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Comparing Self-Management of Oral Anticoagulant Therapy with Clinic Management

A Randomized Trial

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Background: **Control of oral anticoagulant treatment has been reported to be suboptimal, but previous studies suggest that patient self-management improves control.**

Objective: **To compare the quality of control and the clinical outcomes of oral anticoagulant treatment in self-managed patients versus patients following conventional management.**

Design: **Randomized, controlled trial.**

Setting: **University-affiliated hospital in Spain.**

Patients: **737 patients with indications for anticoagulant treatment.**

Intervention: **The self-management group (*n* = 368) received simple instructions for using a portable coagulometer weekly and self-adjusting treatment dose. The conventional management group (*n* = 369) received usual care in an anticoagulation clinic (monthly measurement and control of international normalized ratio [INR], managed by hematologists).**

Measurements: **Percentage of INR values within the target range and major related complications.**

Results: **The median follow-up period was 11.8 months (range, 0.3 to 16.9 months). The unadjusted percentages of in-range INRs were 58.6% in the self-management group and 55.6% in the conventional management group (difference, 3.0 percentage points [95% CI, 0.4 to 5.4 percentage points]). Twenty-seven patients (7.3%) in the conventional management group and 8 (2.2%) in the self-management group had major complications related to anticoagulant treatment. The unadjusted risk difference for major complications between groups was 5.1 percentage points (exact 95% CI, 1.7 to 8.5 percentage points). Fewer patients had minor hemorrhages in the self-management group (14.9%) than in the conventional management group (36.4%). Fifteen patients (4.1%) in the conventional management group and 6 (1.6%) in the self-management group died (unadjusted risk difference, 2.5 percentage points [exact 95% CI, 0.0 to 5.1 percentage points]).**

Limitations: **The trial was performed at only 1 center and was not blinded. The dropout rate in the intervention group was 21%.**

Conclusions: **Compared with conventional management by an anticoagulation clinic, self-management of oral anticoagulant treatment achieved a similar level of control. Of note, major complications and minor hemorrhages were less common in the self-management group.**

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Trial EC/00/111/1439 HSCSP.

Indications for oral anticoagulant treatment to prevent thromboembolic disease have increased in recent years (1). Prothrombin times must be monitored frequently in patients taking oral anticoagulants to determine the safest dose and to minimize the risk for complications. The clinical management of oral anticoagulant treatment improved greatly after the international normalized ratio (INR) was introduced as a measurement of anticoagulation intensity (1). The establishment of accurate therapeutic INR ranges was also beneficial. Target ranges include the safest INR values that carry the lowest risk for hemorrhagic or thromboembolic complications (2). Despite these improvements, however, serious complications are still associated with oral anticoagulant treatment (3, 4), and management by specialized staff at anticoagulation clinics seems to be safer than other clinical strategies in terms of numbers of complications (5–7).

Currently, portable coagulometers are available for determining INR easily and reliably (8). This technology provides interesting clinical models for the control of oral anticoagulant treatment, the most promising of which are patient self-testing and patient self-management. For patient self-testing, patients measure INRs themselves and ask their referring physicians for the proper anticoagulant dose. Patient self-management assumes that patients will adjust their own doses and is the most autonomous strategy. Several published studies have compared these strategies with usual care (that is, monitoring of oral anticoagulant treatment by practitioners) (9–13) or with specialized anticoagulation clinics (14–18). Although these studies showed that both patient self-testing and patient self-management are feasible, their samples were relatively small (9, 11, 13, 14–18) or included selected patients with mechan-

See also:

Print
Editors' Notes 2
Editorial comment 73
Summary for Patients I-14

Web-Only
Appendices
Appendix Tables
Conversion of figures and tables into slides

Context

Although many outpatients require oral anticoagulation, the optimal management of outpatient anticoagulation remains uncertain. Studies have demonstrated the feasibility of patient self-management using portable coagulometers, but the studies that compared patient outcomes with self-management and those with conventional management in an anticoagulation clinic did not find a better outcome with self-management.

Contribution

In this randomized, controlled trial of 737 patients, patients assigned to self-management of anticoagulation achieved a similar level of control and had fewer adverse events than patients assigned to conventional management.

Implications

Health care providers should begin to implement patient self-management of oral anticoagulation with portable coagulometers in mainstream practice.

