Bleeding Evaluation During Single Tooth Extraction in Patients With Coronary Artery Disease and Acetylsalicylic Acid Therapy Suspension: A Prospective, Double-Blinded, and Randomized Study

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Purpose: Acetylsalicylic acid (ASA) has been used for the primary and secondary prevention of cardiovascular events. To reduce bleeding, the administration of ASA has traditionally been suspended before dental procedures; however, this suspension potentially increases the risk of thromboembolic events. The effect of ASA on the amount of bleeding that occurs during tooth extraction procedures is controversial, and perioperative guidelines recommend that ASA administration should not be altered for such procedures. The aim of this study was to evaluate the amount of bleeding that occurs during the intraoperative period of tooth extraction procedures in patients with coronary artery disease who are either undergoing acetylsalicylic acid (ASA) therapy or who have been instructed to suspend their ASA use.

Patients and Methods: Sixty-three patients with coronary artery disease who required tooth extraction were enrolled in this study. All patients were receiving 100 mg/d of ASA at the time of enrollment and were randomly placed into 2 groups: group S, which was comprised of patients whose ASA therapy was suspended 7 days before tooth extraction, and group NS, comprised of patients whose ASA therapy was unaltered. A platelet aggregation test was carried out on the day of the operation, and the amount of bleeding was measured during the intraoperative period by means of aspirated blood collection. All the extractions were performed by the same surgeon, who was unaware of whether the patient's ASA therapy had been suspended.

Results: The mean (± SD) volume of bleeding was 12.10 ± 9.37 mL for patients who underwent ASA therapy suspension and 16.38 ± 13.54 mL for those patients whose treatments were unaltered (P = .151). Local hemostatic methods were sufficient to control bleeding, and there were no reported episodes of hemorrhaging during the intra- and postoperative periods. The platelet reactivity index values exhibited statistically significant differences between the 2 investigated groups (P = .004). The platelet reactivity index values for group S and group NS were 242.58 ± 71.26 and 192.09 ± 60.54, respectively.

Conclusion: There was no difference in the amount of bleeding that occurred during tooth extraction between patients who continued ASA therapy versus patients who suspended their ASA therapy. The

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0278-2391/11/6912-0009$36.00/0
doi:10.1016/j.joms.2011.02.139

platelet reactivity test demonstrated a reduction in platelet aggregation in the ASA therapy group (group NS), but this reduction was without clinical consequence.

J Oral Maxillofac Surg 69:2949-2955, 2011

Medical care and optimized pharmacological therapy have facilitated prolonged survival in certain kinds of patients with cardiovascular disease (CVD) because of a reduction in risk factors, such as hypertension, dyslipidemia, stress, diabetes, obesity, tobacco consumption, and sedentary lifestyle. Within this CVD group, there are patients who present with coronary artery disease (CAD), which results in the deposition of fat over cells that cover the wall of a coronary artery, leading to blockage of the flow of the bloodstream and atherothrombotic accidents. In recent years, CAD patients have comprised an increasing proportion of dental patients; therefore, it has become compulsory for professionals to acquire a greater understanding of CVDs and the medications that are used by this group of patients.

Acetylsalicylic acid (ASA) is the most commonly used antiplatelet medication by CVD patients for the primary and secondary prevention of cardiovascular events because of its effects on reducing platelet aggregation by irreversibly blocking the cyclooxygenase enzyme (COX). Unfortunately, ASA may cause additional bleeding during dental surgical procedures. Therefore, a number of dentists have recommended the suspension of ASA therapy before oral surgical procedures; however, any interruption or alteration of antiplatelet therapy may expose CVD patients to an increased thromboembolic risk.

Although there is a significant threat of hemorrhaging for patients who are receiving ASA therapeutics and who undergo surgical procedures, some studies have suggested that most of these patients can be operated on safely, with no need for a suspension in ASA therapy; however, few studies have randomized the suspension of ASA therapy, and the amount of bleeding in such studies cannot therefore be adequately determined.

The goal of this study is to evaluate the amount of bleeding that occurs during the intraoperative period of tooth extraction procedures in patients with CAD who are being administered 100 mg/d of ASA for the prevention of thromboembolic events. These results are compared with patients who have had their treatment suspended.

