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Should warfarin be discontinued before a dental extraction? A decision-tree analysis

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Objective. The aim of this study was to determine if warfarin should be withdrawn before a single tooth extraction on a patient with a prosthetic heart valve.
Study design. A quantitative decision tree was constructed to assess the expected utility values of 2 typical strategies to manage the dental extraction on a patient currently medicated with warfarin. Probabilities and utilities for a cardiovascular accident and major bleeding from a dental extraction were taken from the literature.
Results. The decision slightly favors withholding warfarin: generating an optimal expected utility value of 0.976 utile. This was only 0.02 utile higher than the alternative option of continuing warfarin for a dental extraction.
Conclusion. The decision to withhold or continue warfarin before a dental extraction depends more on the relative risk of a major bleeding between the 2 medical management strategies than on the consequences of a cardiovascular accident. **(Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2010;110:691-697)**

Warfarin in one of the top 100 drugs prescribed in North America, with >21 million prescriptions filled in 2008.[1] This oral anticoagulant is commonly prescribed for long-term continuous use to reduce the risk of thromboembolism, particularly in patients with prosthetic heart valves. Two percent of people above the age of 65 years have an aortic stenosis which is usually managed with a prosthetic valve.[2] These patients often require a dental extraction.[3-5]

Historically, the medical management of patients on oral anticoagulants slated for dental extractions has been inconsistent.[6,7] Conventional wisdom in the past suggested that the dentist instruct the patient to stopping taking their oral anticoagulant medication 2 days before surgery and then continue with their regular oral anticoagulant regiment immediately after the dental extraction.[8]

However, in recent years this conventional wisdom has been challenged. Aframian et al. concluded that withholding warfarin before dental extractions could not be justified based on the devastating consequences of a thromboembolic event.[9] Guidelines published in the *British Dental Journal* recommend that oral anticoagulants should not be discontinued in the majority of patients requiring dental extraction.[10] These recommendations were made despite the fact that there has been no reported case of a dental extraction causing a cardiovascular accident (CVA) in a patient whose warfarin was temporarily discontinued. Although these authors' conclusion may intuitively make sense based on the precautionary principle, their recommendations neither consider the quantitative risks nor the patient's subjective preferences of the consequences for each treatment option.

Clinical decision-tree analysis (DTA) is a quantitative approach that considers both research evidence and patient preferences with the objective of optimizing clinical decision making in a world of variability and uncertainty. Decision-tree analysis has been successful used in medical practice for over two decades.[11] Only recently has its application to dentistry been demonstrated.[12-14] The concept and application of DTA to health care decision making is described elsewhere.[15,16]

Essentially, DTA considers both the probability of an outcome and its perceived utility into a unified term, referred to as the expected utility value (EUV) with a unit of utile. The utile is a value between a perfect

