REVIEW ARTICLE
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Prophylactic blood transfusion prior to elective invasive procedures

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INTRODUCTION

In Brazil, approximately 3.3 million blood transfusions are performed annually, of which 62.4% correspond to packed red blood cells (PRBCs), 17% to platelet concentrates (PC), and 13% to fresh frozen plasma[1]. The use of blood products (BPs) is one of the most common interventions in clinical practice and can save lives when indicated.

In both developed and developing countries, inappropriate prescription of blood components occurs in up to 36% of cases[2]. The rational prescription of transfusion therapies is essential due to limited resources and growing demand[3]. Moreover, several studies have shown that aggressive correction of anemia, thrombocytopenia, and coagulopathies does not necessarily result in better clinical outcomes[4].

These factors show the importance of individually tailoring the indications and establishing evidence-based transfusion programs[5]. However, several international medical guidelines still recommend the prescription of BP based on low-quality studies or expert opinion[6,7].

In this study, a narrative review of the literature was conducted regarding the evidence for the prescription of BP prophylaxis for elective invasive procedures in clinically stable patients with anemia, thrombocytopenia, or coagulopathies.

The included studies were classified according to the quality of the scientific evidence following the 2011 Oxford Center for Evidence-Based Medicine recommendations (Table 1)[8].

CENTRAL VENOUS CATHETER PUNCTURE-RELATED TRANSFUSION

Evidence regarding the use of blood components prior to central venous catheter (CVC) puncture in patients with blood dyscrasias is scarce. Most international guidelines recommend performing thrombocytopenia and international normalized ratio (INR) correction before the puncture but at variable cut-off points[7,9]. Nevertheless, classic coagulogram parameters (i.e., prothrombin time, INR, and platelet count) have been poor predictors of bleeding-related complications after CVC puncture[10].

A meta-analysis including 4,387 CVC insertions revealed a 5.1% risk of bleeding complications. The efficacy of blood transfusions in preventing these complications could not be determined due to the high heterogeneity and low methodological quality of the studies[11].

ESOPHAGOGASTRODUODENOSCOPY

In clinical practice, esophagogastroduodenoscopy (EGD) plays an essential role in the diagnosis and treatment of severe digestive bleeding. This is a heterogeneous clinical context, which may involve patients with or without hemodynamic instability, coagulation disorders, and/or thrombocytopenia.

Based on low-quality evidence, the American Society for Gastrointestinal Endoscopy recommends a minimum value of

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Table 1. Oxford Centre for Evidence-Based Medicine levels of evidence according to the study design.

Grades of recommendation	Level of evidence	Therapy, prevention, and etiology	Prognosis	Diagnosis	Differential diagnosis or prevalence
A	1A	Systematic review of RCTs	Systematic review of cohort studies. CDR validated in different populations	Systematic review of Level 1 diagnostic studies. CDR with 1b studies from different clinical centers	Systematic reviews of cohort studies (current or prospective)
	1B	RCT with narrow confidence interval	Cohort study with <20% loss. CDR validated in a single population	Validating cohort study with good reference standards. CDR tested within one clinical center	Prospective cohort study with good follow-up
	1C	Results of all or none studies	All or none case-series	Sensitivity and specificity close to 100%	All or none case-series
B	2A	Systematic review of cohort studies	Systematic review of retrospective cohort studies	Systematic review of Level >2 diagnostic studies	Systematic review of 2b and better differential diagnosis studies
	2B	Cohort study or low-quality RCT	Retrospective cohort study, CDR validated on split-sample	Exploratory cohort study with good reference standards. CDR validated only on split samples or databases	Retrospective cohort study or poor follow-up
	2C	"Outcomes" research. Ecological studies.	"Outcomes" research	–	Ecological studies
	3A	Systematic review of case–control studies	–	Systematic review of 3b and better studies	Systematic review of 3b and better studies
	3B	Case–control study	–	Nonconsecutive study or without consistently applied reference standards	Nonconsecutive cohort study, or very limited population
C	4	Case-series, poor quality cohort, and case–control studies	Case-series, poor quality prospective cohort studies	Case–control study, poor or nonindependent reference standard	Case-series or superseded reference standards
D	Expert opinion without explicit critical appraisal or based on basic science (physiology, bench research)				

RCT: randomized clinical trial; CDR: clinical decision rule.

