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RISK FACTORS LINKED TO GASTROINTESTINAL BLEEDING CAUSING SUBSTANTIAL HEMATOCRIT REDUCTION AND REQUIRING BLOOD PRODUCT TRANSFUSION

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ABSTRACT

Background: Haemorrhagic gastrointestinal bleed (GIB) remains one of the most threatening and Life-threatening emergencies with substantial morbidity and mortality. Acknowledging specific characteristics that predict serious GIB that requires a blood product transfusion is crucial to enhance the patient's results and tailor the therapy strategy. Identifying the risk factors for worsening bleeding thus translates to an understanding of the early management factors associated with the demographic, clinical, and laboratory data

Aim: Thus, the purpose of this investigation is to examine respective risk factors of GIB which led to a significant decline of hematocrit levels and requiring transfusion of blood products for managing severe GIB in a clinical setting.

Method: The study design used in this paper was a retrospective cohort study, data from the patients' records, charts, and cross-matched transfusion records were used. For patients, inclusion criteria comprised of patients diagnosed with GIB with need for blood product transfusion; patients with incomplete records or ill-defined bleeding source were excluded. Age, gender, comorbidities, initial hematocrit, bleeding severity scores, transfusion requirements, HS and clinical outcome of the patients were documented. Descriptive analysis and logistic regression to the significant risk factors were used on statistical models. Participants' ethical approval was sought while patient anonymity was preserved throughout the given study.

Results: Patient characteristics that were noted in the study include variety of patients with all ages represented and a dominance of the male gender. Some of the features deemed to increase the risks included age, male gender, PU disease, liver cirrhosis, chronic kidney disease, and coagulopathies. A significantly low value of initial hematocrit concentration was directly related to higher levels of RBC transfusion. Organizations found out that the bleeding severity scores were producing an accurate prediction of the blood product transfusion necessity. The parameters for clinical outcomes showed that patients with major comorbidity conditions received a larger number of transfusions and experienced a greater number of complications. The hypothesis of this study was to validate that

initial hematocrit levels and bleeding severity scores positively correlate in patient transfusion requirements.

Conclusion: The study focuses on the essential aspects that define the risks of developing a severe GIB requiring transfusion of blood products. Prompt detection and intervention of these risk factors are essential in improving patients' prognosis and minimizing the overall demands on health care systems. Thus, the study presents significant findings relevant to the advances of gastrointestinal care and transfusion medicine, underlining the importance of cost-effective risk assessment approaches and protective strategies. There is need for future studies to undertake more prospective studies to establish these findings as well as identify new bleeding risk biomarkers.

Keywords: Gastrointestinal Bleeding, Hematocrit Reduction, Blood Product Transfusion, Risk Factors, Retrospective Cohort Study, Comorbidities, Bleeding Severity Scores, Clinical Outcomes.

Introduction

Gastrointestinal bleeding (GIB) defines an acute condition that indicates bleeding process in the gastrointestinal tract with the mild blood loss to massive haemorrhage. This condition becomes a nightmare in clinical practice because of the propensity of bleeding and the risk of developing shock, organ failure and even death in the absence of proper management. The knowledge of gastrointestinal bleeding is important to health care practitioners since early recognition of factors characterizing severe gastrointestinal bleeding for which the patient might need a blood transfusion is vital in enhancing the patient's care and match appropriate therapeutic interventions. In clinical practice, gastrointestinal bleeding is presented by hematemesis, noticed melena, hematochezia and clinical features of impaired circulation. Such symptoms call for urgent doctor's visits, which in turn, demonstrates the need for, and seriousness of the disorder. The pathophysiologic causes of GIB vary and may be due to peptic ulcer disease, gastritis, oesophageal varices, diverticula, colon polyps, inflammatory bowel disease, and malignancy. Thus, both etiologists remain as management and diagnosis challenges in which the treatment regimen depends on the type of bleeding event and the patient's medical condition [1].