Patients and Methods

PATIENTS

Eighty-three patients with CAD who were undergoing ASA therapy were selected between February 2007 and April 2009 at a tertiary cardiology hospital. The inclusion criteria for this study included an indication of the need for at least 1 molar extraction (superior or inferior) and the presence of CAD that was being treated with an ASA therapy of 100 mg/d. Patients were excluded if they were receiving anticoagulation treatment or undergoing any other type of antiplatelet therapy; had blood dyscrasia; exhibited alcoholic abuse, tobacco consumption, or unstable angina; had a recent (less than 6 months earlier) acute myocardial infarction; exhibited clotting and/or platelet alterations; or were using a drug-eluting stent (DES, a pharmacologic stent). Patients with bare-metal stent (a noncovered stent) or who had received ASA therapy for an indefinite amount of time could be enrolled only after 3 months of implant placement and clopidogrel suspension.

METHODS

The selection of patients was carried out by the Dentistry Department of the Instituto Dante Pazzanese de Cardiologia (IDPC). The selection process included oral and physical evaluations, medical and dental queries, and a radiographic examination (to assess the need for tooth extraction). For the dental examination, inflammation of the support tissues of the teeth that was associated with bleeding and loss of insertion was considered a criterion for the presence of periodontal disease that was defined in the charts as an external factor; preoperative tests that involved platelet aggregation, and a schedule of the dental surgery procedure. In addition, the IDPC required a signature of informed consent from each patient to be enrolled in the tests, which were approved by the local research ethics committee.

Patients were randomly divided into 2 groups by a staff member who was not involved in performing the clinical research. Group S patients had their ASA therapy suspended for 7 days before tooth extraction and were restarted on ASA therapy the day following the surgical procedure. Group NS patients did not have their ASA therapy suspended at any point before or after the procedure. This was a double-blind and randomized study, and all tooth extractions were performed by a single dentist.

Patients were advised to undergo the platelet aggregation test on the morning of the day of the dental procedure, which was to be performed at the Clinical Research Laboratory of the IDPC. The blood sample was collected by vein puncture using

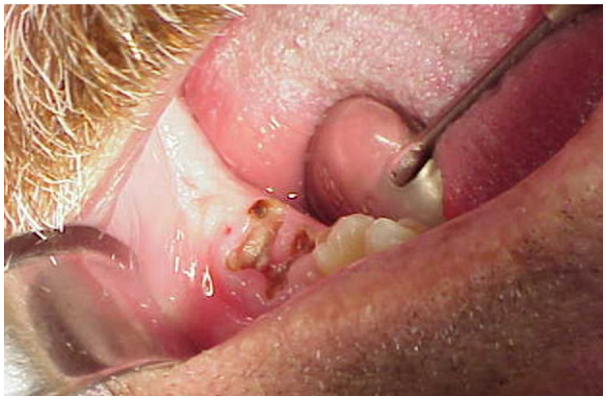

FIGURE 1. The residual root.

Medeiros et al. Single Tooth Extraction in Patients With CAD. J Oral Maxillofac Surg 2011.

a disposable Vacutainer material and 20-mL lure syringes before being transferred to a 4.5-mL vacuum silicone tube that contained 1.0 mL of 3.2% sodium citrate as an anticlotting agent. These procedures were carried out by nurses at the Clinical Research Laboratory of the IDPC. A platelet reactivity index test was carried out on the same day of the sample collection to verify the extent of platelet aggregation.

The dental surgical procedure was performed with a local anesthetic, 3% mepivacaine, without a vasoconstrictor. The extracted teeth were either superior or inferior molars (Fig 1). A 3.0 nylon suture was used after the syndesmotomy, dislocation, tooth avulsion, curettage, and after abundant irrigation with a 0.9% physiological saline solution (Figs 2, 3). A biological adhesive (Polysuture; Polysuture Indústria E Comércio, Minas Gerais, Brazil) was then applied over the suture in cases of more intense bleeding episodes to promote better control of the hemostasis.

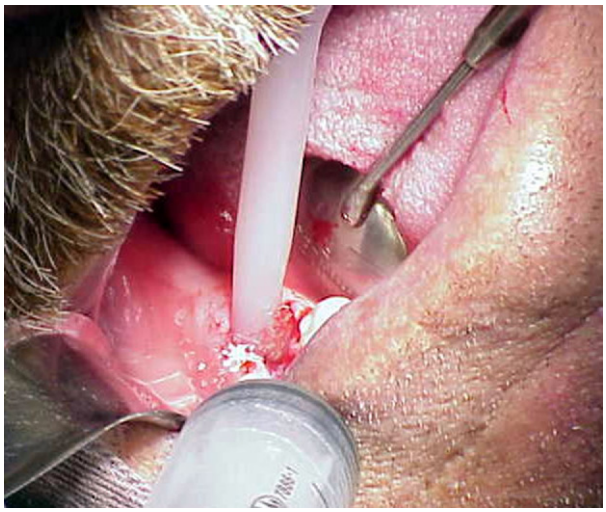

FIGURE 2. The 0.9% physiological saline irrigation and aspiration.