–The Editors

ical valve prostheses (10) or patients older than 65 years of age (12). In general, previous studies indicate that patient self-management may be superior to management by general practitioners or anticoagulation clinics in quality of INR control (10–18). In addition, Körtke and Körfer (10), Beyth and associates (12), and Sawicki (13) reported a decrease in major complications among self-managed patients compared with patients managed by general practitioners. To date, no published data have suggested a better clinical outcome (decrease in associated complications) with patient self-management than with specialized management at an anticoagulation clinic (5, 19). We performed a randomized, controlled trial to directly compare self-management of oral anticoagulant treatment, as evaluated in terms of efficacy and safety in unselected patients, with management in an anticoagulation clinic.

METHODS

Study Design

The Alternative Control of Oral Anticoagulant Treatment (ACOA) trial is a single-center, centrally randomized, controlled study that was performed at Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, from January 2001 to July 2002. The hematologists who manage our anticoagulation clinic use a homogeneous dosing protocol and standard protocols to manage situations that increase clinical risk. The clinical staff includes trained nurses. Computers control the clinical data and INR records, ensuring excellent follow-up. Patients and their relatives receive basic education at the beginning of oral anticoagulant treatment, including information on the main characteristics of oral anticoagulants, potential risks, rationale for periodic monitoring, and drug interactions. Samsa and Matchar (20) recommended that these characteristics be used to provide an appropriate control group in a trial on patient self-management. The institutional review board of our hospital approved the study.

Recruitment Phase

The recruitment phase began with computerized random selection of 1500 patients from the more than 5000 who were receiving oral anticoagulant treatment controlled in our hospital. We included any ambulatory patient 18 years of age or older who had been receiving long-term anticoagulant therapy for at least 3 months before entering the study. We excluded patients who were younger than 18 years of age, who had a severe physical or mental illness without a responsible caregiver, or who were of foreign origin and were unable to understand Spanish.

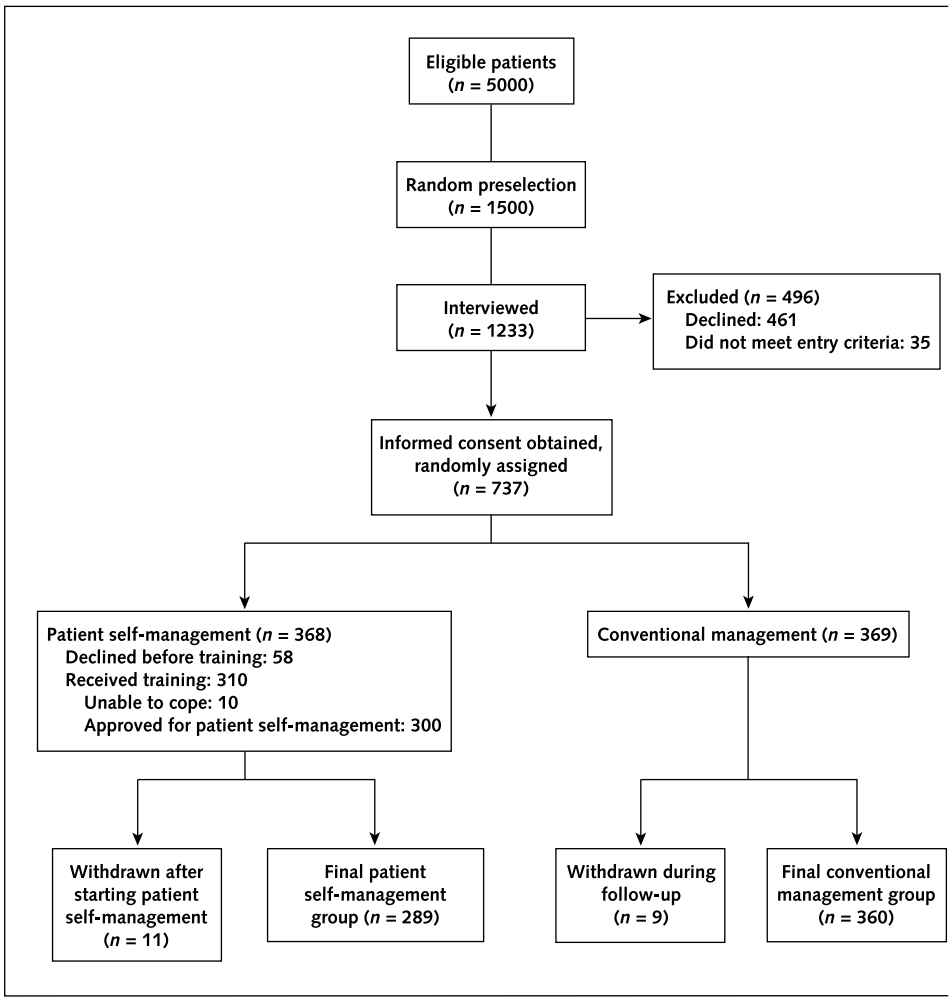
Once the patient (or his or her caregiver) agreed to participate, written informed consent was obtained. Next, centralized telephone randomization assigned the patient to the experimental group (patient self-management) or to the control group (conventional management). The allocation sequence was generated at the hospital's epidemiology department, and the sequence of randomization was concealed until the patient was assigned to a group. To facilitate comparability between study groups, this randomization was stratified according to sex, age ($\geq$70 years of age or $<$70 years of age), and indication for oral anticoagulant treatment (4 groups). Members of our anticoagulation clinic enrolled participants and assigned them to groups. Baseline data included demographic details, clinical information on associated risk factors, other medications, previous length of anticoagulant therapy, bleeding or thromboembolic complications during oral anticoagulant treatment, and target INR range.

