thromboembolism (12%), heart valvulopathy (10%), and other indications (3%). All the procedures were carried out by the same oral surgeon. Before undertaking 511 dental extractions (in average four teeth per patient), six fixture insertions and six exeresis of cystic neoformations, patients were randomized to two treatment groups. In group A (mean age 64 ± 11 years), OAT dosage was reduced during the 72 h before surgery to attain INR values between 1.5 and 2.0 (target 1.8) on the day of surgery. The mean INR value actually attained in this group was 1.77 ± 0.26. In group B (mean age 61 ± 12 years), OAT dosage was not reduced, but hemostatic agents such as tranexamic acid, oxidized cellulose or collagen sponges were applied on the surgically treated region. The mean INR measured in this group was 2.89 ± 0.42 on the day of surgery.

After 2 h of postsurgical observation, all patients were discharged and received written instructions to avoid non-steroidal anti-inflammatory drugs (only paracetamol was allowed), to record the length and severity of any bleeding and to contact the center immediately in case of bleeding not controlled by compression for 20 min. Patients in group A were required to restore oral anticoagulant treatment to return to their regular INR on the day after the procedure, while those of group B were asked to continue their regular dosage. All patients were summoned 7 days after the procedure for the removal of the sutures. During this examination, the presence or absence of late bleeding was also recorded. Only patients in group B (OAT not reduced) were instructed to perform mouthwashing with tranexamic acid at home (10 mL for 2 min, four times daily, for 6 days after procedure), and a daily telephonic contact by a nurse was arranged for 6 days after the procedure. Bleeding was considered as an 'event' if any intervention by the surgeon was needed to stop it either with a new suture or with placement of other local hemostatic agents. Bleeding successfully managed at home by patients were not considered an event.

Bleeding excessive enough to warrant adoption of supplementary local hemostatic measures was observed, in 10 cases (15.1%) in group A (reduced dosage) and in six (9.2%) in group B (unmodified dosage). Bleeding, irrespective of the group, was treated with the insertion of oxidized cellulose inside the procedural area. There was no thrombotic complication in these patients. This randomized study shows that, using simple and inexpensive measures for local hemostasis, it is not necessary to reduce OAT intensity in patients undergoing oral surgery. The adoption of this procedure may prevent thromboembolic complications associated with subtherapeutic INR values.

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Thromboembolic risk and bleeding in patients maintaining or stopping oral anticoagulant therapy during dental extraction

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Most patients on oral anticoagulant therapy (OAT) belong to an old age characterized by high incidence of dental diseases that necessitate surgical interventions [1]. Therefore, the evaluation of the risks of bleeding (with OAT) or thromboembolism (stopping OAT) is important. Owing to serious complications associated with the modification [2] or cessation of OAT before during or after oral surgery [3,4], the dilemma continues to exist and no universal consensus has

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Table 1 International Normalized Ratio (INR), healing and bleeding percentage within the different groups at different time points

Study group	Age (mean ± SD)	Parameters	Before dental extraction	Day 1	Day 3	Day 7
1 (−W−S)	53.6 ± 15.3	INR ratio	1.7 ± 0.6	1.5 ± 0.5	2.0 ± 0.8	2.2 ± 0.7
		Healing (% of patients)	–	27	50	71
		Bleeding (% of patients)	–	12	4	0
2 (+W−S)	51.2 ± 14.0	INR ratio	2.3 ± 0.7	2.4 ± 0.7	2.5 ± 0.7	2.4 ± 0.6
		Healing (% of patients)	–	26	50	72
		Bleeding (% of patients)	–	23	3	0
3 (+W−S)	49.3 ± 12.3	INR ratio	1.7 ± 0.5	1.7 ± 0.5	1.9 ± 0.7	2.2 ± 0.7
		Healing (% of patients)	–	45	65	76
		Bleeding (% of patients)	–	18	3	4
4 (+W−S)	54.5 ± 14.6	INR ratio	2.6 ± 0.7	2.6 ± 0.8	2.5 ± 0.6	2.6 ± 0.8
		Healing (% of patients)	–	36	59	69
		Bleeding (% of patients)	–	31	6	0

been reached thus far. The objective of this study was to evaluate the consequences of the temporary withdrawal of OAT on bleeding following the dental extractions. One hundred and sixty-eight patients on warfarin therapy with a maintenance dose (2–10 mg daily) for more than 1 year and scheduled for dental extractions were evaluated, after excluding those with a history of chronic liver disease or those on drugs that could affect liver function or hemostasis. They were randomized into four groups: no socket suturing with discontinued warfarin (−W−S, group 1) or continued warfarin (+W−S, group 2), suturing with discontinued (−W+S, group 3) or continued warfarin (+W+S, group 4). Patients of groups 1 and 3 were instructed to discontinue warfarin 2 days prior to oral surgery and to resume treatment 12 h after dental extractions. Blood was obtained preoperatively and on postoperative days 1, 3, and 7 to measure the International Normalized Ratio (INR). The status of scarring and healing was objectively monitored by independent-blinded examiners during the 7 day follow-up.