$20'10^3$ platelets/mm^3 to perform EGD in patients at low risk of bleeding and $50'10^3$ platelets/mm^3 in those at high risk[12]. Meanwhile, the British guidelines recommend performing EGD with platelet reserve in patients with less than 50–$80'10^3$ platelets/mm^3 [13]. However, two systematic reviews demonstrated that the existing evidence is insufficient to establish a cutoff point for performing EGD in thrombocytopenic patients and that the current recommendations are based on expert opinion[14,15].

Some randomized controlled trials (RCTs) evaluated the transfusion of PRBCs in patients with upper gastrointestinal

bleeding and showed lower mortality associated with the use of restrictive strategies (transfusion to maintain Hb 7–8 g/dL)[16]. The European Society of Gastrointestinal Endoscopy guideline corroborates this strategy recommending Hb values between 7 and 9 g/dL[17].

As for coagulopathy, no study demonstrated the risk of a new bleeding event in patients with elevated INR (2.5 or higher) or the use of anticoagulants[18]. Despite this, a cohort indicates that performing early EGD (<24 h) is safe in patients after partial INR correction, with a similar risk to patients with no coagulopathies[19]. The International Consensus Group recommends the correction of coagulopathies in advance due to the benefits of early EGD and low evidence of complications, provided this does not delay endoscopy[20].

BRONCHOSCOPY

Bronchoscopy is a well-established complementary method for investigating respiratory system pathologies, including bronchoalveolar lavage, lung parenchyma biopsy, and therapeutic procedures. The incidence of hemorrhagic complications after bronchoscopy is approximately 0.44%[21].

According to the latest guideline of the American Association of Blood Banks, bronchoscopy can be safely performed in patients with a platelet count ≥20´10³/mm³. This recommendation is mainly based on observational studies with limited sample sizes[22]. Despite this, a recent cohort study observed a low rate of bleeding complications in 1,711 cancer patients with thrombocytopenia, including those with a platelet count <20´10³/mm³. Approximately, 45% of the patients with 10–20´10³ platelets/mm³ did not receive prophylactic PC transfusion, and even so, there was no significant difference in bleeding complications[23]. In the case of levels <10´10³ platelets/mm³, PC transfusion before the procedure is plausible due to the high risk of spontaneous bleeding[10].

RENAL BIOPSY

A major complication associated with renal biopsy is hemorrhagic bleeding, occurring in approximately 0.6–4.9% of cases[24]. Some of the risk factors for post-biopsy bleeding are as follows: female sex, advanced age, elevated INR, hypertension, and increased baseline creatinine levels[25,26]. The use of ultrasound in clinical practice allowed the use of open biopsies in some specific cases, as well as CT-, laparoscopic-, or transjugular-guided biopsies.

The use of BPs, especially PRBCs, tends to be more strongly influenced by pre-procedure baseline hemoglobin values rather than by the decrease in hemoglobin levels during the biopsy, the presence of perinephric hematoma, or the need for post-procedure surgical approach[27]. In a large meta-analysis of randomized clinical trials, Salpeter et al. do not recommend routine blood transfusion after renal biopsy because of increased mortality, higher incidence of acute myocardial infarction, pulmonary edema, and bacterial infections[28]. However, the cutoff point for blood transfusion in these patients is controversial, and there are no major RCTs on the use of blood concentrates before or after this procedure[27].

Regarding platelet transfusion, the thrombocyte level decrease is associated with the development of symptomatic hematoma[29]. In a retrospective study, Simard-Meilleur et al. demonstrated that the risk of this complication is inversely proportional to the serum platelet level, being 11% in patients with >200´10³ platelets/mm³ and 40% in those with levels <100´10³ platelets/mm³ [29].

LIVER BIOPSY

The most severe complications of liver biopsies are intraperitoneal hemorrhage, hemobilia, and hematoma formation. The risk of clinically relevant bleeding complications that result in hemodynamic compromise or require some form of intervention ranges from 0.01 to 0.5%[30,31].

