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ORIGINAL ARTICLE

Clinical factors influencing the decision to transfuse after percutaneous native kidney biopsy

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Abstract

Background: Transfusion of erythrocytes is the most common intervention after a complicated percutaneous renal biopsy (PRB). Anemia is considered to be a leading risk factor for bleeding following a PRB, and based on recent studies of transfusions in hospitalized patients, many institutions are restricting the threshold for erythrocyte transfusion to a lower hemoglobin concentration (Hgb). The purpose of this study is to analyze factors that influence the transfusion decision after a PRB, and to determine whether anemia is truly a risk factor for bleeding or anemic patients are simply more likely to receive a transfusion because of their already lower pre-PRB Hgb.

Methods: PRB of native kidneys was performed using real-time ultrasound with automated biopsy needles from January 1990 to April 2014. All patients were prospectively followed for bleeding with a 24-h inpatient observation. An intervention for a bleeding complication (BL-I) was defined by undergoing a procedure (cystoscopy, embolization), receiving a blood transfusion (BL-T), death and/or readmission related to the biopsy. To further define the effect of anemia, patients were divided into three pre-PRB Hgb groups: <9.0 g/dL (n = 79), 9.0–11.0 g/dL (n = 266) and >11.0 g/dL (n = 565).

Results: BL-I occurred in 71/910 (7.8%) of PRBs. The majority of these were BL-T (57/71, 80%; 57/910, 6.3% overall). Patients with BL-I had lower pre-PRB Hgb than those without BL-I (mean \pm SD; 10.3 \pm 2.0 versus 12.0 \pm 2.1 g/dL, P < 0.0001) and a greater change (Δ) in Hgb (2.1 \pm 1.6 versus 1.0 \pm 0.8 g/dL, P < 0.0001). When compared with higher Hgb, patients with Hgb <9.0 g/dL had more traditional risk factors for bleeding (older age: 49 \pm 18 versus 48 \pm 18 versus 45 \pm 16 years, P = 0.02; female: 72 versus 70 versus 56%, P < 0.0001; higher serum creatinine: 4.0 \pm 2.9 versus 2.9 \pm 2.6 versus 1.7 \pm 1.4 mg/dL, P < 0.0001; higher systolic blood pressure: 138 \pm 18 versus 133 \pm 19 versus 133 \pm 18 mmHg, P = 0.06; higher bleeding time: 7.6 \pm 1.8 versus 7.4 \pm 2.0 versus 6.7 \pm 1.8 min, P < 0.0001). When BL-T was stratified by pre-PRB Hgb, there were more transfusions in those with lower pre-PRB Hgb (24 versus 9 versus 3%, P < 0.0001). However, these patients not only had fewer hematomas (58 versus 83 versus 87%, P = 0.04) but also demonstrated a smaller Δ Hgb post-PRB (1.3 \pm 1.0 versus 1.8 \pm 0.8 versus 3.2 \pm 1.6, P < 0.0001) compared with patients with higher pre-PRB Hgb, yet still received a transfusion.

Conclusions: While patients with lower pre-PRB Hgb have more of the traditional risk factors for a complication after PRB, there was actually less clinically evident bleeding in these patients who were transfused. Although anemia itself has been considered to be a risk factor for a complication in the past, it more accurately represents only a predictor of receiving an erythrocyte transfusion. In the setting of the PRB, the decision for transfusion is influenced more by the severity of anemia at baseline as opposed to clinically evident bleeding.

Key words: anemia, bleeding, renal biopsy, transfusion

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In the practice of medicine before the 1960s, perioperative transfusions were given based on the '10/30 rule', which arose from the belief that oxygen extraction deteriorated when the levels of hemoglobin concentration (Hgb) fell below 10 g/dL or the hematocrit fell below 30%. Although physiologic and clinical evidence began mounting to refute this hypothesis, this transfusion practice was still widely performed and was not questioned broadly until the blood-borne human immunodeficiency virus (HIV) epidemic. In 1988, a consensus conference challenged the '10/30 rule', stating that transfusions should not be administered based on a single measure, that there is no evidence for mildto-moderate anemia contributing to perioperative mortality and that clinical judgment should be the basis for the decision to transfuse [1].

