

# Bleeding during and after dental extractions in patients with liver cirrhosis

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**Abstract.** Little is known about the prevention and management of acquired coagulopathies, such as those affecting cirrhotic patients. The objective of this analytic retrospective observational study was to evaluate patients on the liver transplant waiting list according to the following outcomes: (1) presence of unusual intraoperative bleeding (>10 min after routine haemostatic procedures); and (2) presence of postoperative haemorrhagic complications. The outcomes were analysed according to clinical and laboratory variables. A total of 190 visits were performed for extraction of 333 teeth (ranging from 1 to 9 teeth per visit), with platelet count ranging from 16,000 to 216,000 and international normalized ratio (INR) below 3. Twelve cases (6.31%) had unusual intraoperative bleeding and 12 had postoperative haemorrhagic complications. All the events were controlled by local measures. Intraoperative bleeding was associated with low count of platelets ( $P = 0.026$ ). However, this counting could explain only 16% (adjusted  $R^2 = 0.16$ ) of the cases of bleeding ( $P = 0.44$ ), meaning that platelet function changes might be involved. Our results show that cirrhotic patients presenting platelet count above 16,000 and INR below 3 need no previous blood transfusion, with local measures being enough to manage haemorrhagic events.

**Key words:** blood coagulation; intraoperative complications; dental care for chronically ill; tooth extraction; haemorrhage; end-stage liver disease; cirrhosis.

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Hepatic cirrhosis is the result of all chronic diseases affecting the liver in the long term, being characterized by replacement of liver parenchyma with fibrotic tissue and nodules<sup>1</sup>. Regardless of the cirrhosis aetiology, the patient will have to face its two major consequences, namely, liver failure (LF) and portal hypertension (PH). The former is related to changes in the liver functions and is responsible

for signs and symptoms characteristic of the organ's physiological impairment (e.g. jaundice, malnutrition, deregulation of the glycine mechanism, oedemas and metabolic abnormalities), whereas the latter is the result of a greater intrahepatic resistance combined with an increase in the portal blood flow, thus triggering the formation of collateral portosystemic vessels (i.e. varices) and splenomegaly as well as

hypersplenism and thrombocytopenia consequently<sup>2</sup>.

The coagulopathies seen in cirrhotic patients depend on several mechanisms involving both LF and PH. In the former case, the extensive replacement of hepatocytes with fibrotic tissue compromises the liver's routine physiological functions, such as synthesis of all coagulation factors, except the von Willebrand factor<sup>3–5</sup>.

Another component of the coagulopathy found in liver cirrhosis is the thrombocytopenia, which can be mostly explained by the hypersplenic sequestration of platelets. Because portal vein is derived from the splenic vein and from both upper and lower mesenteric veins, the increase in portal pressure ends up extending into the splenic vein, which leads to splenomegaly and hypersplenism and consequent sequestration of platelets. Thrombocytopenia can also be explained by the reduced production of thrombopoietin – the megakaryocyte growth factor, which is exclusively produced by the liver<sup>6</sup>.

These multiple and complex alterations suggest that haemostasis is impaired and the main cause of haemorrhagic diathesis, being frequently seen in cirrhotic patients<sup>7</sup>.

In dentistry, one of the main concerns regarding the management of patients with chronic systemic diseases is the risk of haemorrhagic accidents. However, the vast majority of scientific studies address the management of patients with inherited haemorrhagic disorders or those related to the use of medications<sup>8–18</sup>.

The management of patients with acquired haemorrhagic diseases, such as cirrhosis, was initially addressed through literature review. It was recommended that patients presenting PT (prothrombin time)/aPTT (activated partial thromboplastin time) levels 1.5 higher than the reference value (or international normalized ratio (INR) above 3) were given fresh-frozen plasma (FFP), whereas those patients presenting platelet count less than 50,000 received blood transfusion<sup>19–24</sup>.