Both organ dysfunction and hepatosplenomegaly as a result of chronic liver diseases may result in blood dyscrasias, either by INR change or by platelet destruction and dysfunction. Thus, the American Association for the Study of Liver Diseases recommends the correction of thrombocytopenia to serum levels below 50–60´10³ platelets/mm³ [32]. Regarding INR, the Society of Interventional Radiology defines its cutoff point for performing biopsy as an INR ≤1.5–1.8 and <2.5 for the general population and for patients with chronic liver disease (CLD), respectively[33].

In the largest RCT evaluating the performance of percutaneous liver biopsy in patients with advanced CLD, the HALT-C indicated an increased risk of post-procedure bleeding in patients with platelet counts ≤60´10³/mm³ (5.3% versus 0.4%; p<0.001) and INR≥1.3[34]. However, this study excluded thrombocytopenia <50´10³/mm³, and no patients with INR>1.5 experienced bleeding events.

FINAL ANALYSIS

This study found few and sometimes contradictory data on the indication of blood component transfusion before invasive procedures. Most published studies correspond to observational studies with heterogeneous results and several methodological limitations.

This study found a significant inconsistency in recommendations between the guidelines evaluated and also regarding the evidence available in the literature, indicating that such recommendations are based on expert opinion.

Table 2 shows a synthesis of the main studies, their recommendations, recommended cutoff values for platelet count and INR, and data on the quality of evidence. Figure 1 presents the final recommendations based on these results.

Table 2. Synthesis of evidence levels and recommendations for studies evaluating prophylactic blood transfusion and/or bleeding risk related to elective invasive procedures.