Even though HIV and other known viruses are tested on blood products currently, and the blood transfusion (BL-T) is, therefore, safer than it was in the 1980s, it still can carry risks of immunity, volume overload and potentially unknown infections. In addition, it is the most common procedure performed in hospitalized patients, and is much more frequent in the USA compared with other nations [2]. Because of the unknown benefit of this frequent procedure, several randomized controlled trials have been undertaken to help define a more optimal Hgb threshold for transfusion in the perioperative and/or hospitalized setting [3-9]. Almost universally, with the exception of cardiac surgery [10], liberal transfusion strategies have been proven to not be superior to restrictive strategies that target a Hgb threshold of 7 g/dL [3, 6, 7, 11], and moreover, in many studies, liberal use of transfusions has led to worse outcomes [4, 5, 9, 12–15]. Although clinical judgment still has a role, these trials and studies have led to recommendations that 7.0 g/dL be the new threshold for transfusion [16], and many hospital institutional policies have followed, turning the clock back to the 1960s, by restricting the use of transfusion to a single measure.

In the percutaneous renal biopsy (PRB), the most frequent complication is bleeding, and transfusion of blood products is the most common intervention used to help manage the complication [17]. There are presently no randomized controlled trials to help define an Hgb threshold in this specific population, and furthermore, very little information exists which explores factors that influence the transfusion decision. By multivariate analysis in prospective studies of native kidney biopsies, women, older age, hypertension (HTN), anemia, elevated partial thromboplastin time (PTT), elevated bleeding time (BT) and elevated serum creatinine (SCr) are independent risk factors for bleeding complications [18–21]. The baseline Hgb may, therefore, influence the decision to transfuse, but the optimal threshold is unknown, as limited data exist about which factors influence the decision in this setting.

The purpose of this prospective study is to define the frequency and explore the triggers of transfusion of blood products in patients who are undergoing a native PRB. In addition, we aim to determine whether anemia, which is one of the leading risk factors for a complication, is truly a risk for bleeding as defined in the literature or anemic patients are simply more likely to receive a BL-T because of their already lower pre-biopsy Hgb.

Materials and methods

PRB of native kidneys was performed in 910 adult patients (≥15 years of age) from January 1990 to April 2014 at Rush University Medical Center. Renal biopsies were performed by an attending

nephrologist or a nephrology fellow under the supervision of an attending nephrologist. Imaging was performed by a radiologist using real-time ultrasound (U/S) as previously described [22]. A 14- or 16-gauge automated biopsy needle (Bard Biopsy gun, CR Bard Inc., Covington, GA, USA) was used for the procedure, and as reported previously, there was no difference in major complications or interventions based on needle gauge [23].

Information collected at the time of biopsy included age, gender, race, systolic and diastolic blood pressure, SCr, BT, prothrombin time (PT), activated PTT and Hgb. It is our practice to perform the procedure in patients off aspirin and/or anticoagulants/antiplatelet agents, as well as in those with no evidence of coagulopathy as determined by BT, PT and PTT. No patients were on erythropoietin-stimulating agents. If the BT was elevated, desmopressin acetate (DDAVP) was administered prior to the biopsy. In cases where anticoagulation was necessary or a bleeding diathesis was present, non-percutaneous approaches were used and these patients are excluded from this study.

After the procedure, the patient remained supine in bed for 4–6 h and then stayed in bed for 24 h of observation. Patients were monitored after biopsy for signs or symptoms of complications such as gross hematuria, flank pain or hypotension and/or hemodynamic instability. Vital signs were checked every 15 min for 2 h, every hour for 4 h, every 2 h for 6 h and then every 4 h thereafter. Each urine void was visually inspected for gross hematuria. Hgb levels were checked at ~5–8, 10–13 and 18–20 h post-biopsy. The lowest Hgb level after biopsy was recorded.

Beginning in 2002, all patients were moved to the interventional radiology suite following the biopsy for an initial observation period of at least 1 h. Following this, a screening U/S was performed on all patients to evaluate for perinephric bleeding. After the screening U/S, if considered stable, the patient was transferred to a hospital room. Additional follow-up studies and treatment were determined by an attending nephrologist based on the individual assessment of the severity of clinical signs and symptoms or laboratory results. Patients were reevaluated in the outpatient setting ~1 week after discharge.