Clinical research has not changed much within this panorama. Five articles on this theme were identified on the MEDLINE database, with all invasive procedures in thrombocytopenic patients being preceded by blood transfusions, and in patients presenting INR higher than 2 or 3, FFP was administered<sup>25–29</sup>. The platelet counts considered for blood transfusion were, respectively, 100,000, 50,000, 40,000 and 30,000 according to Helenius-Hietala et al.<sup>26</sup>, Ward and Wiedman<sup>25</sup>, Cocero et al.<sup>28</sup> and Perdigão et al.<sup>29</sup>. Hong et al. just cited that patients presented more than 45,000 platelets and that no haemorrhagic event was observed<sup>27</sup>.

All the studies concluded that it is difficult to predict the risk of bleeding in cirrhotic patients, since no correlation was found between laboratory tests and haemorrhagic complications. Studies using FFP and/or platelets on a prophylaxis basis concluded that this procedure does not ensure an adequate haemostasis<sup>25–29</sup>.

Therefore, the objective of this study was to assess the prevalence and severity of the intra- and postoperative bleeding in cirrhotic patients on the liver transplant waiting list and to verify whether there is a correlation between laboratory tests and cirrhotic complications with presence of bleeding.

## Materials and methods

This project was approved by the Research Ethics Committee according to protocol number 1906327 and the study was conducted in accordance with the STROBE guidelines for observational studies.

## Study Design and Setting

An analytic, observational, retrospective study was performed at the Centro de Atendimento a Pacientes Especiais (CAPE) of the School of Dentistry, University of São Paulo, São Paulo, Brazil, from December 2002 to June 2017.

## Participants and Study Size

The study was performed with a convenience sample, obtained consecutively, of male and female adult cirrhotic patients on the liver transplant waiting list who had been submitted to tooth extraction.

Patients who had other blood dyscrasias not associated with hepatic disease, who used anticoagulants or antiplatelet drugs, who had no valid laboratory tests (i.e. collected up to 1 week before the surgical procedure), and who had been previously transfused or treated with any medication affecting haemostasis were excluded.

## Variables and Data Sources/Measurement

Data on the clinical conditions of the patients, laboratory tests and procedures performed were transferred from the medical records to computer software (Epiinfo<sup>TM</sup> 7).

The following data on the patients were collected: gender, age, medications used, cause of cirrhosis, MELD score (Model for End-Stage Liver Disease), cirrhotic complications (i.e. PH, hepatic encephalopathy, hepatocellular carcinoma, collateral circulation, spontaneous bacterial peritonitis, ascites, hepatorenal syndrome), laboratory tests, number of extracted teeth, type of tooth extraction (i.e. simple or surgical), outpatient bleeding duration (unusual intrasurgical bleeding) and postoperative haemorrhagic complications. The minimum labora-

tory tests required to perform dental extraction were INR and blood count (platelets count), although some patients also underwent additional tests (aPTT, urea, creatinine).

Next, the patients were categorized as being compensated or decompensated depending on the classification established by Garcia-Tsao et al.<sup>30</sup>. According to the authors, decompensated cirrhosis is defined by the development of clinically evident complications of PH (e.g. ascites, variceal haemorrhage, hepatic encephalopathy) or LF (e.g. jaundice).

The Lockhart's criteria were used for definition of the postoperative haemorrhagic complications, namely: bleeding for more than 12 h; need for return visit; presence of extensive haematomas or ecchymosis; and need for blood transfusion<sup>31</sup>.

For this study, unusual intraoperative bleeding was defined as being one lasting longer than 10 min after routine haemostasis procedures (i.e. surgical compression, intra-alveolar haemostatic sponge and suture) and requiring other containment manoeuvres (extra-alveolar use of N-butyl-2-cyanoacrylate or a paste made of macerated tablet of tranexamic acid (250 mg) mixed with saline solution inserted into the dental alveolus or onto the suture)<sup>18</sup>.