Medeiros et al. Single Tooth Extraction in Patients With CAD. J Oral Maxillofac Surg 2011.

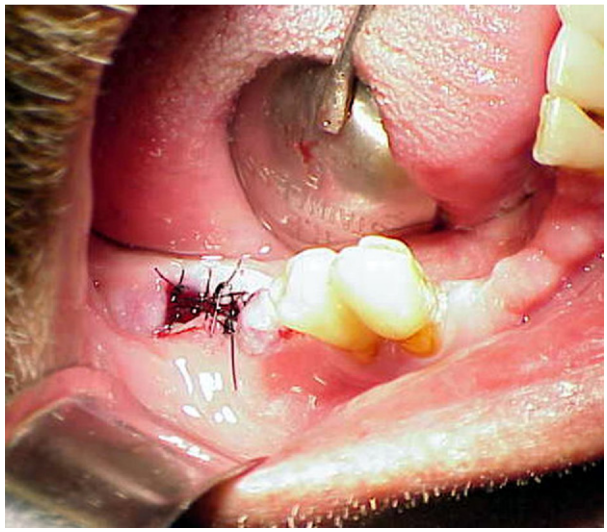

FIGURE 3. Suture.

Medeiros et al. Single Tooth Extraction in Patients With CAD. J Oral Maxillofac Surg 2011.

The amount of bleeding that occurred during the intraoperative period was calculated (Fig 4) by subtracting the final amount of removed blood during tooth extraction from the amount of 0.9% physiologic solution that was used during the irrigation period. A

FIGURE 4. Intraoperative bleeding.

Medeiros et al. Single Tooth Extraction in Patients With CAD. J Oral Maxillofac Surg 2011.

Table 1. THE HOMOGENEITY CORRELATION BETWEEN GROUPS S (ACETYLSALICYLIC ACID SUSPENDED) AND NS (NOT SUSPENDED) REGARDING QUALITATIVE VARIABLES

	Group S (n = 31)	Group NS (n = 32)	Total (N = 63)	*P* Value
Gender*				
Male	13%–41.9%	9%–28.1%	22%–34.9%	.250
Female	18%–58.1%	23%–71.9%	41%–65.1%	
Tooth*				
Superior	19	15	34	.251
Inferior	12	17	29	
External factors†	6	8	14	.590
Biological adhesive‡	2	5	7	.426

*Pearson χ^2 test.
†Periodontal disease.
‡Fisher exact test.

Medeiros et al. Single Tooth Extraction in Patients With CAD. J Oral Maxillofac Surg 2011.

vacuum pump was used for bleeding quantification, and a dental aspirator was used to remove the secreted saliva. After considering all postoperative recommendations, patients were advised to return a week later for suture removal; in cases of hemorrhagic complications, patients were advised to return to the dental department of the IDPC for further evaluation.

STATISTICAL ANALYSIS

All conclusions were statistically evaluated at a significance level of 5%.

The Pearson χ^2 test or the Fisher exact test was performed for sample sizes of less than 5 individuals to verify the homogeneity of the 2 groups (group S and group NS). The qualitative variables included gender, tooth type, the presence of external factors, and the presence of the biological adhesive (Table 1). Student *t* test or the Mann-Whitney test was performed when there was not a normal distribution of the values. These tests were both carried out to verify group homogeneity for the quantitative variables of age, surgical time, platelet count, and platelet reactivity index (Table 2).

Results

Eighty-three coronary patients were initially evaluated, and 20 of these patients were excluded from the investigation for a variety of factors, including the presence of an impacted third molar (4 patients), dental abscess (2 patients), absence of a blood test (9 patients), laboratory technical errors (9 patients), thrombocytopenia (1 patient), and an accident with the aspiration pump during the intraoperative procedure (2 patients).