Previously, a major complication has been defined as requiring an intervention after the procedure [22]. However, as receiving a BL-T is part of that definition, and the purpose of this study is to evaluate factors that influence the decision to transfuse, we have defined the complications as follows: an intervention for a bleeding complication (BL-I) is defined by readmission related to the biopsy, undergoing an invasive procedure (radiographic or surgical), receiving a BL-T and/or resulting in acute renal obstruction or failure, septicemia or death. Asymptomatic, or clinically silent, hematomas found on routine screening U/S as well as gross hematuria and/or flank pain were not included if no intervention was performed.

Data from all patients (1990–2014) were gathered prospectively and used to assess baseline characteristics and complications. To further characterize the effect of anemia, the patients were divided into three pre-PRB Hgb groups (<9.0, 9.0–11.0 and >11.0 g/dL).

This study was approved by the Institutional Review Board of Rush University Medical Center, Chicago, IL, USA.

Statistical analyses

Categorical data were analyzed using the Fisher's exact test and χ^2 test. Continuous data were analyzed with the Mann–Whitney test and analysis of variance using Dunn multiple comparison test. Data are reported as mean ± SD and P < 0.05 is considered significant.

Table 1. Baseline	characteristics of	patients $(N = 910)$
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	Bleeding with intervention	No intervention	P-value
N	71	839	
Age (years)	50 ± 18	46 ± 17	0.05
Male (%)	24	40	0.02
Systolic blood pressure (mmHg)	140 ± 21	133 ± 18	0.002
Diastolic blood pressure (mmHg)	81 ± 13	79 ± 13	0.20
SCr (mg/dL)	3.4 ± 3.3	2.1 ± 1.9	< 0.0001
BT (min)	7.7 ± 1.9	6.9 ± 1.9	0.002
PTT (s)	27 ± 4.3	26 ± 4.6	0.13
PT (abnormal)	14 (20%)	111 (13%)	0.15
Pre-Hgb (g/dL)	10.3 ± 2.0	12.0 ± 2.1	<0.0001
Post-Hgb (g/dL)	8.3 ± 1.6	11.0 ± 2.0	< 0.0001
∆Hgb (g/dL)	2.1 ± 1.6	1.0 ± 0.8	<0.0001
∆Hgb (%)	20.1 ± 10.7	8.7 ± 5.7	<0.0001

Results

Baseline characteristics

An BL-I occurred in 71/910 patients (7.8%) (Table 1). Patients who were older, female and hypertensive were more likely have a BL-I as well as those with renal dysfunction, anemia and elevated BT compared with no intervention. There was no difference in the proportion of patients with abnormal PT or PTT values. Those with BL-I had a greater change (Δ) in Hgb compared with those without an intervention (absolute \triangle Hgb 2.1 ± 1.6 versus 1.0 ± 0.8 g/dL, P < 0.0001; percent Δ Hgb 20.1 ± 10.7 versus 8.7 ± 5.7%, P < 0.0001). Characteristics were also evaluated based on pre-PRB Hgb (Table 2). There were 79/910 patients (8.7%) with a baseline Hgb <9.0 g/dL, and these patients were more often older and/ or female compared with those with higher Hgb. In addition, patients with Hgb <9.0 g/dL had a higher SCr, BT and PT compared with those with higher Hgb. Compared with higher pre-PRB Hgb, more patients with Hgb <9.0 g/dL had an SCr >5.0 mg/dL (30 versus 15 versus 4%, P < 0.0001). Despite displaying more of these traditional risk factors for a bleeding complication, they did not have a greater drop in Hgb.

Interventions for bleeding

The majority of interventions for bleeding involved receiving a BL-T (57/71, 80%; 57/910, 6.3% overall). At a lower baseline Hgb, more patients developed a BL-I (25 versus 11 versus 4%, P < 0.0001) (Table 3). The baseline Hgb was not an influencing factor for patients who required an intervention without a transfusion (P = 0.53). However, it was a significant factor in those who did receive a transfusion. A greater proportion of patients with Hgb <9.0 g/dL received a transfusion compared with those with a higher baseline Hgb (24 versus 9 versus 3%, P < 0.0001) (Table 3). Of the patients with BL-I, those with BL-T started at a lower pre-Hgb compared with those without BL-T (BL-T, 9.9 ± 1.6 versus BL-I without transfusion, 12.1 ± 2.7 g/dL, P = 0.0002), yet there was no difference in Δ Hgb (BL-T, 2.0 ± 1.3 versus BL-I without transfusion, 2.4 ± 2.5 g/dL, P = 0.49) (Table 4).