The outcomes of interest were the following: (1) presence of unusual intraoperative bleeding; (2) Presence of delayed postoperative bleeding complications.

## Bias

Because the patients presented with different clinical and laboratory conditions in each return visit for tooth extraction, the sampling number was determined as the number of appointments for assessment of the outcomes of interest.

## Quantitative Variables and Statistical Methods

The outcomes were evaluated according to the following variables: MELD, cirrhotic complications, characterization of cirrhosis (i.e. compensated or decompensated), laboratory tests, number of extracted teeth and type of tooth extraction.

The resulting data were analysed using IBM SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk, NY, USA) and the Kolmogorov–Smirnov test was used to assess the hypothesis performed. Descriptive analysis of the data on frequencies, mean, standard deviation, median, and

minimum and maximum values was also performed.

In the bivariate analysis for qualitative variables, Fisher's exact test was used to determine associations between bleeding events (intra- and postoperative) and independent variables, including non-adjusted odds ratio (OR) and 95% confidence interval (95% CI).

As for quantitative variables, Student's *t*-test was used for independent samples and Mann-Whitney's test for normality distribution of the variables being tested. *P*-values  $\leq 0.05$  were considered statistically significant. In order to verify the relationship between platelet counts and bleeding duration during surgical procedure, Spearman's correlation test was used before linear regression analysis, with the results being expressed by the coefficient of determination ( $R^2$ ) and 95% CI. All statistical analyses were performed at a significance level of 5%.

## Results

### Participants

Within the period between December 2002 and June 2017, a total of 224 patients on the liver transplant waiting list were attended at the CAPE and 99 needed tooth extraction, but the sampling number was determined as the number of appointments ( $n = 190$ ) for assessment of the outcomes of interest.

### Descriptive data

The majority of the patients were male (75.44%) with mean age of 51.27 years old and whose major causes of cirrhosis were hepatitis C (40.18%), alcoholic cirrhosis (26.79%) and cryptogenic cirrhosis (10.27%).

As for the cirrhotic complications, all the patients had PH, but none of them had hepatorenal syndrome. More than a half had portosystemic varices (collateral circulation) (66.8%), hepatic encephalopathy (55.8%) or ascites (63.2%) and the great majority had decompensated cirrhosis (86.80%).

One week before each appointment, the patients underwent basic preoperative examinations as recommended by the dental literature (i.e. blood count and INR). Tests for aPTT levels, urea and creatinine were not mandatory before tooth extractions, but some patients underwent them up to 1 week before (Table 1). Almost all patients exhibited changes in their laboratory tests, that is, thrombocytopenia (platelet count  $<150,000$ ) was identified

Table 1. Descriptive analysis of laboratory tests.

Variables	Minimum	Maximum	Median	Mean	Standard deviation
aPTT (s) $n = 63$	22.80	88.30	37.50	38.65	9.60
INR $n = 190$	1.00	3	1.45	1.54	0.31
Haemoglobin $n = 190$	7.00	16.50	11.85	12.01	1.96
Platelets ( $\times 10^3$ ) $n = 190$	16	216	69.50	76.38	38.96
Urea $n = 54$	8.00	90.00	27.00	29.39	13.35
Creatinine $n = 93$	0.50	2.10	0.80	0.84	0.27

Reference values: INR (0.96–1.30); haemoglobin (13.5–17.5 g/dL); platelets (150,000–450,000); creatinine (0.6–1.2); urea (21–53 mg/dL), aPTT (27–37.5 s).

in 183 patients (95.80%), anaemia in 129 (67.90%) and white blood cell alterations in 110 (57.80%).

A total of 190 appointments were made for extraction of 333 teeth in total, with the number of extracted teeth ranging from 1 to 9. More than 95% of the tooth extractions were simple procedures in which only forceps and elevators were used. The use of burs for dental sectioning or osteotomy was required in eight cases. Haemorrhagic events were uncommon in both intra ( $n = 12$ ; 6.31%) and postoperative ( $n = 12$ ; 6.31%) procedures. None of the patients presenting unusual bleeding during tooth extraction had postoperative haemorrhagic complications. Also, no patients presented more than one case of intraoperative bleeding or postoperative haemorrhagic complications.