Follow-up for patients assigned to the conventional management group was done immediately. Patients in the self-management group received a training course first, and follow-up was not performed until the nurse teaching the course judged that the patients had acquired a minimum of expertise in self-management.

Training Course

An educational program was designed to optimize the number of patients able to understand and safely perform self-management (Appendix, available at www.annals.org). It was similar to the German program developed by Sawicki (13) but was demographically adapted to the characteristics of the Spanish population, considering differences in daily schedules, diet, educational level, and other idiosyncratic factors. The program consisted of 2 sessions of 2 hours each on consecutive days. A specially trained nurse was responsible for teaching the patients in small, organized groups. The lessons included basic theoretical and practical concepts involving the use of a coagulometer, interpreta-

Figure. **Flow of patients in the Alternative Control of Oral Anticoagulant Treatment (ACOA) trial.**



tion of INR, and adjustment of dose. The concepts of target range and dose modification were emphasized when necessary. A simple card system was designed to help the patient select the correct dose. For each target range, a specific card was provided. Patients were taught to use the portable coagulometer CoaguChek S (Roche Diagnostics, Mannheim, Germany) with the appropriate reagent strips.

Follow-up Phase

Normally, the patients in the conventional management group visited our hospital every 4 weeks to check their INRs. When the INR result was out of target range, our dosing protocol indicated that we should advance the next appointment for INR testing to 1 or 2 weeks. International normalized ratio was determined by means of a standard KC 10 coagulometer (Amelung, Lemgo, Germany). As a thromboplastin, we used Thromborel S (Behring, Marburg, Germany). A hematologist experienced in oral anticoagulation management adjusted the dose and made the appointment for the next INR test. Patients in the self-management group performed the INR tests at home once per week using the CoaguChek S kit. They determined the appropriate dose of oral anticoagulant and the time of the next INR test. All of the INR results in both groups were entered into a computer (in the central system of our anticoagulation clinic or in the portable coagulometers) to facilitate data management.

Patients in both groups were interviewed monthly by telephone to record any complications or changes in their health status. For the conventional management group, these interviews were done approximately midway between hospital visits. The questions addressed minor or major bleeding, thromboembolic events, episodic diseases, changes in long-term medications, and hospital stays. Associated complications were diagnosed and evaluated by a third physician who was not involved in the trial and was unaware of patients' study group. Standard criteria were used to diagnose any thromboembolic complications. Transient ischemic attack was diagnosed clinically by a neurologist, and superficial thrombophlebitis was diagnosed clinically

by an angiologist. To diagnose stroke, arterial embolism, venous thromboembolism, pulmonary embolism, or valve thrombosis, we used widely accepted methods (computed tomography or magnetic nuclear resonance imaging, angiography, surgical diagnosis, Doppler ultrasonography, phlebography, lung angiography or ventilation–perfusion lung scanning, cardiac ultrasonography, or fluoroscopy). All thromboembolic complications were considered major events. Life-threatening bleeding or bleeding requiring transfusion or hospital admission was considered a major event. Any other bleeding was considered a minor event.