Sixty-three patients (22 females and 41 males) attended the meetings. These patients were between the ages of 35 and 81 years with an average age of 58 years. Thirty-one patients comprised group S (13 females; 18 mol/L), and 32 patients comprised group NS (9 females; 23 mol/L). There were no statistically significant differences between the groups for the variables, including gender, tooth type, the presence of external or biological adhesive, age, surgical time, and platelet count (Tables 1 and 2).

The platelet reactivity index (PRI) exhibited a statistically significant difference ($P = .004$) between group S = 242.58 (± 71.26) and group NS = 192.09 (± 60.54). According to the PRI values of the patients in groups S and NS, the greatest numbers of patients were at the moderate level of 141 to 240, whereas 17 patients from group S were at the severe level (Table 3).

Local bleeding was controlled in 56 patients (88.9%) using a 4.0 nylon simple suture, which resulted in good coaptation of the wound edges and efficient local hemostasis. More intense bleeding was clinically observed in 7 patients (11.1%), such that a biological adhesive was applied over the suture to induce hemostasis. No hemorrhagic episode occurred in the intraoperative or postoperative periods for patients in either group. In addition, no statistically significant difference was observed between groups when the biological adhesive ($P = .426$) was used (Table 3).

Table 2. THE HOMOGENEITY CORRELATION BETWEEN GROUPS S (ACETYLSALICYLIC ACID SUSPENDED) AND NS (NOT SUSPENDED) REGARDING QUANTITATIVE VARIABLES

	Group S (n = 31)	Group NS (n = 32)	Total (N = 63)	*P* Value
Age*	57 (11)	59 (9)	58 (10.05)	.373
Surgical time (min)†	16.77	20	18,41	.058
Platelet count*	222.23 (58.63)	210.72 (52.74)	216.38 (55.56)	.417

*Mean values (SD), Student *t* test.
†Mann-Whitney test.

Medeiros et al. Single Tooth Extraction in Patients With CAD. J Oral Maxillofac Surg 2011.

Table 4. MULTIPLE LINEAR REGRESSIONS CONSIDERING THE AMOUNT OF BLEEDING AS THE DEPENDENT VARIABLE

	Estimation	Standard Error	*P* Value
Age	−0.018	0.088	.841
Surgical Time	1.052	0.130	<.001*
PC	0.002	0.016	.876
PRI	0.026	0.014	.076
Group NS	1.605	2.957	.209
Gender (female)	−4.704	3.868	.352
Tooth (superior)	2.351	2.981	.422
External factors	2.121	5.208	<.001*
Biological adhesive	−0.168	4.701	.049*

Abbreviations: Group NS, patients in whom acetylsalicylic acid was not suspended; PC, platelet count; PRI, platelet reactivity index.

*Statistical significance at $P < .05$.

Medeiros et al. Single Tooth Extraction in Patients With CAD. J Oral Maxillofac Surg 2011.

anson et al[1] have shown that relatively low dosages (150 mg/d ASA) can cause a significant alteration in platelet function, which can result in serious physiologic complications.

Some authors have stated that a continuation of ASA therapy before dental surgical procedures may greatly benefit patients in terms of the prevention of thromboembolic events with high morbidity potential, even at the risk of hemorrhagic episodes.[2-5]

Doubts concerning the suspension or maintenance of antiplatelet agents before elective interventions and also the period that such procedures should be suspended before the procedure are very common. According to Daniel et al,[6] antiplatelet therapy should be suspended 7 days before a surgical procedure to minimize hemorrhagic complications. This assertion reinforces the results of Sonis et al,[7] which indicate that the suspension of ASA therapy should occur 7 days before tooth extraction procedures. In addition, they have stated that ASA should be restarted after adequate healing of the soft tissues, which usually forbids the use of ASA therapy for up to 1 week postsurgery. Interestingly, other studies have advised the suspension of such therapy for up to at least 5 days before an elective surgery when patients are undergoing ASA therapy or being administered any other type of platelet aggregation inhibitor drugs. These studies have affirmed that treatment should be restarted the day after the surgery and on confirmation that there is no additional bleeding.[8,9] This advice contradicts Medeiros et al,[10] who have proposed that medication should be suspended 24 to 48 hours before the surgery and restarted 24 to 48 hours after the procedure. In some cases, this interval can be increased, depending on disease complexity. It should be noted that the mean platelet lifetime is between 7 and 10 days and cannot be used to justify a suspension in ASA therapy less than this period.