Patients with transfusions

The change in Hgb in patients receiving a transfusion was 2.0 ± 1.3 g/dL (range of pre-PRB Hgb: 7.2–13.9 g/dL) (Table 4). Despite

Table 2. Baseline characteristics stratified by baseline (pre-PRB) Hgb

	Pre-PRB Hgb (g/dL)			
	<9.0	9.0–11.0	>11.0	P-value
N	79	266	565	
Fellow	72 (91%)	228 (86%)	480 (85%)	0.34
Age (years)	49 ± 18	48 ± 18	45 ± 16	0.02
Male	22 (28%)	81 (30%)	249 (44%)	< 0.0001
Systolic BP (mmHg)	138 ± 18	133 ± 19	133 ± 18	0.06
>140	27 (34%)	89 (33%)	151 (27%)	0.09
>170	2 (3%)	9 (3%)	14 (2%)	0.57
Diastolic BP (mmHg)	80 ± 12	78 ± 13	80 ± 13	0.46
>90	10 (13%)	33 (12%)	82 (15%)	0.68
>100	3 (4%)	7 (3%)	14 (2%)	0.79
BP > 140/90 mmHg	9 (11%)	24 (9%)	51 (9%)	0.79
SCr (mg/dL)	4.0 ± 2.9	2.9 ± 2.6	1.7 ± 1.4	< 0.0001
BT (min)	7.6 ± 1.8	7.4 ± 2.0	6.7 ± 1.8	< 0.0001
>9.0	8 (10%)	32 (12%)	27 (5%)	0.0006
PTT (s)	27 ± 6	27 ± 5	26 ± 4	0.07
>33	7 (9%)	23 (9%)	27 (5%)	0.06
PT (abnormal)	18 (23%)	44 (17%)	63 (11%)	0.006
Pre-Hgb (g/dL)	8.2 ± 0.5	10.1 ± 0.5	13.2 ± 1.5	< 0.0001
Post-Hgb (g/dL)	7.6 ± 0.8	9.3 ± 0.9	12.0 ± 1.6	< 0.0001
∆Hgb (g/dL)	0.6 ± 0.8	0.8 ± 0.7	1.2 ± 1.0	< 0.0001
ΔHgb (%)	10 ± 8	9±6	10 ± 7	0.31

demonstrating less of a drop in Hgb post-PRB, patients with a lower pre-Hgb were more likely to receive a transfusion (Figure 1). Patients with a pre-Hgb of <9.0 g/dL who were transfused had a Δ Hgb of 1.3 ± 1.0 g/dL, while those with a pre-Hgb of >11.0 g/dL had a significantly higher Δ Hgb of 3.2 ± 1.6 g/dL (P <0.0001) (Table 5, Figure 1). Among all patients who experienced a Δ Hgb of >1.5 g/dL (207/910, 22.7%), if the pre-Hgb was <9.0 g/dL, 100% (7/7) of patients received a transfusion, whereas only 8.7% (14/ 161) were transfused if the pre-Hgb was >11.0 g/dL (P <0.0001). In addition, among the patients receiving BL-T, only 58% with a pre-Hgb of <9.0 g/dL had a clinically significant hematoma post-procedure, while 87% of those with a pre-Hgb >11.0 g/dL had a clinically significant hematoma post-biopsy (P = 0.04) (Table 5, Figure 1).

Discussion

We conclude that the erythrocyte transfusions post-PRB is significantly influenced by the baseline Hgb, more so than other factors such as a drop in Hgb, perinephric hematoma or need for a radiologic or surgical procedure. The rate of interventions for bleeding complications in our single center prospective study was 7.8%, and most of these were transfusions (6.3% overall). Patients with a pre-PRB Hgb <9.0 g/dL were more often female, older and had more systolic HTN, elevated SCr, prolonged BT and abnormal PT, all of which are considered to be traditional risk factors for bleeding [19]. Despite the higher prevalence of risk factors in patients with a Hgb < 9.0 g/dL, they received a transfusion even though there were fewer hematomas and a less severe drop in Hgb compared with those patients with higher baseline Hgb concentrations. Thus, anemic patients are more likely to receive a BL-T because of their already lower pre-biopsy Hgb rather than as a result of a bleeding complication.