Statistical Analysis

Study outcomes were evaluated on an intention-to-treat basis and also on an on-treatment basis. The primary outcome with respect to efficacy was the individual percentage of INR values within the target range. Also, related to efficacy, we evaluated the individual percentage of time within target range, calculated by a linear interpolation (21). A Student *t*-test was used to compare these 2 variables in the 2 groups. The mean distance of individual INRs to the central point of target range was used as a measure of dispersion of INR values. Since these mean distances were not normally distributed, a Mann–Whitney test was used to compare the 2 treatment groups.

The secondary outcome, related to safety, was the occurrence of major thromboembolic and hemorrhagic complications. Occurrence of minor bleeding was also evaluated. We computed unadjusted risk differences for complications and death. There were no clinically relevant differences in baseline characteristics between the 2 groups. Because of this and because of insufficient outcome events, we did not provide adjusted risk differences. Statistical comparisons included 95% CIs, and a P value less than 0.05 was considered statistically significant. We used SPSS software, version 11.5, for all analyses (SPSS, Inc., Chicago, Illinois). In addition, exact 95% CIs for the risk differences between groups were calculated by using StatXact for Windows, version 6 (Cytel Software Corp., Cambridge, Massachusetts). A minimum of 250 patients was required in each comparison group; from data from previous publications (10, 11, 13–17), we expected a difference of 10% among in-range INR tests ($\alpha = 0.05$; $\beta = 0.10$).

Role of the Funding Sources

The funding source, Roche Diagnostic S.L., had no role in the design or conduct of this study or in the decision to submit the manuscript for publication.

RESULTS

The **Figure** shows the flow of patients through the study. The recruitment phase lasted 8 months. After we interviewed the first consecutive 1233 of 1500 randomly preselected patients, 737 (60%) agreed to participate and signed the informed consent form. All 737 patients were treated with acenocoumarol. Of the 1233 consecutive patients, 496 were not included because they declined to participate ($n = 461$) or did not meet the inclusion criteria ($n = 35$). Using stratified randomization, we assigned 369 patients to the conventional management group and 368 to the patient self-management group. **Table 1** shows the baseline characteristics of both groups.

In the intention-to-treat analysis, no statistically significant differences were observed in the distribution of the baseline variables (in addition, the size of the observed differences was not clinically relevant), except that a higher proportion of patients in the self-management group (13.5% vs. 7.9%) had had thromboembolic events during previous anticoagulant treatment. Theoretically, this difference implies a higher risk for complications in the self-management group. For the on-treatment analysis, the self-management group was also slightly younger and had a higher proportion of patients within the INR target range of 2.5 to 3.5.

Between randomization and the beginning of training, 58 of 368 patients in the self-management group (16%) declined to participate, most because they lacked self-confidence. Nine of 369 patients in the conventional management group (2.4%) withdrew after randomization. We trained 310 patients in the self-management group. It took approximately 4 hours for patients to learn to evaluate themselves reliably; some older patients needed 5 to 6 hours. Only 10 patients (3%; mean age, 70 years) could not pass the course and returned to conventional management. In the intention-to-treat analyses, these 10 patients were considered part of the self-management group. Thirty-nine of the patients trained (13%) required some help from a relative or caregiver to perform self-management reliably; the mean age of these nonindependent patients was 71 years.

The observation period ranged from 0.3 to 16.9 months (median, 11.8 months). The results of the intention-to-treat analysis of efficacy are shown in **Table 2**. The mean percentage of INR determinations within the individual target range was higher in the patient self-management group than in the conventional group (58.6% vs. 55.6%; difference, 3.0 percentage points [95% CI, 0.4 to 5.4 percentage points]). The time within target range and the INR distance were not statistically different in the 2 treatment groups. **Table 2** also shows the comparison between groups separately according to the 3 intended target ranges. The worst outcomes in the 3 efficacy measures occurred in patients whose target INR range was 3.0 to 4.5. There was no relationship between the percentage of INR tests within target range and age, educational level, or indication for oral anticoagulant treatment. In addition, these variables were not associated with the time within target range (data not shown).