Postoperative haemorrhagic events were controlled on an outpatient basis using local haemostasis and suture, with patients needing neither blood transfusion nor presenting ecchymosis after surgery.

### Outcome Data and Main Results

Correlations were made between qualitative variables and intraoperative haemorrhage in order to verify whether the unusual bleeding (longer than 10 min) might be associated with some of the variables. Quantitative variables (i.e. INR, platelets, haemoglobin, aPTT levels, urea and creatinine) were divided dichotomically into 'normal' and 'altered'. There was a correlation between absence of collateral circulation and presence of uncommon intraoperative bleeding ( $P = 0.022$ ), which was confirmed by OR (0.22) (Table 2).

By correlating the quantitative variables with intraoperative bleeding, we observed a significant difference in the distribution of platelet counts and unusual bleeding ( $P = 0.026$ ). Individuals with intraopera-

tive bleeding longer than 10 min had a low count of platelets (Table 3).

Linear regression analysis confirmed the significant difference found with the Mann-Whitney test, but the platelet count could only explain 16% (adjusted  $R^2 = 0.16$ ) of the cases of intraoperative bleeding ( $P = 0.044$ ) (Table 4).

The sample power was calculated using the OpenEpi software, version 3, showing that the sample of 190 appointments had a 64% power to reaffirm the correlation found between platelet count and intraoperative bleeding.

There was no correlation of qualitative and quantitative variables with postoperative haemorrhagic complications (Tables 5 and 6).

## Discussion

Although all scientific works on dental surgery in cirrhotic patients have pointed to the necessity to perform platelet count and PT/INR before surgical procedures, none of them found any correlation between bleeding and the laboratory tests performed<sup>25–29</sup>.

The premise that platelet count below 50,000 can lead to haemorrhagic events in cirrhotic patients, which thus should be treated before surgical procedures<sup>19–24</sup>, may be misleading. In our treatment centre, the thrombocytopenic patients on the liver transplant waiting list are not submitted to blood transfusion before tooth extraction. This approach was based on the assumption that tooth extraction would not be a surgical trauma sufficiently strong to indicate blood transfusion, since the literature points to the fact that significant bleeding is unlikely to occur in patients with platelet counts above 10,000<sup>32,33</sup>. In addition, it does not seem to be reasonable to expose the patient to biological risks resulting from plasma transfusions, such as transmission of pathogens and adverse

Table 2. Correlation between qualitative variables and intraoperative bleeding.

Variables	Intraoperative bleeding		<i>P</i> *	Gross OR 95% CI
	≤10 min ( <i>n</i> = 178, 93.7%) <i>n</i> (%)	>10 min ( <i>n</i> = 12, 6.3%) <i>n</i> (%)		
Tooth sectioning/osteotomy			1.000	0.93 (0.90–0.97)
No	170 (93.4)	12 (6.6)		
Yes	08 (100.0)	00 (0.0)		
INR			0.735	1.59 (0.33–7.55)
Normal	43 (95.6)	02 (4.4)		
Altered	135 (93.1)	10 (6.9)		
Haemoglobin			1.000	1.14 (0.29–4.38)
Normal	49 (94.2)	03 (5.8)		
Altered	129 (93.5)	09 (6.5)		
Platelets			1.000	1.07 (1.03–1.11)
Normal	08 (100.0)	00 (0.0)		
Altered	170 (93.4)	12 (6.6)		
aPTT (s)			0.305	0.23 (0.02–2.33)
Normal	24 (8.9)	03 (11.1)		
Altered	35 (97.2)	01 (2.8)		
Urea			1.000	0.90 (0.82–0.99)
Normal	46 (90.2)	05 (9.6)		
Altered	03 (100.0)	00 (0.0)		
Creatinine			1.000	0.94 (0.89–0.99)
Normal	82 (94.3)	05 (5.7)		
Altered	06 (100.0)	00 (0.0)		
Encephalopathy			0.371	0.53 (0.16–1.74)
No	76 (91.6)	07 (8.4)		
Yes	102 (95.3)	05 (4.7)		
Ascite			0.121	0.37 (0.11–1.22)
No	61 (89.7)	07 (10.3)		
Yes	117 (95.9)	05 (4.1)		
Disease stage			0.198	0.42 (0.11–1.68)
Compensated	22 (88.0)	03 (12.0)		
Decompensated	156 (94.5)	09 (5.5)		
Collateral circulation			<b>0.022</b>	0.22 (0.06–0.77)
No	55 (87.3)	08 (12.7)		
Yes	123 (96.9)	04 (3.1)		