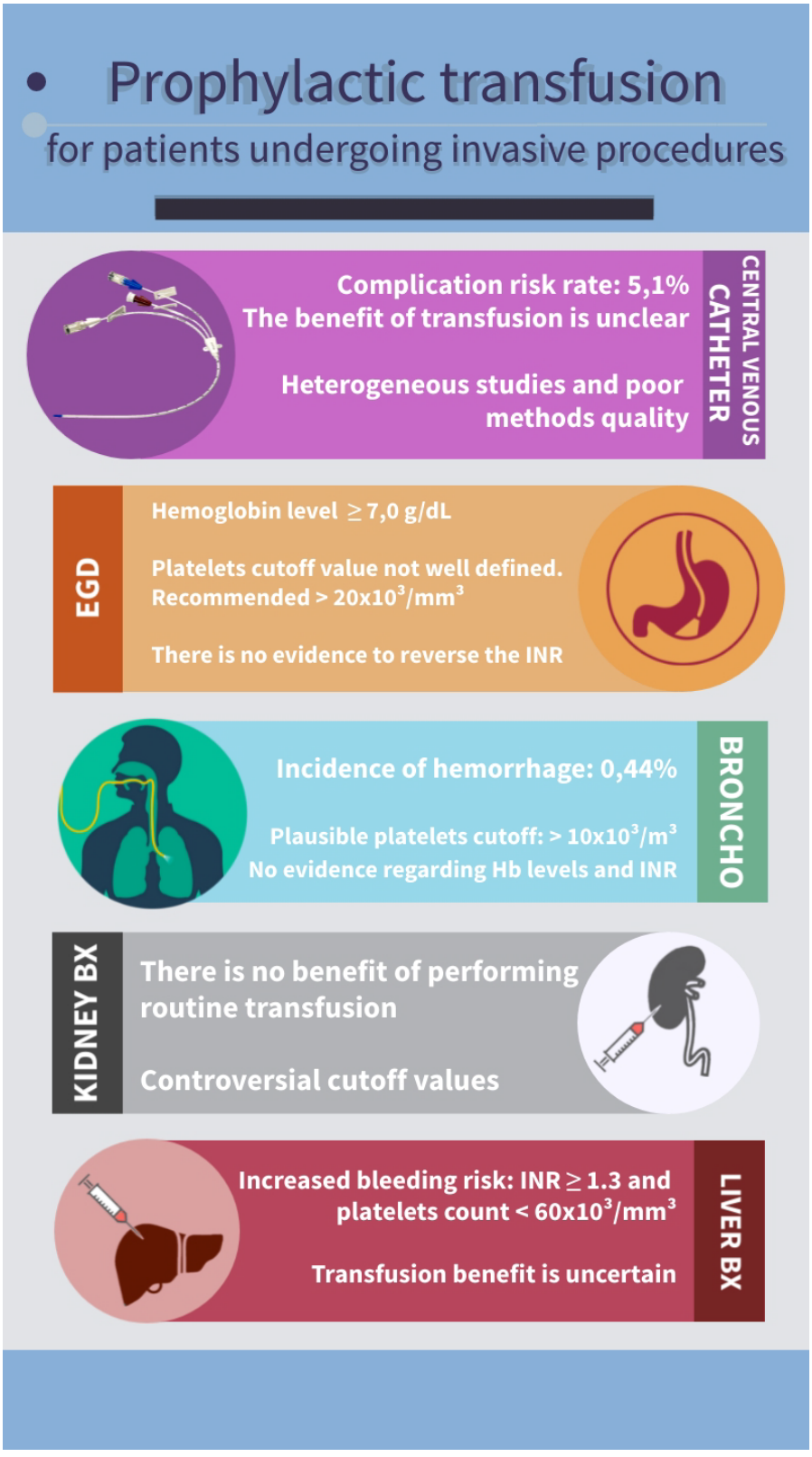
Procedure	Platelet count[π]	INR	Recommendation*	LOE[¥]	Comments	References
CVC puncture	–	–	Benefit is unclear. Prophylactic transfusion or if bleeding after the procedure seems equally acceptable alternatives	2a	Systematic review of 13 observational studies. High heterogeneity	Cabrini L. et al. 2017[11]
	20´10³	3.0	The benefit of prophylactic reversion of coagulopathies or thrombocytopenia correction is unclear	2a	Systematic review: 01 RCT e 21 observational study. High heterogeneity. Studies of poor to moderate quality	van de Weerdt E.K. et al. 2017[35]
	30´10³	1.5–3.0	Prophylactic reversion of coagulopathies with FFP could not be evaluated	2b	Open-label RCT, concealed, 4 centers, with 81 patients. Compared FFP versus placebo. Truncated due to slow recruitment	Müller M.C. et al. 2015[36]
	50´10³	1.5	Thrombocytopenia or increased INR were not related to the risk of bleeding. Prophylactic correction is not recommended	2c	Open-label not randomized trial with 196 subjects in 02 intensive care units	Weigand K. et al. 2009[37]
EGD	50´10³	–	The platelet count cutoff of 50´10³ is safe to perform EGD. In patients in which this value is difficult to reach, a cutoff of 20´10³ is reasonable	4	Retrospective study in one site with 588 oncology patients, which of 20% had a performance status of 3 or 4	Abu-Sbeih H. et al. 2019[38]
	20–50´10³	–	Safe procedure in thrombocytopenic patients. Low risk of bleeding, no severe or fatal bleeding. Prophylactic platelet transfusion should be individualized	2b	Systematic review of 11 observational studies. High heterogeneity. High proportion of oncology patients	Tong M.C. et al. 2015[15]
	50´10³	–	The study results demonstrate a trend to no difference in risks for a platelet count 10–20´10³. Conversely, the authors suggest transfusion for a platelet count <50´10³ based on guideline recommendations	2a	Systematic review of 20 studies: 4 RCT and 16 observational studies. High proportion of oncology patients	Razzaghi A. and Barkun A.N. 2012[14]
Bronchoscopy	10´10³	–	Prophylactic transfusion is not routinely recommended. In patients whose platelet count is <10´10³, transfusion seems reasonable due to spontaneous bleeding risk	4	Retrospective cohort in one center with 1,711 patients. Only pre-procedure platelet count was analyzed. The authors could not assure the absence of transfusion during or after the procedures in patients without evidence of bleeding. Lung biopsy and BAL were not assessed	Faiz S.A. et al. 2019[23]

Continue…

Table 2. Continuation.