The incidence and prevalence of gastrointestinal bleeding also differ by patient's demographic characteristics, presence of co-morbid conditions, and region of the world. This research shows that causes of acute gastrointestinal bleed led to substantial number of cases presenting the emergency department and admission to hospital worldwide. This work emphasizes the necessity of efficient proactive approaches to risk assessment as well as the means of timely intervention and complex management to decrease prevalence of the mentioned outcomes and enhance patients' condition. Thus, there is need to define clinical variables that will be considered to have severe gastrointestinal bleeding this being characterized by at least 6% drop in the hematocrit level as well as a need to have the patient treated through transfusion of blood product. Listing down is some of the risk factors causing the vulnerability of a person to have grave bleeding incidents: The risk factors that are well recognized are therefore based on age and or diseases like peptic ulcer diseases, liver cirrhosis, chronic kidney diseases, coagulopathy, as well as use of anticoagulant or antiplatelet agents [2]. Some of these conditions may affect the ability of haemostasis mechanisms, reduce the mucosal barrier, or worsen pre-existing vascular pathology; therefore, making patients more vulnerable to gastrointestinal haemorrhage and challenging the management of the condition [3].

In evaluating gastrointestinal bleeding, timely identification of the etiology and assessment of the patients' risk factors are the first steps to determine the right treatment approaches. The first assessment entails taking of history to establish potential risk factors and symptoms, physical examination, and stabilization of the patient's circulation. In assessing the bleeding, diagnostic investigations are very central in locating the origin and the degree of bleeding. Blood count, prothrombin test, and renal function help in understanding patient's physiological state and management plan since patient's laboratory tests were elevated [4]. The diagnostic tests including abdominal ultrasound, computed tomography, and endoscopy are some of the paramount techniques

that can be used in identifying and determining the origin of the bleeding. In particular, diagnostic and therapeutic possibilities of endoscopy are highly appreciated, and through the endoscopy the doctor can inject the medication, coagulate temperature, apply clips and ligation bands. The management is based on the site and extent of bleeding and the goal is to stop bleeding as much as possible and in a safe manner without increasing the chance of rebleeding [5].

Blood transfusion, including packed red blood cells, platelets, and fresh frozen plasma is determined by patient's stability, bleeding profile, and hematocrit value. Transfusion is mainly used to revive an acceptable tissue perfusion and oxygenation, reduce the potentiality of hypovolemic shock, and promote coagulation. Yet, it is necessary to admit that blood product transfusion should be employed sparingly because, in some cases, further administration contributes to undesirable effects, such as fluid overload, transfusion reactions, and immune responses. Objectives of this research include the identification and explanation of the risk factors seen in patients who present with gastrointestinal bleeding and experience a significant decrease in hematocrit requiring transfusion. Based on these factors and their effects on patients' outcomes, the stated goals of the study are to advance the understanding of antecedents and risk indicators for the development of the complications as well as to enhance the formulation of risk assessment tools, early intervention techniques, and preferable management strategies in clinical practice. The findings from this analysis can be the knowledge about potential patient populations for the future, better estimate of patients' outcomes, and better distribution of limited resources in the domain of emergency and gastroenterology field [6].

Methodology

Since this analysis of risk factors concerning gastrointestinal bleeding (GIB) necessitating transfusion of blood products is a retrospective cohort study, the methodology used to analyse the patient data for clinical outcomes and the relevant risk factors is critical during the research process as it enables research to be done based on the data collected from practice settings of the past. This part explains why the study was conducted in this design, where data was obtained, what criteria were used to recruit participants, how data was collected, how it was analysed, and how patient identity was protected, and legislation complied with. The specific study approach used, retrospective cohort study, is selected based on the study's aim of using data from patients to establish relationships between factors that may lead to a specific outcome. Thus, the researchers can follow the clinical history of patients with the diagnosis of GIB, who received blood transfusion, using the data from hospital databases, patient records, and transfusion sheets. It enables a review of the various clinical patient factors including the demographics, clinical descriptors, management, and the results within the given time frame. It will be useful to return to this method for several reasons because of the intrinsic value of the retrospective approach. Firstly, it makes it possible to analyse a greater number of patients than those enquired in the prospect study within the time and resources available. Collection of data also enables researchers study outcomes that are out of the norm, for instance, cases of serious bleeding complications that may necessitate transfusion, this may be quite hard to study at real time because they may be ethically sensitive or practically Impossible. Moreover, the data derived from retrospective studies give information regarding follow-up and prognosis which should be useful for subsequent prospective studies and clinical practice [7].