Table 3 shows the numbers and risk differences for each type of complication. All of the results were unadjusted because the number of outcome events was low. **Table 4** describes the type of associated complications and

Table 1. **Baseline Characteristics of Patients, according to Study Groups and Analysis***

Variable	Intention-to-Treat Analysis		On-Treatment Analysis	
	Conventional Management Group	Patient Self-Management Group	Conventional Management Group	Patient Self-Management Group
Patients, *n*	369	368	360	289
Sex, *n* (%)				
Men	201 (54)	190 (52)	198 (55)	148 (51)
Women	168 (46)	178 (48)	162 (45)	141 (49)
Mean age ± SD, *y*				
Men	64 ± 12	64 ± 13	63 ± 12	61 ± 12
Women	67 ± 11	65 ± 15	66 ± 12	62 ± 15
Indication for oral anticoagulant treatment, %				
Atrial fibrillation, dilated cardiomyopathy, valve disease, biological prosthesis	50.4	50.3	49.4	46.0
Mechanical aortic prosthesis	18.4	15.6	16.7	18.7
Mechanical mitral, tricuspid, or multiple prosthesis	17.6	22.7	18.6	24.6
Venous thrombophilia	13.6	11.4	15.3	10.7
Intended INR target range, %				
2–3	77.5	72.8	78.1	68.8
2.5–3.5	19.0	24.5	18.3	27.7
3–4.5	3.5	2.7	3.6	3.5
Risk factors, %				
Arterial hypertension	42.8	48.6	45.8	45.5
Diabetes mellitus	13.6	15.4	19.5	13.6
Gastric ulcer	15.7	17.8	16.4	18.1
Cancer	8.7	9.2	8.5	7.4
Liver disease	8.4	9.7	9.1	9.5
Previous complications, %				
Severe hemorrhagic	9.8	11.1	10.0	12.8
Thromboembolic	7.9	13.5	7.8	13.5
Median previous time receiving anticoagulation (IQR), *y*	5.1 (2.2–12.0)	5.0 (2.0–11.7)	5.0 (2.2–12.0)	5.8 (2.1–12.4)
Other long-term medications, %				
Antihypertensive agents	11.9	12.0	11.6	11.8
Antiplatelet agents	1.1	1.6	1.1	1.4
Diuretics	34.7	35.1	33.8	34.2
Antiarrhythmic agents	44.9	47.8	43.9	49.4
Vasodilators	13.9	14.2	13.5	13.8
Antilipemic agents	17.0	20.3	17.5	20.6
Oral antidiabetic agents	5.6	5.4	5.4	5.1
Antidepressants	21.1	18.7	20.5	20.8
Antiulcer agents	17.8	16.9	17.3	16.4
Anticonvulsants	2.4	1.9	2.2	2.1
Other demographic data, %				
Accompanied attendance†	26.8	24.6	25.6	21.4
Educational level‡				
High	9.2	7.8	10.6	9.3
Low	88.4	89.0	86.0	89.7
Illiterate	2.4	3.2	3.4	1.0

* INR = international normalized ratio; IQR = interquartile range.
† Patients who usually brought a companion (relative or friend) to the scheduled visits.
‡ High = university or advanced education; low = intermediate or primary education.

causes of death. When the 37 severe complications described in **Table 4** were diagnosed, the INRs were within target range in most patients and no differences between groups were observed (data not shown). In the conventional management group, 27 patients had major complications (20 thromboembolic events and 7 hemorrhagic events). One hundred thirty-four patients reported minor hemorrhagic events. Fifteen patients died during the study, and 3 of the deaths were directly associated with anticoagulant therapy. In the self-management group, 8 patients had