Reference values: INR (0.96–1.30); haemoglobin (13.5–17.5 g/dL); platelets (150,000–450,000); creatinine (0.6–1.2); urea (21–53 mg/dL), aPTT (27–37.5 s). CI, confidence interval; OR, odds ratio.

\*Fisher's exact test.

effects (e.g. minor allergic reactions, anaphylactic reactions, non-haemolytic febrile reactions, acute pulmonary lesion, circulatory overload, bacteremia, sepsis and haemolysis)<sup>34</sup>.

In this context, it is important to highlight that the new medical guidelines for liver transplantation or biopsy do not recommend prophylactic transfusions based on INR and platelet counts. Instead, transfusions or anti-fibrinolytic drugs should be performed for active haemorrhages only (during and after surgery) and prophylactic approaches should be restricted to the treatment of infections and improvement of renal function of the patient<sup>35</sup>. Therefore, we agree with Weeder et al., who reported that it would be difficult to imagine any greater haemostatic challenge for the patient than the liver transplantation, and consequently, they also state that minor invasive procedures should not be preceded by prophylactic blood transfusions to improve the INR and platelet levels<sup>35</sup>.

Differently from other authors<sup>25–29</sup>, whose studies could not find any relationship between platelets count and bleeding, the present study has identified an inversely proportional correlation between intraoperative bleeding and quantity of platelets, probably because the platelet levels of our patients were much lower than those reported elsewhere. However, despite the fact that some of our patients had extremely low platelet counts (reaching 16,000), all haemorrhagic events were controlled with local haemostatic measures.

Indeed, the platelet counts can only partially explain the intraoperative bleeding, as shown by the linear regression analysis. It is possible that there is an improvement in other primary haemostatic events<sup>36</sup>. This

Table 3. Correlation between quantitative variables and intraoperative bleeding.

Variables	Intraoperative bleeding	Minimum	Maximum	Median	Mean	Standard deviation	<i>P</i>
Number of extracted teeth	≤10 min	1	9	1	1.77	1.32	0.346*
	>10 min	1	2	1	1.33	0.49	
MELD	≤10 min	12	29	17	17.05	4.66	0.400*
	>10 min	15	21	17	17.4	1.81	
Haemoglobin	≤10 min	7.00	16.50	11.80	11.99	1.98	0.188**
	>10 min	10.00	16.20	12.45	12.29	1.75	
Platelets	≤10 min	16	216	71	77.81	39.05	<b>0.026*</b>
	>10 min	23	121	42	55.25	32.11	
INR	≤10 min	1.00	3.00	1.45	1.54	0.31	0.114*
	>10 min	1.00	2.00	1.71	1.69	0.36	
aPTT (s)	≤10 min	22.80	63.00	37.60	38.24	7.21	0.615**
	>10 min	27.80	88.30	31.55	44.80	29.10	
Urea	≤10 min	16.00	90.00	27.00	29.82	13.61	0.881*
	>10 min	8.00	36.00	29.00	25.20	10.85	
Creatinine	≤10 min	0.50	2.10	0.80	0.84	0.27	0.805*
	>10 min	0.50	0.90	0.81	0.76	0.15	

\*Mann–Whitney test.