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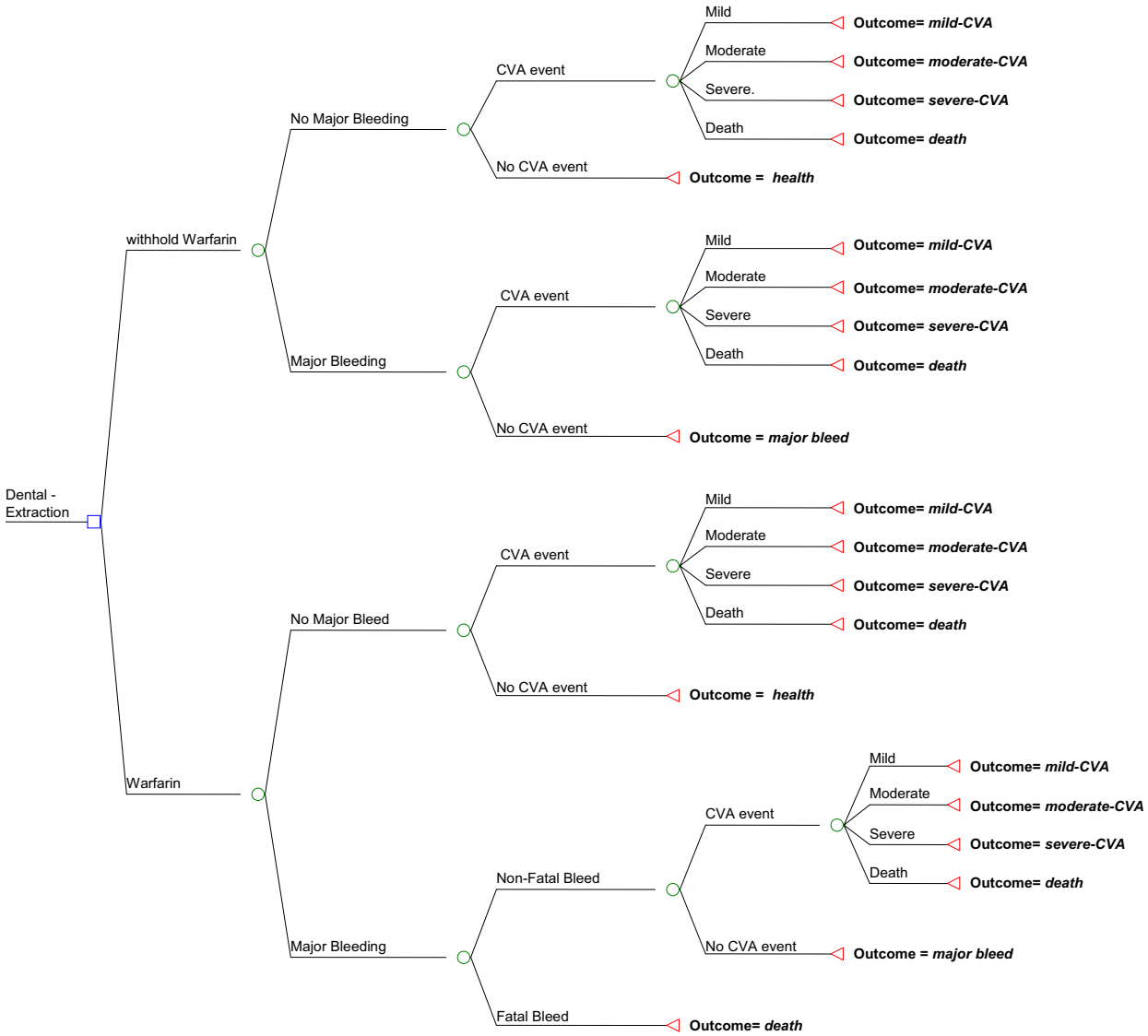

Fig. 1. Decision tree for the medical management of the oral warfarinised patient scheduled for a dental extraction. (The square box indicates decision node, chance nodes are depicted by circles and the final outcome nodes are shown as triangles. CVA refers to Cardio-Vascular-Accident. Refer to textbooks on healthcare decision making for a further explanation on the construction of decision trees. [15,16]).

health state of 1 utile and the worst health state of 0 utile. One can think of the utile as the proportional value judgment a patient or decision maker places on a nonideal health state relative to the ideal health state (having a value of 1 utile) and death (having a value of 0 utile). For example, a utility of .75 utile implies a health state perceived to be about 75% of ideal.[13]

Dunn et al. published a DTA on the medical management of patients on oral anticoagulants slated for dental extraction.[17] However, their analysis considers the decision of the preoperative withdrawal of oral anticoagulants and replacing with heparin versus the decision of not withdrawing the oral anticoagulant before a dental extraction. In the typical outpatient private dental practice, bridging therapy with heparin is not a practical option.

Therefore, the objective of the present paper is to apply quantitative DTA to a common clinical question confronting dentists in practice: Should oral anticoagulants be withdrawn or not before a dental extraction in patients with a history of a prosthetic heart valve and an international normalized ratio (INR) of <4?

METHODOLOGY

Decision tree construction

The decision tree model (Fig. 1) depicts the possible

outcomes of 2 preextraction approaches of managing a dental patient's warfarin medication. The hypothetical clinical scenarios of the extraction of a single tooth on a 60-year-old patient with a medical history of a prosthetic heart valve and a pretreatment INR of <4 were analyzed using this model.