Traditionally, a major complication of PRB has been defined by the need for any intervention after the procedure, including readmission, radiologic or surgical procedure, or a transfusion. Table 3. Bleeding requiring interventions (BL-I) stratified by baseline (pre-PRB) Hgb

	Pre-PRB Hgb (g/dL)			
	<9.0	9.0–11.0	>11.0	P-value
N	79	266	565	
Bleeding requiring intervention (BL-I)	20 (25%)	29 (11%)	22 (4%)	<0.0001
Interventions without transfusion				
Interventional radiology embolization	0	0	3	
Obstruction and/or cystoscopy	0	1	2	
Readmission	1	4	2	
Death	0	1 ^a	0	
Total	1 (1.2%)	6 (2.3%)	7 (1.2%)	0.53
Interventions with transfusions (BL-T)				
Interventional radiology embolization	1	7	1	
Obstruction and/or cystoscopy	1	1	0	
Readmission	0	0	3	
Transfusion without procedure	17 ^b	15	11	
Total	19 (24%)	23 (9%)	15 (3%)	<0.0001

^aDeath was not attributed to the renal biopsy.

^bOne death in a patient with baseline Hgb of 7.8 g/dL, dropped to 4.7 g/dL and was transfused four units of packed red blood cells.

Table 4. Bleeding interventions (BL-I) with and without transfusion

	With transfusion (BL-T)	Without transfusion	P-value
N	57	14	
Pre-Hgb (g/dL)	9.9 ± 1.6	12.1 ± 2.7	0.0002
Post-Hgb (g/dL)	7.9 ± 1.4	9.8 ± 1.5	< 0.0001
∆Hgb (g/dL)	2.0 ± 1.3	2.4 ± 2.5	0.49
∆Hgb (%)	20 ± 10	20 ± 19	0.81

Our data suggest that a transfusion is not given for a bleeding complication, but more often given because of an Hgb threshold, as it is in other patient populations [24]. This is relevant especially to patients undergoing the PRB because even in uncomplicated procedures, the Hgb will drop on average by 1 g/dL [22, 25-28]. Preexisting anemia has classically been considered to be a risk factor for bleeding complications in the PRB. Corapi et al. [29] found the risk of transfusion of erythrocytes to be five times greater if the baseline Hgb was <12.0 g/dL. Although anemia itself has been shown to be a risk factor for actual bleeding, due to the rheology of red blood cells and platelets in circulation [30], we did not find this to be the case. Our association with the degree of preexisting anemia and complications is linked to a lower threshold for transfusion in patients starting with a lower pre-biopsy Hgb as opposed to clinically evident bleeding. In the past, patients with lower pre-PRB Hgb values have been traditionally thought to bleed more. This, however, is an artifact of the classic definition of a major complication, which includes transfusions. Therefore, the rate of actual bleeding requiring an intervention after the PRB is lower than 7.8%, and suggests that the definition of a complication should change to reflect this.

As bleeding is the most common complication from the PRB, identifying factors associated with hemorrhage has persistently been a focus to help risk-stratify for this procedure [31, 32]. In prospective studies in the native PRB that utilize multivariate analysis, clinical factors such as age, female gender and elevated blood pressure have been associated with increased risk of complication [18–20]. In addition to a low baseline Hgb, other laboratory tests, such as elevated SCr, prolonged BT, increased

international normalized ratio and increased PTT (even within the reference range), are also independent risk factors for complications after PRB [18, 20, 22]. In the largest registry study of 9288 biopsies, low estimated glomerular filtration rate (GFR), older age and elevated systolic HTN have been confirmed as increasing risk [33], and in the meta-analysis by Corapi *et al.* [29], age, female gender, HTN, increased SCr and use of a 14-gauge needle were all associated with increasing risk of complication. All of these studies, however, used transfusion post-procedure in the definition of a complication, and anemia itself is more common in females, older individuals and those with a reduced GFR.

The current decision to transfuse in acute anemia is based on the level of Hgb, the amount of blood loss and the clinical condition of the patient [1, 34]. In open surgical procedures, a 15% drop in Hgb is typically tolerated without symptoms postoperatively, unless preexisting anemia is present [34]. It is, therefore, not surprising that, in a closed procedure, where the rate and amount of blood loss is more difficult to quantify, a lower Hgb level alone may trigger the decision to transfuse. The presence of a hematoma on routine screening U/S at 1-h post-PRB has a low positive predictive value (43%) but a high negative predictive value (95%) for developing a clinical complication [35]. Thus, the absence of a hematoma 1-h post-PRB may be helpful in determining which patients may be safely managed as a 'same day' procedure. While the routine use of renal U/S 1-h post-PRB is not universal, we believe it can be helpful in post-PRB observation decisions.