\*\*Student's *t*-test for independent samples.



Table 4. Linear regression analysis to correlate platelet counts and intraoperative bleeding duration.

Variables	$\beta$	95% CI	P	Adjusted $R^2$
Intraoperative bleeding duration				
Constant	77.94	72.21–83.68	<0.001	0.16
Platelet count	–5.47	–10.80 to 0.14	0.044	

CI, confidence interval.

hypothesis is supported by our results, demonstrating that patients with normal platelet counts had intraoperative bleeding as well as postoperative haemorrhagic complications.

Primary haemostatic events, such as vasoconstriction, and platelet adhesion, activation and aggregation might be impaired as a result of accumulation of nitrogenated compounds, nitric oxide (NO), urea and ammonium ( $\text{NH}_4$ ), which occurs in the cirrhotic patient's body. NO is a powerful vasodilator acting on the relaxation of the vessel walls<sup>37</sup> and the

platelet function may be impaired due to an increase in NO and  $\text{NH}_4$  levels or in urea levels (in patients with hepatorenal syndrome)<sup>7</sup>. In addition to these factors, the impairment of circulating immunity may consequently allow bacterial infections to occur, which can trigger the release of endogenous heparinoids<sup>38</sup>.

Nitrogenated compounds are also closely related to the development of ascites and hepatic encephalopathy<sup>39,40</sup> and, in theory, by analogy these clinical complications of cirrhosis could be used as clinical parameters to predict haemorrhagic

events. However, in the present study, it was not possible to correlate these complications to bleeding.

The incidence of unusual bleeding (longer than 10 min) during and after surgical procedures was 6.31% in both cases, which is a low figure, thus indicating no correlation between intraoperative and postoperative haemorrhagic events. This may suggest that the origin of these two types of events is different, showing that it is important to further study the coagulation in cirrhotic patients.

The understanding that liver is an organ responsible for the production of both coagulation and anticoagulation factors (anti-thrombin, heparin cofactor II, protein C, protein S, tissue factor inhibitor, and fibrinolytic system components – plasminogen,  $\alpha_2$ -anti-plasmin, plasmin inhibitor) and the concept of 'state of re-balanced haemostasis' have led the medical professionals to revise the indications for blood transfusions<sup>35</sup>. In this context, the increase in von Willebrand factor and the decrease in metalloproteinase ADAMTS 13 also participate. This panorama causes the cirrhotic patient to present a more balanced coagulation picture, even when INR and platelet count have alterations which may seem numerically significant<sup>7,41</sup>.

Although intrinsic and extrinsic coagulation pathways may be impaired in these patients, it is known that only 20–50% of the normal level of the majority of procoagulants is actually necessary for haemostasis. PT and aPTT tests do not reflect the reality of the coagulation picture of a cirrhotic patient<sup>42</sup>.

The limitations of the present study were the sample (190 appointments), which had a 64% statistical power for prediction of the type of association being assessed, and the retrospective design. With a very small incidence of bleeding events, it is possible that distortions in the statistical analysis may be found, such as the association between lack of collateral circulation and longer bleeding ( $P = 0.022$ ). Physiologically, this type of association is meaningless as patients with collateral circulation would be, in theory, more likely to have haemorrhagic events due to the increased circulating NO, for instance.

The clues found in this study can help in guiding future works. The present work identified low intra- and postoperative complication rates in spite of the poor lab tests and outpatient setting safety for such patients. Moreover, our results showed evidence that there is no need for previous transfusion in cirrhotic

Table 5. Correlation between qualitative variables and postoperative haemorrhagic complications.

