to blood loss <1.0 mL/min, Grade 1 to bleeding between 1.0 < mL/min > 5.0, Grade 2 to bleeding between 5.0 < mL/min > 10.0, Grade 3 to bleeding between 10.0 < mL/min > 50.0, and Grade 4 to bleeding with blood loss > 50 mL/min. This division corresponds to a severity threshold and relative life-threatening risk based on the quantity of bleeding. Medical professionals who intervened or were responsible for follow-up visits were given a mini-questionnaire in which they were asked to classify the outcome success rate based on the percentage, assessing the cessation of bleeding considering the initial severity according to the FDA scale. The obtained responses were classified as perfect, good, sufficient, or failed based on the achieved outcome, also correlated with the type of hemostatic device and/or drug used for each individual treatment. The considered therapies involving hemostatic devices and/or drugs were evaluated for total cost. Responses that initially failed were subsequently reclassified as at least sufficient, in order to understand the economic impact of less consistent choices in the treated cases and the related financial expenditure. Within the costs assessed for therapies from sufficient to perfect, all costs related to cases where therapy needed to be modified to improve the outcome were already included.
Results:
During the 36 months of the study, the outcomes of the 75,000 cases were collected, and each of them was attributed to a grade on the FDA scale. Considering the outcomes, the observed responses were effective, with just under 7% of the total not reaching the levels from perfect to sufficient. The threshold for a failed outcome was intentionally set very high (positive outcome less than 49%) to maintain high performance levels to ensure a good average success rate of the therapies. It is worth noting that out of the 7% of failed responses, only 2% yielded a positive outcome of less than 22%, indicating a significant deviation from the average positivity standards achieved. The outcomes are influenced by the choices made during the bleeding treatment phase, particularly when considering the total for each group. This allowed for the identification of the best therapeutic choices for each grade on the FDA scale. Thus, adhesive sealants were classified as Perfect for Grade 0 cases with only Blood Loss, hemostatic patches for Grade 2, and surgical adjuvants with thrombin and coagulation factor for Grade 4 cases where the patient's life is seriously at risk. Hemostatic powders and dressings were classified as Sufficient for Grade 1 cases, while the hemostatic matrix performed well for Grade 3 cases.
When considering the percentage impact on the total cost of the individual observed responses, it was revealed that perfect responses account for 43%, while failed responses account for 10%. In conclusion, the average costs of treatments resulting in a failed response were approximately €135,000. The costs related to the change of

therapy to improve the initially obtained response were also calculated.
Conclusions:
The appropriate classification of the type of bleeding allows for swift intervention and a higher accuracy in selecting the appropriate medical device and/or medication. By using the FDA-validated bleeding scale, optimal results for the patient's life can be achieved quickly, which is highly significant for their recovery.
Simultaneously, making the correct choice regarding the use of medication and/or devices to stop bleeding leads to continuous cost monitoring for the corresponding therapies, achieving efficiency and effectiveness while containing costs. The total costs of the 75,000 observed therapies conducted over 36 months in the departments, including the Emergency Room and outpatient clinics of San Giuliano Hospital to address hemorrhages, amounted to approximately €1,500,000. Out of this, around €150,000 could have been saved with a targeted and appropriate choice of the most suitable therapy.

INTRODUCTION

Bleeding can result from inadequate blood coagulation and represents a relevant clinical aspect in medical practice, even for non-specialist doctors. In Italy, around 10,000 people are affected by disorders related to this phenomenon. In most cases, these are genetically determined disorders that persist throughout life, leading to a significant cost impact on the National Health System and also affecting the quality of life of the affected patients.
On the other hand, the bleeding phenomenon can be influenced in its potential complications by various factors such as pharmacological therapies, autoantibodies, clinical situations, lifestyle, and other factors related to possible genetic predispositions. These unwanted effects present a diagnostic and therapeutic challenge that often takes on urgent and dramatic characteristics due to the disruptions in the patient's hemostatic balance.