When such a patient is scheduled for dental extractions, the dentist must decide between instructing the patient to continue with their regular warfarin medication or instructing them to withhold their warfarin regimen for 2 days before dental surgery. Then the patient is told to start their medication immediately after the dental extraction. The option to withhold warfarin assumes that the patient is still anticoagulated (i.e., therapeutic) for the 2 days up to the moment of extraction. This implies that the risk of a thrombosis before surgery is the same between the alternative strategies.[17] Both management strategies present the possibility of a CVA and its associated levels of complications occurring after oral surgery with or without the occurrence of major bleeding. However, it is assumed that a possible fatal outcome from major bleeding can only occur to patients still on warfarin during the surgical procedure. The description of stroke severity is described by Dunn et al.[17]

Determination of outcome probabilities and utilities

The range and case-base probabilities' and utilities' for each outcome are presented in Table I.

The probability of a CVA is based on results of a literature review conducted by Dunn et al.[17] It is assumed that the warfarin-withheld patient is subtherapeutic just before the extraction and that it takes about 3 days after restarting warfarin for the patient to return to therapeutic levels. The probability of developing a stroke for the warfarin-withheld patient for 3 days after extraction was determined by dividing the annual stroke rate for a nonanticoagulated patient by 365 days and then multiplying the result by 3 days. This probability was reduced by the reported relative risk reduction to determine the 3-day probability of a stroke for the warfarin-continued patient.[17]

The probability of major bleeding on a warfarin-continued and a warfarin-withheld patient was determined by a literature search. Pubmed was searched for articles on December 2, 2009. The following MeSH and text terms were used: warfarin, anticoagulants, tooth extraction, oral anticoagulant, and coumadin. The search was limited to English-language clinical trials, randomized controlled trials, reviews, and meta-analyses. Only studies that investigated dental extractions in patients whose warfarin was continued or withheld were included. Excluded were studies that used adjunctive measures to control hemostatis (i.e., tranexmatic acid, resorbable collagen sponges). Relative risk (RR)—and associated 95% confidence intervals—of major bleeding between the warfarin-continued and the warfarin-withheld patient was calculated from the data extracted from only 2 studies which met the inclusion/exclusion criteria (Table II).[18,19] The probability of major bleeding reported by Evans et al.[18] was used in this analysis, because it was a larger study (Table I).

In the mathematical model of this tree, the probability of major bleeding on warfarin was a function of the RR and probability of major bleeding when warfarin was withheld;

$$p[\textit{major bleed with warfarin}] = p[\textit{major bleed with warfarin withheld}] \times \mathrm{RR}$$

There is no reported cased of fatal bleeding after dental extraction in a patient with warfarin. However, fatal bleeding of 1% has been reported in patients with anticoagulatants who underwent other types of surgery.[20] For the sake of creating balance in this decision

Table I. Model estimates of probabilities and utilities

Event	*Probabilities (%)*	*Range (%)*	*Reference(s)*
Major bleeding after extraction			
Warfarin	25	25-37	[18,19]
Warfarin withheld	14	14-25	
Relative risk (RR)*	1.79*		
Death from major bleeding	1	0-2	[17]
CVA with prosthetic mitral valve			
Warfarin			[17]
Annual	7.2	4-12	
3 days	0.059		
Warfarin withheld			
Annual	1.1	0.9-1.5	
3 days	0.009		
Risk of stroke			
Mild	21.1	10-30	[17]
Moderate	9.0	5-20	
Severe	39.6	25-40	
Death	30.3	20-35	
	Utility (utile)		
Health (recovery with no complications)	1		
Major bleeding	0.841		[21]
CVA			
Mild	0.76		[17]
Moderate	0.39		
Severe	0.189		
Death	0		

*Not a probability but a ratio calculated from the above data of a major bleeding with warfarin and wafarin-withold.