Our results indicate that there is no need for the suspension or alteration of ASA therapy consisting of 100 mg/d before tooth extraction procedures. Interestingly, group NS exhibited more bleeding than group S; however, there was no statistically significant difference between the observed bleeding in both groups, at least with respect to the amount of bleeding that occurred during the intraoperative period, even when all the variables (gender, age, tooth type, presence of external factors, biological adhesive, surgical time, and PRI) were evaluated together or individually. These findings reinforce the results of Sonksen et al[2] and Brennan et al,[11] who demonstrated that there is no justification for suspending ASA therapy for a single tooth extraction or for any other invasive tooth procedure. In other reports, the authors have reported that even when there is a more intense bleeding episode, local hemostatic methods are usually effective.[3-5,11-18]

Our results demonstrate that local hemostatic methods are sufficient for the control of bleeding in patients who were receiving ASA therapy. Interestingly, in 88.9% of the patients, local bleeding was controlled with simple sutures that are typically used for wound edge coaptation; in 11.1% of the patients, a biological adhesive was used, which resulted in a 0.168-mL reduction in the amount of bleeding. As a result, the data depicted in Figure 5 demonstrate that there was no significant difference in the amount of bleeding between group S and group NS, which suggests that typical surgical techniques and standard sutures can be used for satisfactory local hemostatic control.

Lemkin et al[19] have reported that significant hemorrhage after multiple tooth extractions following ASA ingestion can occur in patients with no preexisting blood disorders and that a platelet transfusion is required for bleeding control. McGaul[20] stated that postoperative hemorrhage can also occur when ASA is administered as a perioperative analgesia for periodontal surgery. Moreover, Scher[21] reported cases of diffuse postoperative bleeding that were associated using ASA therapy in perioperative procedures; however, the patients that were involved in this study were already receiving high doses of ASA therapeutics. Foulke et al[22] reinforced this concept, but they also described 1 hemorrhage episode that occurred after dental cleaning with an ultrasound device in a patient who ingested 2 tablets of ASA the night before the dental procedure. In our results, there were no observed long bleeding episodes in the intraoperative or postoperative conditions of patients who were being treated with 100 mg/d ASA therapy, which

contradicts the results of other studies. Despite this contradiction, there is agreement in the literature that a 100 mg/day dosage of ASA does not significantly increase intraoperative and postoperative bleeding during teeth extraction procedures[3,11,12]

The incidence and severity of oral bleeding can be reduced with local hemostatic methods when they are employed during and after surgery. These methods include the use of an absorbable sponge, an oral rinse (with tranexamic acid or aminocaproic acid), electrocautery, fibrin sealants, and sutures.[13,23,24] After the initial clot is formed, the bleeding probability is small, with minimal or no indication for the need to suspend the use of antiplatelet medication during dental procedures.[24] Ardekian et al[3] and Madan et al[16] confirmed that the bleeding process can be controlled with a good suture, local gauze compression, and antifibrinolytic agents, such as tranexamic acid.

The purpose of evaluating the platelet reactivity index in our study was to identify whether the suspension of ASA therapy increased the platelet reactivity index values, thus increasing the probability of a thromboembolic event. Our results indicate that there was a significant difference in the index values between the 2 investigated groups. The group that suspended ASA therapy exhibited a greater average PRI value than the group that did not suspend ASA therapy. Nevertheless, it is important to draw attention to the fact that both groups exhibited mean values that were in excess of the reference values considered by Manrique.[25] This finding is contradictory because it suggests that a 100 mg/d ASA dosage is not sufficient to prevent the risk of thromboembolic events in CAD patients. Notably, Manrique[25] reported on the presence of hyperaggregant platelets in people with CAD. In addition, he has stated that low dosages of ASA cannot protect against thromboembolic events, and therefore, therapy should be personalized for each patient. This approach seems to agree with some reports in the literature that have proposed this dosage because of its positive preventive effects. The purpose of this study was not to evaluate the risk of thromboembolism; only hemorrhagic risks were evaluated. The evaluation of thromboembolism risks is left to future investigations.

In conclusion, our results demonstrate that there is no need for ASA therapy suspension for single tooth extractions. In cases in which ASA therapy has been suspended, local hemostasis seems to control bleeding sufficiently. The PRI test demonstrated a reduction in platelet aggregation in the ASA therapy group (group NS), but this was without clinical consequence. Additional studies are required to evaluate more complex dental procedures to measure the amount of bleeding in CAD patients.