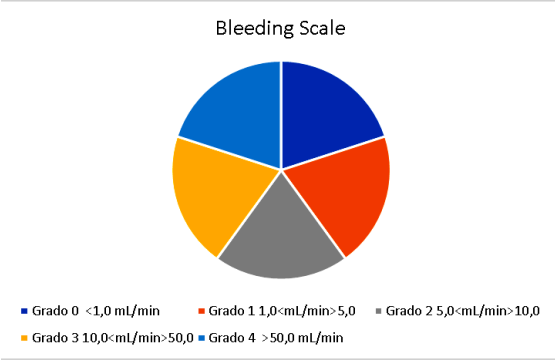
Factors Influencing Bleeding		
Pharmacological Therapies	Anticoagulant Drugs	
Autoantibodies	Autoimmune Diseases	
Clinical Situations	Post-Surgery and Postpartum	Previous Illnesses
Lifestyle Situations	Traumas	Accidents
Genetic Predispositions	Blood Group	

Table 1: *Factors that Can Influence Bleeding*

Pharmacological therapy with anticoagulants, whether they are heparins or NOACs (Non-Vitamin K Oral Anticoagulants), influences the duration and quantity of bleeding. Therefore, it is always necessary to inform the surgeon and the medical team before undergoing any surgical procedure if you are on anticoagulant therapy. The decision to replace or interrupt these medications should only be made under the guidance of a medical professional, especially if such changes are necessary to prepare for a minor or major surgery.
The formation of a blood clot also involves the activation of various blood coagulation factors, which are proteins primarily produced by the liver. There are over a dozen blood coagulation factors, and they generate thrombin. Thrombin converts fibrinogen, a normal blood coagulation factor, into long fibrin filaments that extend from the aggregated platelets, forming a network that traps other platelets and red blood cells. The fibrin filaments add mass to the forming clot and help to securely seal the vessel wall injury.
Recent studies have shown that genetics play a role in the outcomes related to bleeding. Patients with blood type O have lower levels of coagulation factors responsible for preventing potentially lethal bleeding. The mortality rate among individuals with severe trauma, which remains the leading cause of death in such patients, is 28% higher for those with blood type O compared to other blood types. Severe liver conditions (such as cirrhosis or liver failure) can reduce the production of coagulation factors and increase the risk of excessive bleeding. Since the liver requires vitamin K to produce some of the coagulation factors, a deficiency in vitamin K can lead to excessive bleeding.
Stopping bleeding is an essential medical procedure both in the operating room and in outpatient settings. The choice of hemostatic drug or device to use is based on the type of bleeding to be treated and can be a life-saving measure for the patient, as well as an accelerator of recovery times. Making the most suitable choice quickly can lead to significant cost savings, becoming an effective and efficient practice that avoids waste related to inappropriate choices.

MATERIALS AND METODS

The study is observational and multicenter, lasting for 36 months, with data collected from a cohort of 75,000 patients treated at various departments, including the Emergency Room, and outpatient clinics of the San Giuliano Hospital located within the territory of ASL Napoli 2 Nord in the northern area of the Campania region.
The degree of bleeding from the lesions was classified using a scale validated by the FDA, dividing the phenomenon into grades from 0 to 4. Grade 0 refers to bleeding with a rate of <1.0 mL/min, Grade 1 indicates bleeding at a rate of 1.0 < mL/min > 5.0, Grade 2 represents bleeding at a rate of 5.0 < mL/min > 10.0, Grade 3 corresponds to bleeding at a rate of 10.0 < mL/min > 50.0, and Grade 4 indicates blood loss exceeding 50 mL/min. Such division has been correlated, based on the amount of bleeding, with a threshold of severity and the related risk to life.