TABLE II. Summary of reported risk of major bleeding after dental extractions

Reference	Major bleeding after extraction	Relative risk [95% CI (calculated)]
Al-Mubarak et al. (2007)[19]	+W = 37% (n = 51) −W = 25% (n = 48)	1.48 [0.807-2.71]
Evans et al. (2002)[18]	+W = 25% (n = 57) −W = 14% (n = 52)	1.79 [0.82-4.17]

CI, Confidence interval; *+W,* warfarin; *−W,* warfarin withheld.

tree, the risk of a fatal bleed was included in this analysis.[22]

Sensitivity analyses

A sensitivity analysis is necessary to see how robust the tree's conclusions are under different levels of uncertainty. One-way sensitivity analyses were conducted on varying the RR of major bleeding and on varying the patient's perceived utility of major bleeding after a dental extraction.

DTA software

This decision model was analyzed with TreeAge Pro 2009 (TreeAge Software, Williamstown, MA).

RESULTS

Figure 2 presents the detailed DTA with each strategy's optimal EUV.

The DTA favors the strategy of withholding warfarin; generating an optimal EUV of .976 utile. This is only .02 utile higher than the alternative option of continuing warfarin.

A sensitivity analysis (Fig. 3) demonstrates that the decision threshold occurs with an RR of 1. In other words, the EUVs of the 2 strategies are essentially the same when there is no difference in the risk of major bleeding after a dental extraction on the warfarin-continued and warfarin-withheld patient with a prosthetic valve. An RR >1 favors withholding warfarin.

Figure 4 shows no effect on the decision when varying the patient's utility of major bleeding after a dental extraction.

DISCUSSION

All clinical decisions are made in a world of uncertainty. The rational decision maker will choose the course of action that maximizes their net desired expectation (i.e., expected utility value). This expectation is a balance between the chances of success of each strategy and the patient's perceived value judgment (i.e., utility) of its outcome.

The analysis here found that in a world of uncertainty, the decision slightly favors withholding warfarin from a 60-year-old prosthetic valve patient scheduled for a dental extraction. This is because the risk of a CVA is so small compared with the risk of major bleeding after a dental extraction when the patient is on warfarin. However, if the risk of major bleeding after a dental extraction is equal between the warfarin-continued and warfarin-withheld patients, then either strategy is equally favorable.

Although Evans et al.[18] and Al-Mubarak et al.[19] reported a higher risk of major bleeding in the warfarinized patient, the difference was not statistically significant. This may be because both studies' sample sizes did not have the statistical power to show a difference (i.e., type II error).

The utility of major bleeding was taken from a source including major bleeding from surgery but not necessary dental extraction.[21] As such, the author may have overestimated or underestimated this value. However, a sensitivity analysis on this issue showed that this had no effect on the final decision.

Despite the fact that there are no reported cases of a fatal bleeding on a warfarin-continued patient after a dental extraction, the present DTA considered its possibility. However, even when the probability of such an event is taken as 0, the EUV of continuing with warfarin is 0.958 utile, which is still below the EUV of withholding warfarin.

The definition of what constitutes major postextraction bleeding is inconsistent in the literature. Nemutalla et al. made reference to this heterogeneity in their systematic review that queried the medical management of warfarin-continued patients scheduled for minor dental surgery.[23] However, they suggested that warfarin not be discontinued before minor oral surgery, because their meta-analysis of the literature found no statistical difference in the risk of a major postextraction bleeding event between the 2 medical management options. This is consistent with the conclusion of the present study's sensitivity analysis. Nevertheless, a potential flaw with this analysis is with the data used in the model and not the model itself. However, this DTA can be updated in the future as more accurate and up-to-date data for each of the variables in the model become available.