Procedure	Platelet count[n]	INR	Recommendation*	LOE[¥]	Comments	References
Bronchoscopy	30´10³	–	Prophylactic transfusion recommended for a platelet count <30´10³, including diagnosis purposes and BAL	4	Retrospective cohort with 150 patients. Prophylactic transfusion was routinely performed. Confusion bias. Biopsies not assessed	Nandagopal L. et al. 2016[39]
	20´10³	–	Bronchoscopy, including with biopsy, is safely performed for a platelet count ≥20´10³	2b	Prospective observational study with 234 patients, with a follow-up of 18 months. Bronchoscopist blinded. Thrombocytopenia <20´10³ and INR<1.3 were excluded. No occurrence of bleeding or hemorrhage with hemodynamic instabilities	Carr I.M. et al. 2012[40]
Renal biopsy	–	–	Lower pre-procedure Hb is associated with the higher risk of transfusion after biopsy despite the absence of bleeding. Transfusion prescription should be individualized and consider other risk factors instead of only Hb	2c	Prospective study with 910 adults which evaluated bleeding, need for transfusion or death 24 h after percutaneous biopsy	Whittier W.L. et al. 2016[27]
	–	–	No recommendations. Symptomatic hematoma was associated with platelet count and hemodialytic therapy	4	Retrospective cohort study with 287 inpatients and outpatients. No cutoff defined to guide blood product transfusion. Desmopressin was used in 33% of patients	Simard-Meilleur M.-C. et al. 2014[29]
	≥50´10³	1.3	No recommendations. A platelet count <150´10³ was associated with increased risk of hemorrhagic complications	2b	Retrospective cohort study with 219 patients with SLE in a tertiary center. Desmopressin use was excluded. Possibility of information bias	Chen T. et al. 2012[41]
Liver biopsy	60´10³	–	Indication and benefit of prophylactic blood product transfusion prior to liver biopsy in cirrhotic patients is unclear	5	Narrative review including 15 studies with cirrhotic patients. Heterogeneous studies. No systematic approach or critical information appraisal	Alvaro D. et al. 2021[30]
	50´10³	–	Image-guided liver biopsies are safe in patients with a platelet count >50´10³/mm³	2b	Retrospective cohort study in one center with 5,987 patients. Information bias, events identified from medical records. Small number of events	Boyum J.H. et al. 2016[31]
	60´10³	1.3	Percutaneous liver biopsy should be avoided in patients with a platelet count <60´10³ due to increased risk of bleeding	2b	Multicentric open-label RCT including 2,749 percutaneous biopsies. No stratification to the usage of an ultrasound device, needle type, or the number of attempts. Thrombocytopenia <50´10³/mm³ was excluded and no patients with INR>1.5 has bleed	Seeff L.B. et al. 2010[34]

INR: international normalized ratio; LOE: level of evidence; CVC: central venous catheter; RCT: randomized clinical trial; FFP: fresh frozen plasma; EGD: esophagogastroduodenoscopy; BAL: bronchoalveolar lavage; Hb: hemoglobin; SLE: systemic lupus erythematosus.
*Recommendations of international guidelines were not listed in this table, since they are already mentioned in the text and mostly based on the opinion of experts (LOE 5).
[n]Platelets/mm³.
[¥]According to the Oxford Centre for Evidence-Based Medicine Classification.



EGD: esophagogastroduodenoscopy; Broncho: bronchoscopy; Bx: biopsy; INR: international normalized ratio.

Figure 1. Recommendations for prophylactic blood transfusion prior to main elective invasive procedures.

CONCLUSIONS

Few studies evaluated the indications of prophylactic blood transfusion for bleeding complications in patients with anemia, thrombocytopenia, or coagulopathies. The recommendations of international guidelines do not always reflect critical analyses of the available scientific evidence and should be reviewed and applied in clinical practice with caution.

AUTHORS' CONTRIBUTIONS

MAOSV: Conceptualization, Formal Analysis, Investigation, Methodology, Project Administration, Writing – Original Draft, and Writing – Review and Editing. **GLOS:** Conceptualization, Formal Analysis, Investigation, Methodology, and Writing – **ORIGINAL DRAFT. AFS:** Supervision and Writing – Review & Editing.

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