References

1. Thomason JM, Seymour RA, Murphy P, et al: Aspirin-induced post-gingivectomy haemorrhage: A timely reminder. J Clin Periodontol 24:136, 1997
2. Sonksen JR, Kong KL, Holder R: Magnitude and time course of impaired haemostasis after stopping chronic low and medium dose aspirin in healthy volunteers. Br J Anaesth 82:360, 1999
3. Ardekian L, Gaspar R, Peled M, et al: Does low-dose aspirin therapy complicate oral surgical procedures? J Am Dent Assoc 13:331, 2000
4. Aframian DJ, Lalla RV, Peterson DE: Management of dental patients taking common hemostasis altering medications. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 103(suppl 1): S45.e1S45.e1, 2007
5. Pototski M, Amenábar JM: Dental management of patients receiving anticoagulation or antiplatelet treatment. J Oral Sci 49:253, 2007
6. Daniel NG, Goulet J, Bergeron M, et al: Antiplatelet drugs: Is there a surgical risk? J Can Dent Assoc 68:683, 2002
7. Sonis ST, Fazio RC, Fang L, et al; Princípios e Prática de Medicina Oral (ed 2). Rio de Janeiro: Guanabara Koogan, 1996, chap VII., p 491
8. Kreisner PE: Procedimentos cirúrgicos em pacientes que fazem uso de ácido acetilsalisílico ou anticoagulantes orais. Rev Facodontoluniv Passo Fundo 8:22, 2003
9. Peterson LJ, Ellis E, Hupp JR, et al: Cirurgia Oral e Maxilofacial (ed 4). Rio de Janeiro: Elsevier, 2005, p. 795.
10. Medeiros PJ, Miranda MS, Ribeiro DPB, et al: Cirurgia dos Dentes Inclusos (ed 1). São Paulo: Santos, 2003, p. 147.
11. Brennan MT, Valerin MA, Noll JL, et al: Aspirin use and postoperative bleeding from dental extractions. J Dent Res 87:740, 2008
12. Valerin MA, Brennan, MT, Noll JL, et al: Relationship between aspirin use and postoperative bleeding from dental extractions in a healthy population. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 102:326, 2006
13. Morimoto Y, Minematsu K, Minematsu K: Hemostatic management of tooth extractions in patients on oral antithrombotic therapy. J Oral Maxillofac Surg 66:51, 2008
14. Ferraris VA, Swanson E: Aspirin usage and intraoperative blood loss in patients undergoing unexpected operations. Surg Gynecol Obstet 56:139, 1983
15. Gaspar, Ardekian L, Brenner B, et al: Ambulatory procedures in patients on low dose aspirin. Harefuah 136:108, 1999
16. Madan GA, Madan SG, Madan G, Madan AD: Minor oral surgery without stopping daily low-dose aspirin therapy: A study of 51 patients. J Oral Maxillofac Surg 63:1262, 2005
17. Krishnan B, Shenoy NA, Alexander M: Exodontia and antiplatelet therapy. J Oral Maxillofac Surg 66:2063, 2008
18. Franken RA, Franken M: Avaliação de risco cardiovascular para procedimentos odontológicos. Rev Soc Cardiol de Sao Paulo 10:406, 2000
19. Lemkin SR, Billesdon JE, Davee JS, et al: Aspirin-induced oral bleeding: Correction with platelet transfusion. J Oral Surg 37: 498, 1974
20. McGaul T: Postoperative bleeding caused by aspirin. J Dent 6:207, 1978
21. Scher KS: Unplanned reoperation for bleeding. Am Surg 62:52, 1996
22. Foulke CN: Gingival haemorrhage related to aspirin ingestion. J Periodontol 47:355, 1976
23. Rogerson KC: Hemostasis for dental surgery. Dent Clin North Am 39:649, 1995
24. Lockhart PB, Gibson J, Pond SH, Leitch J: Dental management considerations for the patients with an acquired coagulopathy. Part 2: Coagulopathies from systemic disease. Br Dent J 195: 495, 2003
25. Manrique R: Antiagregantes plaquetários, *in* Souza JEMR, Gizzi JC, Jatene AD (eds): IV Simpósio Internacional sobre Aterosclerose Coronária (ed 4). São Paulo, Instituto Dante Pazzanese, 1979, pp 168-173