Table 2. **Bivariate Analysis of Efficacy***

Variable	Intention-to-Treat Analysis			On-Treatment Analysis		
	Conventional Management Group	Patient Self-Management Group	*P* Value	Conventional Management Group	Patient Self-Management Group	*P* Value
Patients, *n*	369	368		360	289	
INR tests, *n*†	4712	15 435		4533	14 278	
Dose changes, *n (%)*	1459 (31.0)	4097 (26.5)		1383 (30.5)	3767 (26.4)	
Individual proportion of dose changes, %	28.9 ± 18.6	26.2 ± 13.8	0.03	28.8 ± 18.6	26.3 ± 12.7	0.04
General efficacy analysis, *n*	369	368		360	289	
Individual in-range INRs, %	55.6 ± 19.6	58.6 ± 14.3	0.02	55.8 ± 19.5	58.3 ± 12.5	0.055
Individual time within target range, %	64.9 ± 19.9	64.3 ± 14.3	0.2	65.0 ± 19.8	63.4 ± 12.6	0.20
INR distance	0.59 ± 0.27	0.58 ± 0.18	>0.2	0.59 ± 0.26	0.59 ± 0.18	>0.2
Efficacy analysis by intended INR target range						
2.0–3.0, *n*	285	273		278	202	
Individual in-range INRs, %	58.4 ± 19.1	60.8 ± 14.4	0.07	59.0 ± 19.2	60.9 ± 12.8	0.08
Individual time within target range, %	67.5 ± 19.1	66.6 ± 14.4	>0.2	67.7 ± 18.8	65.8 ± 13.0	0.17
INR distance	0.56 ± 0.25	0.54 ± 0.19	>0.2	0.56 ± 0.24	0.54 ± 0.17	>0.2
2.5–3.5, *n*	74	85		73	87	
Individual in-range INRs, %	46.6 ± 18.9	52.1 ± 11.6	0.03	46.1 ± 17.3	52.5 ± 9.5	0.02
Individual time within target range, %	55.5 ± 21.3	58.0 ± 12.4	>0.2	55.5 ± 21.1	57.9 ± 9.5	>0.2
INR distance	0.65 ± 0.23	0.65 ± 0.16	0.20	0.65 ± 0.22	0.66 ± 0.14	0.15
3.0–4.5, *n*	10	10		9	10	
Individual in-range INRs, %	43.6 ± 14.0	49.2 ± 12.5	>0.2	43.7 ± 14.1	46.6 ± 13.2	>0.2
Individual time within target range, %	57.6 ± 13.0	57.7 ± 10.3	>0.2	57.5 ± 12.9	57.8 ± 10.4	>0.2
INR distance	1.01 ± 0.51	0.85 ± 0.20	0.16	1.10 ± 0.51	0.97 ± 0.39	0.15

* Values presented with a plus/minus sign are means ± SD. INR = international normalized ratio; INR distance = deviation from the central INR values in each target range (i.e., 2.5 for the INR range 2.0–3.0).
† These tests were done monthly for the conventional management group and weekly for the patient self-management group.

major complications (4 thromboembolic, 4 hemorrhagic) and 55 reported minor hemorrhages. Six patients died, but none of the deaths were related to anticoagulant therapy.

According to the intention-to-treat analysis of risks, patient self-management appeared protective in comparison with conventional management for all types of complications. The major complication rate was 7.3% in the conventional management group and 2.2% in the self-management group (risk difference, 5.1 percentage points [exact 95% CI, 1.7 to 8.5 percentage points]). When analyzed separately, the rate of severe hemorrhage was 1.9 in the conventional management group and 1.1 in the self-management group (risk difference, 0.8 percentage point [exact 95% CI, −1.1 to 2.9 percentage points]). The self-management group had lower rates of minor hemorrhages (14.9% vs. 36.4%) and deaths (1.6% vs. 4.1%).

DISCUSSION

In this study, patient self-management of oral anticoagulant treatment was essentially similar to management by a specialized anticoagulation clinic when measured by the quality of INR control. However, self-management was superior in terms of reduction of total major complications. To date, none of the published randomized, controlled trials comparing clinical outcomes of oral anticoagulant treatment in these 2 settings has reported such a difference (14–17). However, all of these clinical trials in-

Table 3. **Risk for Types of Complications***

Variable	Intention-to-Treat Analysis			On-Treatment Analysis		
	Conventional Management Group	Patient Self-Management Group	Risk Difference (Exact 95% CI)†	Conventional Management Group	Patient Self-Management Group	Risk Difference (Exact 95% CI)†
Median follow-up (IQR), *mo*	11.7 (10–14)	12.0 (10–14)		11.7 (10–14)	11.9 (10–14)	
Patients, *n*	369	368		360	289	
Type of complication, *n (%)*						
Severe hemorrhagic complication, *n (%)*	7 (1.9)	4 (1.1)	0.8 (–1.1 to 2.9)	6 (1.7)	2 (0.7)	1.0 (–1.0 to 3.0)
Thromboembolic complication, *n (%)*	20 (5.4)	4 (1.1)	4.3 (1.5 to 7.3)	19 (5.3)	3 (1.0)	4.3 (1.5 to 7.2)
Total major complications, *n (%)*	27 (7.3)	8 (2.2)	5.1 (1.7 to 8.5)	25 (6.9)	5 (1.7)	5.2 (1.9 to 8.6)
Minor hemorrhagic complication, *n (%)*	134 (36.3)	55 (14.9)	21.4 (15.2 to 27.5)	131 (36.4)	49 (16.9)	19.5 (12.7 to 26.0)
Death, *n (%)*	15 (4.1)	6 (1.6)	2.5 (0.0 to 5.1)	15 (4.2)	6 (2.1)	2.1 (–0.7 to 5.0)