Based on recent randomized controlled trials of hospitalized or post-surgical patients [3, 5–7], a Hgb threshold of 7.0 g/dL has been recommended [16, 36] and adopted by many institutions as policy. Universal application of this policy to all patients limits the ability of clinical judgment to be used in specific situations. To follow this target singularly, as may be done by making it policy, eliminates the effect of judgment on the rate or amount of blood loss, and the clinical condition of the patient. Based on our data, there is a suggestion that transfusions are overprescribed in patients with anemia undergoing a PRB, just as they have been proven to be in other clinical situations, such as in patients with sepsis in the intensive care unit [5, 6] or in those with a gastrointestinal bleed [9]. However, without a randomized controlled trial targeting a Hgb threshold in this population,

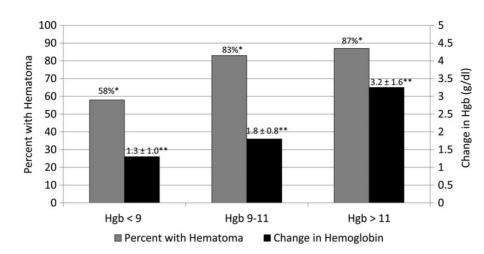


Fig. 1. Change in Hgb and percent of hematomas in patients who received a BL-T, stratified by baseline Hgb. Gray bars, percent of patients with a hematoma. Black bars, average change in Hgb. In patients who were transfused and a lower Hgb baseline (Hgb <9.0 g/dL), a significantly smaller drop in Hgb triggered the transfusion, despite significantly less patients in that group with a hematoma [pre-Hgb <9.0 g/dL, percent with hematoma, 58%; 9.0–11.0 g/dL, 83%; >11.0 g/dL, 87%, *P = 0.04. Pre-Hgb <9.0 g/dL, change in Hgb, $1.3 \pm 1.0 g/dL$; 9.0–11.0 g/dL, $1.8 \pm 0.8 g/dL$; >11.0 g/dL, $3.2 \pm 1.6 g/dL$, **P < 0.0001 (N = 57)].

Table 5. Characteristics of patients who received a BL-T

	Pre-PRB Hgb (g/dL)			
	<9.0	9.0–11.0	>11.0	P-value
Number of patients	19	23	15	
Reason for transfusion				
Isolated drop in Hgb	3 (16%)	2 (9%)	0 (0%)	0.27
Hematoma	9 (47%)	13 (57%)	10 (67%)	0.53
Gross hematuria	6 (32%)	2 (9%)	2 (13%)	0.11
Hematoma and gross hematuria	1 (5%)	6 (26%)	3 (20%)	0.20
Overall hematomas	10 (58%)	19 (83%)	13 (87%)	0.04
Hgb in patients transfuse	ed (BL-T)			
Pre-Hgb (g/dL)	8.2 ± 0.5	9.8 ± 0.6	12.2 ± 0.9	< 0.0001
Post-Hgb (g/dL)	7.0 ± 0.9	8.0 ± 0.8	9.0 ± 1.7	< 0.0001
∆Hgb (g/dL)	1.3 ± 1.0	1.8 ± 0.8	3.2 ± 1.6	< 0.0001
∆Hgb (%)	18±9	18 ± 8	27 ± 13	0.02

restricting transfusions to a specific target for all patients, eliminating the effect of clinical judgment, especially in a closed procedure, is unwarranted.

In summary, patients with preexisting anemia are significantly more likely to receive a BL-T post-PRB despite the absence of evidence for a bleeding complication. Thus, anemia alone should not be considered a significant risk factor for a hemorrhagic complication post-PRB. As the definition of a major complication after PRB includes receiving a BL-T, the rate of intervention for actual bleeding is likely lower than what has been reported. The decision to transfuse after a PRB still depends on many factors (i.e. clinician and center preference, hemodynamic instability, rate of fall of Hgb, anticipation for need of intervention, etc.) and the pre-biopsy Hgb is only one of those factors considered.

Conflict of interest statement

All of the authors disclose that there is no real or perceived conflict of interest. The results presented in this paper have not been published previously in whole or part, except in abstract format.

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