Current data from different types of the hospitals' records such as the electronic health records (EHRs), patient charts kept by different care givers, and transfusion records reflecting blood products used, were used as sources of data in this study. These sources provide a detailed database of patient data consisting of demographics, medical history, laboratory data, procedural details, and outcomes of cases of GIB and transfusion. The use of an MBA as an integration tool means that data from multiple sources is combined as a way of enriching data mining exercises and improving the accuracy of findings. Microscopic records such as the hospital records and patient charts play a very vital role in the documentation of certain details of the patient as they relate with GIB and transfusion events. EHRs allow for more organized data acquisition; they include tabular records with fields and search options for providing quick identification of cases and variables of interest [8]. These records are

supplemented by transfusion logs that provide details of blood products with regard to the type of products, amounts of blood products that were given, and time relationship of the transfusion to clinical procedures. In combination, these sources allow for a thorough evaluation of patient pathways over time from the time they first present to the healthcare system to the data collected post-transfusion, which assists in providing an in-depth examination of risk factors and the patients' response to treatment [9].

The eligibility criteria of the present study comprise patients who are at least 18 years old, presented with GB, the diagnosis of which was made based on clinical assessment, and received one or more blood product transfusion during their hospital stay. These criteria guarantee that the identified cohort is indeed involving cases of active bleeding requiring management, which is in accordance with the objectives of the present study that targets major GIB consequences. Patients with missing data that can prevent comprehensive abstraction are also excluded, as are patients whose bleeding etiologies are uncertain because doing so eliminates potential sources of confounding and ensures the validity of the results [10].

Extraction of data includes a process of systematic collection of patients data from the EHR and a process of going through the patient charts and compile a database. This implies that the patient factors which should be captured include age, sex, co-existing diseases, initial hematocrit level, bleeding severity score or amount while on the aspects related to the transfusion, one should consider type and volume of blood products given to the patients and the clinical outcomes which are the mortality rate, the number of days the patients spent in hospital, and complication arising from the transfusion. Due to the detailed procedure that is followed in data collection, there is always completeness and accuracy that is achieved when gathering some of these important points that are very central for the analysis and interpretation. Descriptive statistics enable analysis of study population features and outcomes of bleeding severity in the subjects and transfusion rates. Frequencies and logistic regression analysis is used to establish that, a number of patients with severe gastrointestinal bleeding will need a transfusion by evaluating risk factors like Age, Comorbidity, Initial Hematocrit levels. It is therefore possible to recognize predictors that anticerebral outcomes and they facilitate the definition of strategies for mid-term survival in the clinical practice [11].

Patient's data privacy to researchers is crucial, and so is the protection of the rights to patients' privacy. Data collection is done in accordance with institutional review board (IRB) to conform to the ethical acceptable use of patients' information as mandated by the law. Techniques that help in the process of data anonymisation are used in the process of the study to protect the identity of the patients at every stage of the work so that in case of data breaches or unauthorized access to the work, the patient's identity is not at risk. Thus, adherence to ethical values enables the researchers to maintain patient trust and respect for patient's well-being as well as contribute to the development of knowledge in the management of GIB [12].

Results

The findings of the research were derived from a retrospective cohort study focusing on GIB requiring blood product transfusion and it covers details of participants' characteristics, important predictors, the severity of bleeding and the clinical implications. In this context, the current study reveals the following patterns of risk, which indicates how patient and clinical characteristics may contribute to severe GIB outcomes and initiates a basis for changes in the practices about severe GIB clinical management. The study population was the patients with gastrointestinal bleeding confirmed at admission and who required blood transfusion. The age distribution analysis indicated that GIB was more rampant in the elderly population and all the patients were 60 years and above. Thus, the level of threat in this age group was significantly higher due to severe bleeding episodes, probably by age-related physiological changes and complex comorbidity. Cohort demographic review pointed to an approximately heightened enrolment of male students which is in correspondence with other studies in this area of epidemiology in regard to cases of gastrointestinal bleeding [13].

These comorbidities were tagged as the most prominent predictors of the more severe bleeding episodes. Specifically, earlier peptic ulcer disease, liver cirrhosis, chronic kidney disease, and coagulopathies were showing a greater risk of severe GIB requiring a blood transfusion. These conditions probably increase the risk of bleeding through factors such as impaired coagulation, friable mucosa, and changes in blood flow. The patients' hematocrit on admission was another factor that worked as an initial determinant of bleeding severity and the necessity of transfusion. It was further confirmed that initial hematocrit was highly negatively associated with overall transfusion needs; therefore, timely determination of hematocrit should be a priority step in the clinical decision-making/ossa and resource utilization [14].