Graph 1: *FDA-validated Bleeding Scale*

GRA-	SEVERITY	RISK
G0	No Bleeding with Blood	No
G1	Minimal Bleeding	No
G2	Moderate Bleeding	No
G3	Heavy Bleeding	YES
G4	Profuse Bleeding	YES

Tab 2: *Association with FDA Severity Scale Grade and Risk of Life*

In essence, Grade 0 corresponds to no bleeding with blood loss, Grade 1 to minimal bleeding, Grade 2 to moderate bleeding, Grade 3 to substantial bleeding, and finally Grade 4 to life-threatening bleeding.

To the doctors who performed the interventions or those responsible for follow-up visits, a brief questionnaire was administered in which they were asked to classify the response based on the percentage of successful outcome, evaluating the cessation of bleeding considering its initial severity according to the FDA scale.

Response	Outcome
Excellent	+ > 95%
Good	80%<+>94%
Satisfactory	79%<+>50%
Failed	+ < 49%

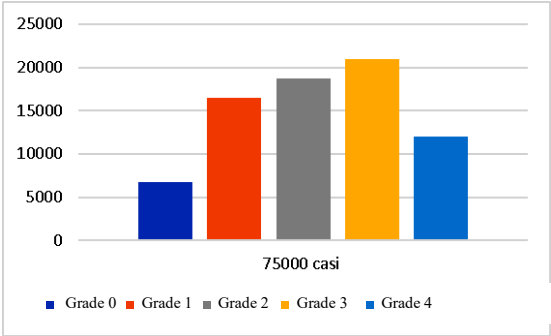
Table 3: *Classification of Response Based on Outcome Percentage out of Total Cases After Follow-up*

The obtained responses have been classified as perfect, good, sufficient, and failed, depending on the achieved outcome, also correlating them with the type of hemostatic device and/or drug used for each individual treatment.

The therapies involving the hemostatic devices and/or drugs used have been evaluated for total cost, as well as the failed responses which were subsequently addressed to generate a sufficient response in order to understand the economic amount of choices not entirely consistent with the treated cases and their corresponding economic expenditure. Within the costs recorded for therapies from sufficient to perfect, all those for which a variation in the therapy was necessary to improve the outcome have already been included.

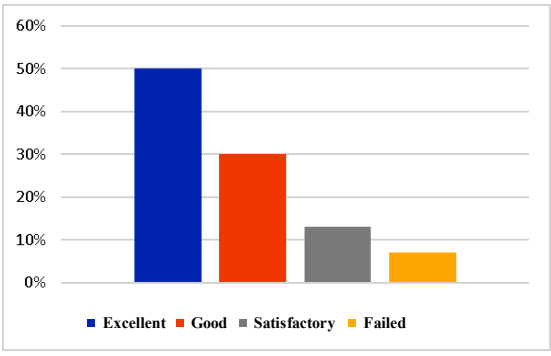
RESULTS

During the 36 months of the study, the outcomes of the 75,000 cases were collected, and each of them was associated with a grade on the FDA scale. Therefore, the following were associated:



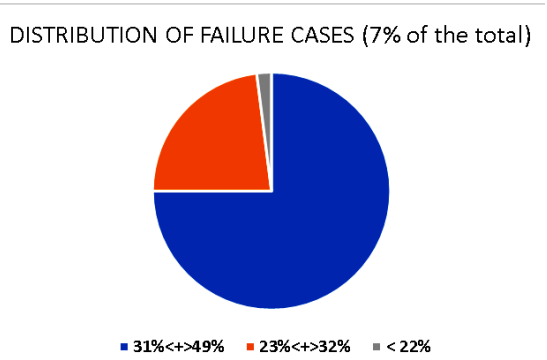
Graph 2: *Percentage of FDA scale grade membership in the 18 months among the observed 75,000 cases*

- 9% of the total with only Minor Bleeding without any life-threatening danger to the patient;
- 22% of the total with Minor Bleeding without consequential life-threatening danger for the individuals involved;
- 25% reported Moderate Bleeding without life-threatening danger for the patient;
- 28% with Abundant Bleeding with consequential life-threatening danger for the patient;
- 16% with Copious Bleeding with consequential life-threatening danger for the patient.