Although the conclusion generated by this analysis is generally in disagreement with the current clinical guidelines by the *British Dental Journal*[10] and Aframian et al.,[9] the spirit of this analysis should be appreciated more than the results it generated. For example, Aframian et al. concluded that "for most patients undergoing simple single dental extractions, the morbidity of potential thromboembolic events if anticoagulants therapy is discounted clearly outweighs

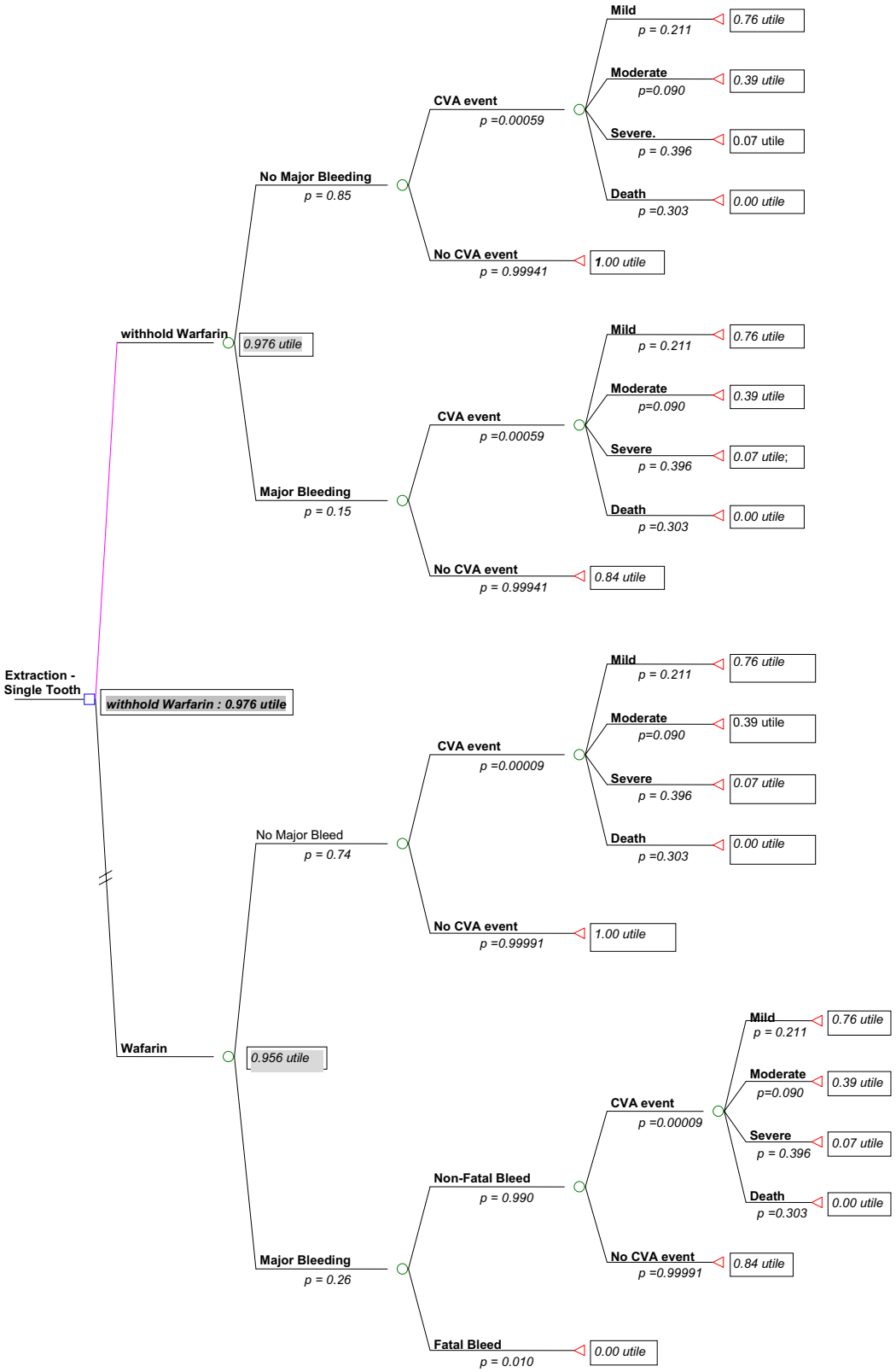

Fig. 2. Decision-tree analysis for the medical management of the oral warfarinised prosthetic-valve patient scheduled for a single-tooth extraction. (Shaded boxes are the EUV of that specific decision node).