The study also reviewed the bleeding severity score that was evaluated with clinical parameters including the amount of blood loss, stability, and laboratory values. These scores indicated a correlation between the need for transfusion of blood products and the corresponding scores. Thus, memorizing or using a higher severity score full point increases the transfusion needs with the viewership stressing on the roles of these scores for the categorization of the patients based on bleeding severity and the estimation of their requirements on transfusion. This correlation elevated the significance of the clinical examination in the identification of the degree of treatment required before stabilising the patients.

The requirement for transfusion in the cohort was not uniform and the most frequently ordered blood components were PRBCs while Platelets and Plasma were the next frequently ordered blood products. Concerning the selection of blood products, it depends on the type and extent of bleeding, the cause of haemorrhage, and other related factors. The study noted that clients who at baseline had lower hematocrit values and higher bleeding severity scores were overall more likely to undergo more aggressive and often more EPUI transfusions, PRBCs, platelets, and plasma, to correct coagulopathy and support haemostasis. The adverse sequelae of transfusion were noted and scrutinized, and transfusion reactions were the most common outcome noted in this regard. The cited side effects varied from simple allergic reactions up to serious consequences that are febrile non-haemolytic transfusion reactions and TDALI. The frequency of such complications remained fairly low but demonstrated that constant supervision and management measures should be provided to prevent injuries related to blood transfusion [15].

The study also analysed the relationships between the identified risk factors to the clinical consequences, giving insights into the effects of comorbidities, starting hematocrit levels on transfusion results. Patients with severe comorbid condition especially those with liver cirrhosis and chronic kidney disease had poorer clinical prognosis characterized by higher mortality rate and longer length of stay. These observations indicate that comorbidities greatly affect the natural history and outcome of GIB and thus require interprofessional care in order to address the needs of the patient. This study also supported the predictions of initial hematocrit values to transfusion requirements on patients. While there was no significant difference in hematocrit between the groups, patients with lower hematocrit levels were more likely to require hastened transfusion support reaffirming the role of early and accurate method of determining an individual's hematocrit level before developing a management plan for it. This association hints at the idea of utilizing the initial hematocrit level as a purpose of risk stratification in GIB, to help predict the necessity of the transfusion and to improve the resource allocation among the clinicians [16].

In conclusion, the data obtained in the course of this work contributes to the assessment of incidence, demographic characteristics, specific causes, severity of bleeding, as well as short-term clinical outcomes in patients with gastrointestinal bleeding who required transfusion of blood products. The results concerning the main topics are presented by the increased rate of GIB in patients over the age of 60 and male, thromboembolic event being related to increased bleeding severity, and initial hematocrit level being important in predicting transfusion requirement. The study therefore confirms the significance of risk assessment in the early period of GIB along with an extensive clinical evaluation to inform the right management strategies for the patient. Through identification of the above factors, the study brings positive contribution to the body of knowledge in emergency medicine

and gastroenterology and provides great insight in the improvement of practice and quality of patient with severe GIT bleeding [17].

Variable	Statistic	Key Insights
Age and Gender	Patients ≥ 60 years, Higher in Males	Elderly patients and males are at higher risk of severe GIB requiring transfusion
Comorbidities	Liver Cirrhosis, CKD, Coagulopathies	These conditions increase the risk of severe GIB and the need for transfusion
Initial Hematocrit	Negative association with transfusion needs	Lower initial hematocrit indicates higher likelihood of requiring transfusion
Bleeding Severity Score	Higher scores correlate with increased transfusion needs	Severity scores are useful in categorizing patients and estimating transfusion requirements
Blood Products Used	PRBCs most common, followed by Platelets and Plasma	Type and extent of bleeding dictate the selection of blood products; PRBCs are frequently used
Transfusion Reactions	Low frequency, but includes allergic reactions and TDALI	Constant supervision and management measures are required to prevent adverse outcomes related to transfusion
Clinical Outcomes	Higher mortality and longer length of stay severe cases	Severe comorbidities and lower initial hematocrit levels result in poorer clinical prognosis

Discussion

The discussion of our retrospective cohort study looking at patients with gastrointestinal bleeding requiring blood product transfusion is to give the rundown and robust assessment of the findings compared with the published work; to identify the potential reasons for modifiable risk factors; and to examine the clinical and practical implications for the desired population and stakeholders. Further, it gives an account of the strength and limitations of the study and puts forward suggestions for effectively enhancing the understanding of the mechanisms and antecedents of severe GIB for more future research.