The sockets had good healing and scar formation at the follow-up visits, irrespective of study groups (Table 1), confirming that the level of anticoagulation has no significant impact on wound healing after dental extractions [4]. Suturing played no role on bleeding because, contrary to expectation, patients from groups 3 and 4 had a slightly higher rate of bleeding than those from groups 1 and 2 who had no suturing (Table 1). Therefore, socket suturing may be avoided for simple extractions.

Table 1 also shows that the preoperative and day 1 postoperative INR of patients from groups 2 and 4 who continued warfarin were significantly higher than those of groups 1 and 3. However, resumption of warfarin gradually increased the INR in groups 1 and 3, so that there was no significant difference among the four study groups on day 7. The percentage of patients who bled on postoperative day 1 was significantly less ($\chi^2 = 21.35$, $P < 0.001$) in patients with INR between 1.0 and 2.0 (12.9 %) or 2.0 and 3.0 (18.9 %) than in those with INR greater than 3.0 (52.38 %). This is in contrast to earlier findings [5]. In no instance, bleeding of clinical significance and intervention was not needed. These findings support earlier studies, suggesting that anticoagulation poses no risk of serious bleeding and that dental extractions can be carried out safely without stopping warfarin, provided the INR is kept within a lower range [6].

In agreement with other studies [7], there was no thromboembolic event, even though the INR in 76 of 87 patients in groups 1 and 3 reached values lower than 1.5. The difficulty in predicting the degree of INR drop and the associated risk of thromboembolism in warfarin-withdrawal patients outweigh the risk of postoperative bleeding in patients on OAT [7]. It has been documented that in patients whose OAT has been interrupted, thromboembolism including death is three times more likely to occur than bleeding complications associated with anticoagulation [8].

In conclusion, dental extractions can be safely performed in patients on warfarin therapy without altering the dose of anticoagulant, provided the INR is ≤3.0 and effective local hemostasis has been ensured. Moreover, suturing and invasive manipulation of soft tissue are not always necessary and should be decided on a case-to-case basis depending on the extent of surgical trauma.

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The effect of vitamin K supplementation on anticoagulant treatment

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Until recently, the view that dietary vitamin K interferes with oral anticoagulant therapy was based on case reports and a few small experimental studies with extremely high vitamin K intake. In two recent studies the effect of dietary vitamin K on oral anticoagulation was systematically investigated [1,2]. These studies showed that, even in patients on an average diet, changes in vitamin K intake affect anticoagulation. When patients decreased their vitamin K intake the International Normalized Ratio (INR) response was more pronounced than when vitamin K intake was increased [2]. Because changes are proportionally larger in people with a low average vitamin K intake, it is likely that the INR is more sensitive to a varying vitamin K intake in those individuals. Sconce *et al.* established that daily intake of vitamin K was indeed lower in patients with unstable anticoagulation than in stably anticoagulated patients [3]. Daily supplementation of low doses of vitamin K might thus be beneficial.

To safely start vitamin K supplementation in patients receiving oral anticoagulants, it is important to know the effect of low doses of vitamin K on the INR and on the dose of the anticoagulant drug. The dose–response relationship of vitamin K supplementation on the INR in healthy subjects who received a fixed dose of oral anticoagulants was established by Schurgers *et al.* [4]. They concluded that 100 μg of vitamin K daily did not significantly interfere with oral anticoagulant therapy. Consequently, Oldenburg suggested 100 μg vitamin K as a recommended supplementation dose in his editorial [5]. However, Kurnik *et al.* found that, in patients with a low vitamin K status, even daily supplement doses as low as 25 μg led to an important reduction of the INR [6].

We performed a pilot study to determine the effect of escalating daily doses of vitamin K on the required dose of the anticoagulant drug phenprocoumon. We included patients from the Leiden Anticoagulation Clinic who took part in a program for self-management of anticoagulant treatment. The total study period was 9 weeks, in which the INR was measured at least 3 times a week with a CoaguCheck S coagulometer (Roche Diagnostics, Almere, Netherlands). Patients received vitamin K for 3 weeks. The first and last 3 weeks served as control periods. Five patients received 50 μg and 10 patients 100 μg of oil-based vitamin K1 (250 μg g^{-1}). The primary endpoint was the percentage change in phenprocoumon dose during and after vitamin K needed to keep the INR within therapeutic limits.

Supplementation of 50 μg vitamin K had little effect on the INR and therefore only slight dose-adjustments were made (mean dose increase after starting vitamin K 3% [95% confidence interval (CI95): −4% to 10%]. Supplementation of 100 μg resulted in a mean dose increase of 9% (CI95: 0–19%, Fig. 1). There was considerable inter-individual variability in response with dose adjustments ranging from −7% to 37%. In the three weeks of follow-up after the vitamin K was discontinued phenprocoumon doses were lowered to pre-substitution values (mean change of −7%, CI95: −15% to 0%).

Our results show that daily supplementation up to 100 μg can be given without a relevant decrease in the INR, on the condition of frequent monitoring during and after the supplementation to allow timely dose adjustments.

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