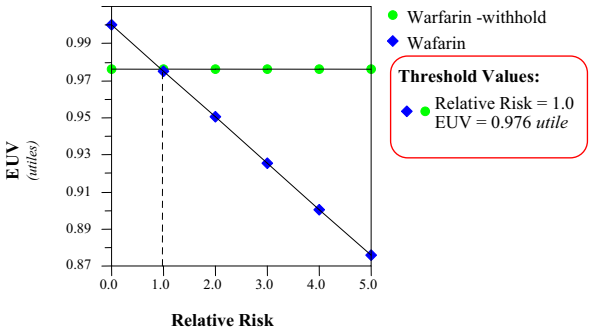

Fig. 3. One-way sensitivity analysis on the effect of each strategy's expected utility value on varying the relative risk of a post-extraction major bleed.

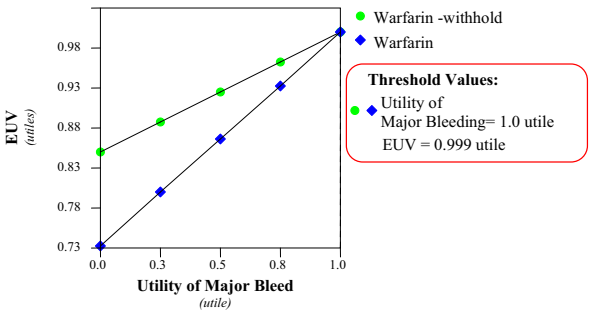

Fig. 4. One-way sensitivity analysis on the effect of each strategy's expected utility value on varying the patient's perceived utility of a major bleed after a dental extraction.

the risk of prolonged bleeding if anticoagulant therapy is continued."[9] The present DTA demonstrates that the risk to consider in the decision to withhold or continue warfarin depends on the probability of major bleeding with either strategy. This is because the risk of a CVA is negligible compared with the risk of a major bleed, regardless of the lower CVA utility.

Therefore, if the decision to continue with warfarin is selected, then the clinician should dentally manage the extraction site with adjunctive hemostatis procedures that would reduce the risk of a major bleeding. Adjunctive procedures such as absorbable sponges, cyanoacrylic glue, tranexmatic acid, and avoiding suturing when possible, have been shown to effectively manage postextraction hemostasis on warfarin-continued patients.[24,25]

If the clinically perceived RR of major bleeding between the 2 strategies is determined to be ~1, then the medical management decision to not interrupt warfarin makes clinical sense because it would be less demanding on the patient. Under these circumstances, Aframian et al.'s[9] conclusion and the *British Dental Journal*'s[10] recommendation are defendable.

CONCLUSION

The decision to withhold or continue warfarin before a dental extraction depends more on the RR of major bleeding between the two medical management strategies than on the consequences of a CVA. For the minimally invasive single tooth extraction, not disrupting the patient's warfarin protocol and using local adjunctive means of hemostasis is defensible. However, in cases that are significantly invasive and/or involve multiple dental extractions, withholding warfarin may be indicated, because of the risk and thus the negative consequences of major bleeding as perceived by the patient.