Thus, our study is in synergy with the previous literature on the highest risk factors of severe GIB, indicating how comorbid conditions and initial hematocrit levels may predispose the patient to bleeding severity and the necessity for transfusion. In line with research done before, we identified higher age and male gender as the key demographic characteristics that increasingly relate to GIB, as seen in other types of ailments. Similarly, the relationship between the comorbidities including peptic ulcer disease, liver cirrhosis, chronic kidney disease, and coagulopathies with the increased bleeding severity complements what has already been acknowledged from prior literature regarding the role of these comorbidities in the haemostatic processes. These comorbidities increase the risk of severe bleeding through such mechanisms as defects in mucus layer integrity, changes in blood circulation patterns, and hew their clotting patterns.

The pathological processes causing the mentioned factors in relation to the development of severe GIB and changes in hematocrit level are diverse. Conditions such as peptic ulcer disease results to mucosal erosion and ulceration hence patients who contract this disease are likely to experience massive bleeding when the gastrointestinal mucosa is compromised. Portal hypertension and variceal bleeding as well as coagulopathies due to the impaired synthesis of clotting factors by cirrhotic liver are the principal complications. Chronic kidney disease increases the risk of bleedings due to the platelet dysfunction caused by uraemia and the presence of uremic toxins that affect normal coagulation. These conditions acting in synergy lead to the development of severe GIB that can be managed only through the use of blood products in an effort to stabilize the patients' hemodynamic as well as correct the hematocrit values [18].

This study's findings of the key risk factors highlight vast implications for clinical practice among patients with chronic diseases, specifically the necessity for screening and intervention among high-risk patients. Using structured risk assessment techniques on the presentation of the patients can enable early identification and management of the patients with severe GIB thus enhancing their result. These include practicing comorbidity identification during the initial and subsequently regular reviews, strict assessment of the first values of hematocrit level, and applying bleeding severity scores that will help the physician to sort out patients on certain tiers allowing the effective management of the treatments. These risk factors are useful to be incorporated into predictive models that can be integrated to decision making processes within the clinic, regarding transfusions and other supporting measures. Also, implementation of practice parameters/protocols for transfusing blood components that incorporate evidence-based literature can have a positive impact for the patient by increasing proper utilization of specific blood products and decrease more potential sequel of transfusion-related complication.
Thus, the study under consideration supports the need for preventive strategies and patient awareness to decrease the occurrence and severity of GIB from a public health point of view. Epidemiological and preventive measures that focus on communication on possible causes, early check-ups, and advocacy for changes in peoples' lifestyle greatly reduce the impact of gastrointestinal Bleeding. Health promotion initiatives like patients' education programs for the conditions associated with the comorbidities, for instance, peptic ulcer disease and liver cirrhosis, should enable a patient to prevent those events that can lead to severe bleeding. Moreover, improving health care infrastructure for screening and early treatment of GIB can help improve patients' prognosis and lower the health care costs of later description for transfusion and long-stay hospitalization [19].

However, the following limitations can be seen as remarkable only if attention should be paid to them: The retrospective design means that some kind of restrictions regarding data quality are involved, such as data accuracy and data completeness as due to the retrospective analysis, certain records may be missing or contain only a part of the information. Although the sample size provided enough statistical power to establish such associations, the results' generalizability to other populations and various healthcare settings can be constrained. Also, the variation in the standards used for documenting and diagnosing the condition can also affect the validity of the findings. These limitations point to the fact that the results obtained here should be interpreted in light of these limitations and that the results should be externally validated through future prospective work.

The future directions of the research field were outlined as follows: Future studies on bleeding risk prediction should overcome the limitations of this study and include prospective studies to confirm the validity of the risk factors that were described and to investigate new biomarkers for bleeding risk assessment. Clearly, prospective variant cohort studies will generate stronger and or more encompassing data sets, which are beneficial for drawing more accurate time sequence analyses of risk predictors and clinical endpoints. Also, the identification of genetic and molecular profiles of subjects to GIB might open a new view on pathophysiology and possible targets for intervention. Multicentre trials that incorporate heterogeneous patient cohorts may increase generalisability of data, and, thus, utility of guidelines that are produced. Future studies should also focus on tracking the follow-up of patients with severe GIB to understanding the effect of the variation in the transfusion practice and management on patients' survival and the quality of life and healthcare cost [20].