Graph 3: *Percentage of responses in the observed 75,000 cases*

Considering the outcomes, the observed responses were effective, with slightly less than 7% of the total not achieving levels from perfect to sufficient. The threshold for failure was intentionally set very high (positive outcome less than 49%) to maintain high performance levels and ensure a good overall success rate of the therapy.



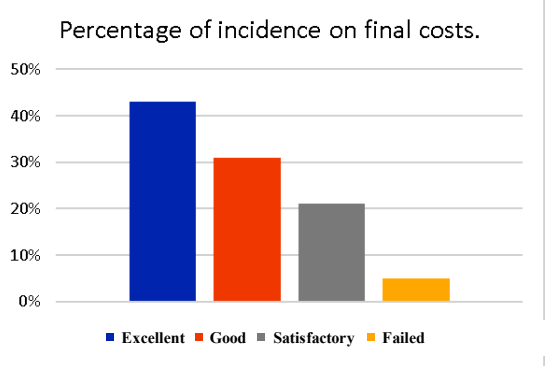
Graph 4: *Distribution of failure cases based on % positive outcome*

It is important to highlight that out of the 7% of failure responses, only 2% resulted in a positive outcome of less than 22%, which is significantly distant from the average positivity standards achieved. The outcomes are influenced by the choices made during the bleeding treatment phase, particularly when considering the total of each group. This allowed for the identification of the best therapeutic choices for each grade on the FDA scale.

GRADE	RESPONSE	TREATMENT PHASE	OUTCOME
G0	Perfect	Sealant adhesives	+ nel 98%
G1	Sufficient	Powders and gauzes	+ nel 90%
G2	Perfect	Hemostatic patches	+ nel 94%
G3	Good	Hemostatic Matrix and Thrombin	+ nel 94.5%
G4	Perfect	Surgical adjunct with Thrombin and coagulation factor	+ nel 97%

Tab 4: *Response observed according to the outcome found based on the type of hemostatic devices/ drugs used in the first intervention treatment.*

It was thus possible to classify hemostatic sealants as "Perfect" in cases of Grade 0 with only Blood Loss, hemostatic patches in Grade 2, and surgical adjuvants with thrombin and coagulation factor in Grade 4 when the patient's life is at serious risk. "Sufficient" was assigned to powders and gauzes in Grade 1, while the hemostatic matrix was found to be "Good" in cases of Grade 3.



Graph 5: *Percentage of incidence on final costs of responses.*

When considering the percentage incidence on the total cost of individual observed responses, it has been highlighted that perfect responses account for 43% and the failure responses for 10%.

RESPONSE	TREATMENT PHASE COST	FINAL RESPONSE
Failure	**€ 135.000**	Failure
65%	€ 87.815	Perfect
25%	€ 33.750	Good
5%	€ 6.750	Sufficient

Tab 5: *Response observed according to the outcome based on the type of hemostatic devices/drugs used in the first intervention.*

In conclusion, the average costs of treatments that resulted in a failure response amounted to approximately €135,000. Additionally, the costs associated with the subsequent change in therapy to improve the initial response were also calculated.

CONCLUSIONS

The proper classification of the type of bleeding allows for prompt intervention and a more accurate selection of the appropriate medical device and/or medication. By using the FDA-validated bleeding scale, optimal results for the patient's life and significant improvements in their recovery can be achieved rapidly.

Simultaneously, making the correct choice in using the appropriate medication or device to stop bleeding leads to continuous cost monitoring for the respective therapies. This approach attains efficiency and effectiveness while containing costs.

The total costs of the 75,000 observed therapies over the 36 months in the departments, including the Emergency Room and outpatient clinics of San Giuliano Hospital, for hemorrhage control, amounted to approximately €1,500,000. Out of this, around €150,000 could have been saved with a targeted and appropriate choice of the most suitable therapy.

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