REFERENCES

1. SDI/Verispan V 2008 top 200 branded drugs by presciptions. Available at: http://drugtopics.modernmedicine.com/drugtopics/data/articlestandard/drugtopics/222009/599845/article.pdf. Accessed December 12, 2009.
2. Chandrashekhar Y, Westaby S, Narula J. Mitral stenosis. Lancet 2009;374:1271-83.
3. Ahluwalia KP, Cheng B, Josephs PK, Lalla E, Lamster IB. Oral disease experience of older adults seeking oral health services. Gerodontology 2009 [Epub ahead of print].
4. Dolan TA, Atchison K, Huynh TN. Access to dental care among older adults in the United States. J Dent Educ 2005;69:961-74.
5. Peltola P, Vehkalahti MM, Wuolijoki-Saaristo K. Oral health and treatment needs of the long-term hospitalized elderly. Gerodontology 2004;21:93-9.
6. Linnebur SA, Ellis SL, Astroth JD. Educational practices regarding anticoagulation and dental procedures in U.S. dental schools. J Dent Educ 2007;71:296-303.
7. Lim W, Wang M, Crowther M, Douketis J. The management of anticoagulated patients requiring dental extraction: a cross-sectional survey of oral and maxillofacial surgeons and hematologists. J Thromb Haemost 2007;5:2157-9.
8. Devani P, Lavery KM, Howell CJ. Dental extractions in patients on warfarin: is alteration of anticoagulant regime necessary? Br J Oral Maxillofac Surg 1998;36:107-11.
9. Aframian DJ, Lalla RV, Peterson DE. Management of dental patients taking common hemostasis-altering medications. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;103(Suppl): S45-11.
10. Perry DJ, Noakes TJ, Helliwell PS. Guidelines for the management of patients on oral anticoagulants requiring dental surgery. Br Dent J 2007;203:389-93.
11. Pauker SG, Kassirer JP. Decision analysis. N Engl J Med 1987;316:250-8.
12. Balevi B, Shepperd S. The management of an endodontically abscessed tooth: patient health state utility, decision-tree and economic analysis. BMC Oral Health 2007;7:17.
13. Balevi B. The management of incipient or suspicious occlusal caries: a decision-tree analysis. Community Dent Oral Epidemiol 2008;36:392-400.
14. Elad S, Thierer T, Bitan M, Shapira MY, Meyerowitz C. A decision analysis: the dental management of patients prior to hematology cytotoxic therapy or hematopoietic stem cell transplantation. Oral Oncol 2008;44:37-42.
15. Sox HC Jr, Blatt MA, Higgins MC, Marton KI. Medical decision making. Boston: Butterworth-Heinemann; 1988.
16. Hunink M, Glasziou P, Siegal J, Weeks J, Pliskin J, Elstein A,

et al. Decision making in health and medicine. Cambridge, U.K.: Cambridge University Press; 2001.
17. Dunn AS, Wisnivesky J, Ho W, Moore C, McGinn T, Sacks HS. Perioperative management of patients on oral anticoagulants: a decision analysis. Med Decis Making 2005;25:387-97.
18. Evans IL, Sayers MS, Gibbons AJ, Price G, Snooks H, Sugar AW. Can warfarin be continued during dental extraction? Results of a randomized controlled trial. Br J Oral Maxillofac Surg 2002;40:248-52.
19. Al-Mubarak S, Al-Ali N, Abou-Rass M, Al-Sohail A, Robert A, Al-Zoman K, et al. Evaluation of dental extractions, suturing and INR on postoperative bleeding of patients maintained on oral anticoagulant therapy. Br Dent J 2007;203:E151.
20. Dunn AS, Turpie AG. Perioperative management of patients receiving oral anticoagulants: a systematic review. Arch Intern Med 2003;163:901-8.
21. Robinson A, Thomson R, Parkin D, Sudlow M, Eccles M. How patients with atrial fibrillation value different health outcomes: a standard gamble study. J Health Serv Res Policy 2001;6:92-8.
22. Detsky AS, Naglie G, Krahn MD, Redelmeier DA, Naimark D. Primer on medical decision analysis: part 2—building a tree. Med Decis Making 1997;17:126-35.
23. Nematullah A, Alabousi A, Blanas N, Douketis JD, Sutherland SE. Dental surgery for patients on anticoagulant therapy with warfarin: a systematic review and meta-analysis. J Can Dent Assoc 2009;75:41.
24. Salam S, Yusuf H, Milosevic A. Bleeding after dental extractions in patients taking warfarin. Br J Oral Maxillofac Surg 2007;45:463-6.
25. Al-Belasy FA, Amer MZ. Hemostatic effect of n-butyl-2-cyano-acrylate (histoacryl) glue in warfarin-treated patients undergoing oral surgery. J Oral Maxillofac Surg 2003;61:1405-9.

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