Conclusion

The findings of this retrospective cohort study describing gastrointestinal bleeding requiring blood transfusion are summarised in the conclusion followed by appreciation of the importance of prompt identification and treatment of GIB and subsequent overall impact of the study in the fields of gastrointestinal and transfusion medicine. In using this analysis, we likewise found out that key predictors that are considered to increase the risk in severe GIB are age, male gender, and comorbid

conditions like peptic ulcer disease, liver cirrhosis, chronic renal disease, and coagulopathy. These, along with initial hematocrit values and bleeding severity scores higher than in the non-trauma group, were associated with higher transfusion needs and worse outcome. Such results can be relevant to previous studies confirming the superposition of both direct and indirect effects of patients' demographic characteristics, co-morbidities, and the pathophysiological process underlying severe bleeding. It is extremely critical to identify bleeding episodes at their early stages and to intervene with proper management methods. Our study underscores the importance of the evaluation of such factors so that efficient risk review procedures can be implemented. Such strategies include general screening for other high-risk associated disease co-morbidities, consistently monitoring of hematocrit levels and the use of bleeding severity scores to ensure that the risk factors are properly put into consideration.

The realization of these measures can help to improve processes of patients' treatment, since timely and correct actions of health care professionals can prevent extensive transfusion requirements and its consequences. Besides, an implementation of the predictive models in the practical work contributes to the improvement of transfusion schedules, which are aimed at the more competent utilization of blood products and rational distribution of resources. The findings of our study in this regard have vast implications for public health. With displaying the key risk factors and demanding for their elimination, the cases and severity of GIB, and thereby the healthcare costs, may be decreased. Preventive measures should target on informing the patients and the public on how to manage comorbid conditions, get regular check-ups, and adopt healthier lifestyles to reduce the risk of developing gastrointestinal bleeding. The education of patient concerning the understanding of relevant symptoms to the heart and the importance of seek medical help as soon as possible will enable individuals to ensure that they seek treatment early thus boosting the chances of recovery and lowering mortality levels. In addition, it is crucial to strengthen healthcare facilities that would improve early diagnosis and treatment of GIB to maximize the delivery of appropriate care to affected patients. Considering the nature of the study and its design, certain limitations should be considered that include for future research, the studies must be done on the predictors rather than the outcomes to ensure the generalizability of the findings made in this study and to identify other biomarkers for predicting bleeding risk. Multicentre trials with patients from different locations, therefore, supplement our results and contribute to the creation of guidelines relevant to all populations. Therefore, future studies should explore the main predictors of survival and quality of life in severe GIB patients focusing on the comparison of the outcomes depending on the applied transfusion regimens and management strategies. Thus, the current findings make the important contribution to the knowledge of GIB and its risk factors on the general background of the fields of gastrointestinal care and transfusion medicine. These contributions are essential in providing practicable recommendations, reshaping policies and advancing patients' well-being and clinical results. This paper's results support a multidisciplinary approach to the management of GIB, where gastroenterologists, haematologists, and emergency medicine specialists could collaborate.

Therefore, based on our understanding of the study design, our presented HIT-CGI analysis delineates the risk factors that contributed to secondary GI bleeding with blood product transfusion highlighting the need for early identification and management to improve patient outcome and alleviate the burden on health care systems. This way, our study adds value to GI care and TM, providing a list of critical risk factors and insisting on the necessity of developing proper protocols in this aspect, raising awareness and contributing to optimal patient outcomes and evidence-based practices. Such conclusion specifies the importance of distinct and early prevention and intervention efforts, elaboration of preventive strategies, as well as a focus on patient's awareness about GIB and its risk factors improving the quality of given treatment, decreasing the rate of mortality among patients. They also emphasize our requirement for prospective verification of the findings and clarification of new biomarkers for bleeding risk estimation, future research directions for GIB prognosis and its

predicting factors elucidation that should contribute to the creation of the effective clinical guidelines suitable for universal practice.

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