Variables	Postoperative haemorrhagic complications		$P^*$	Gross OR 95% CI
	Absent (n = 160, 93.0%) n (%)	Present (n = 12, 7.0%) n (%)		
INR			0.733	1.61 (0.34–7.67)
Normal	39 (95.1)	02 (4.9)		
Altered	121 (92.4)	10 (7.6)		
Haemoglobin			1.000	1.24 (0.32–4.81)
Normal	47 (94.0)	03 (6.0)		
Altered	113 (92.6)	09 (7.4)		
Platelets			0.099	0.19 (0.03–1.09)
Normal	06 (75.0)	02 (25.0)		
Altered	154 (93.9)	10 (6.1)		
aPTT (s)			0.681	0.66 (0.12–3.64)
Normal	20 (87.0)	03 (13.0)		
Altered	30 (90.9)	03 (9.1)		
Urea			1.000	0.91 (0.83–0.99)
Normal	41 (91.1)	04 (8.9)		
Altered	03 (100.0)	00 (0.0)		
Creatinine			1.000	0.86 (0.79–0.95)
Normal	65 (86.7)	10 (13.3)		
Altered	06 (100.0)	00 (0.0)		
Encephalopathy			0.231	2.51 (0.65–9.64)
No	73 (96.1)	03 (3.9)		
Yes	87 (90.6)	09 (9.4)		
Ascites			0.542	1.71 (0.44–6.55)
No	58 (95.1)	03 (4.9)		
Yes	102 (91.9)	09 (8.1)		
Disease stage			0.368	1.09 (1.04–1.13)
Compensated	22 (100.0)	00 (0.0)		
Decompensated	138 (92.0)	12 (8.0)		
Collateral circulation			0.541	0.69 (0.21–2.29)
No	53 (91.4)	05 (8.6)		
Yes	107 (93.9)	07 (6.1)		

Reference values: INR (0.96–1.30); haemoglobin (13.5–17.5 g/dL); platelets (150,000–450,000); creatinine (0.6–1.2); urea (21–53 mg/dL), aPTT (27–37.5 s). CI, confidence interval; OR, odds ratio.

\* Fisher's exact test.

Table 6. Correlation between quantitative variables and postoperative haemorrhagic complications.

Variables	Postoperative bleeding	Minimum	Maximum	Median	Mean	Standard deviation	P
Number of extracted teeth	Absent	1	9	1	1.71	1.14	0.863*
	Present	1	9	1	2.00	2.25	
MELD	Absent	12	29	17	16.92	4.39	0.932*
	Present	12	29	15	17.25	6.04	
Haemoglobin	Absent	7.00	16.50	12.00	12.13	1.99	0.365**
	Present	9.00	14.10	11.40	11.59	1.75	
Platelets	Absent	16	216	70	76.83	39.40	0.796*
	Present	36	163	65	83.16	48.69	
INR	Absent	1.00	3.00	1.46	1.53	0.30	0.422*
	Present	1.00	3.00	1.43	1.67	0.46	
aPTT (s)	Absent	22.80	88.30	38.55	39.12	10.16	0.823**
	Present	26.90	56.00	35.65	38.13	10.65	
Urea	Absent	8.00	90.00	27.40	30.12	14.37	0.808*
	Present	17.00	38.00	29.50	28.50	8.88	
Creatinine	Absent	0.50	2.10	0.80	0.87	0.29	0.060*
	Present	0.50	1.11	0.62	0.71	0.20	

\* Mann–Whitney test.

\*\* Student's *t*-test for independent samples.

patients presenting platelet counts above 16,000 and INR below 3; instead only local measures are enough to control the few bleeding events. We believe that prospective studies should be conducted to further assess the coagulation in these patients so that adequate strategies can be outlined for prevention of haemorrhagic events.

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### Competing Interests

None.

### Ethical approval

This project was approved by the Research Ethics Committee of the Dental School of the University of São Paulo according to Protocol number 1.906.327.

### Patient consent

All the participants read, understood, accepted and signed a written informed consent form.

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