* The risk differences are unadjusted because there were insufficient outcome events to create reliable multivariable models. IQR = interquartile range.
† Values are percentage points.

volved smaller samples (<50 patients per group), much younger patients (average age between 42 and 54 years), and shorter follow-up periods (19). The incidence of clinical complications is of major interest in the investigation of clinical progress attributable to patient self-management, while the time within target range and the proportion of in-range tests are intermediate outcomes that may be more or less highly correlated with these incidence rates (20).

Our unselected sample of patients was older than those in most previous studies (10, 11, 13–18). Major complications occurred in fewer patients in the self-management group (2.2%) than in patients managed conventionally (7.3%). Classically, the factors influencing risk for adverse events are the intensity of anticoagulation, age, indication for anticoagulation, and history of thromboembolism or bleeding (22). These factors did not explain the difference we observed because both study groups had similar distribution (**Table 1**). However, any other potential confounder not included in the statistical analyses could be responsible for the observed differences, although this possibility is difficult to evaluate.

A direct comparison among different studies is not possible. However, the occurrence of major complications in our conventional management group was of the order of magnitude reported by other authors in patients managed by anticoagulation clinics (4.9% to 15.7% of patient-years) (3, 4, 6, 23). On the other hand, a German research team with long-term experience in patient self-management recently reported a rate of severe complications lower than 1% of patient-years in patients with mechanical heart valves, using the same INR target ranges as in our study (24). Another experienced team obtained results close to ours after 5-year follow-up of a self-management group that was included in a previous randomized trial (13). Sixty-two percent of their INR values were in range, and the occurrence of major complications was 1.7% of patient-years (25). These results (24, 25) compare well with ours (major complications in 2.2% of patients) and support the idea that patient self-management is clearly safer than conventional management.

In the patient self-management group, our dropout rate was 21% (**Figure**). Fifty-eight patients declined to participate a short time after signing the consent form but before participating in training; 10 patients could not pass the examination and never began self-management; and another 11 patients withdrew after they began self-management. This relatively high dropout rate is common in patients assigned to self-management and has ranged from 17% to 33% in previous studies (9, 11, 14, 26). In the trials by Sawicki (13) and by Gadisseur and associates (17), which had lower dropout rates (approximately 10%), the patients were 10 years younger than our patients.

In our intention-to-treat analysis, the percentage of in-range INR values was slightly higher in the self-management group than in the conventional management group (58.6% vs. 55.6%; $P = 0.02$). However, when the efficacy was evaluated in terms of time within target range, the difference was in the opposite direction, although it was not statistically significant (64.3% vs. 64.9%). This apparent contradiction may be due to the greater number of INR measurements in the self-management group. In any case, it is important to realize that, from a clinical and practical point of view, both groups obtained similar levels of efficacy in INR testing.

Several previous studies that compared self-management with management in anticoagulation clinics (**Table 5**) reported that self-management was superior in the percentage of INR tests (14–17) or percentage of time within target range (17), although the differences were mostly modest (<10%) (14, 15, 17). It has been argued that the improvement in these variables can be explained by the higher fre-

Table 4. **Associated Major Complications and Causes of Death***

Variable	Conventional Management Group, *n*	Patient Self-Management Group, *n*
Thromboembolic complications		
Stroke	3	2
TIA	10†	1
Mechanical valve thrombosis	1	–
Mechanical valve thrombosis + stroke	2	–
Leg arterial embolism	1	–
DVT	1	–
Superficial thrombophlebitis	1	–
Pulmonary embolism	1	1
Testicle thrombosis	1	–
Central vein retina thrombosis	1	–
Total	22†	4
Hemorrhagic complications		
Hemoptysis	2	–
Abdominal wall	1	–
Buttock	1	
Leg	–	1
Cerebral	1	2
Subdural	1	–
Bowel	1	1
Total events	7	4
Deaths		
Pulmonary embolism	1‡	–
Mechanical valve thrombosis	1‡	–
Massive ischemic stroke	1‡	–
Cardiac arrest	3	3
Septic shock	2	–
Myocardial infarction	2	–
Congestive heart failure	1	–
Renal failure	1	–
Disseminated breast cancer	1	–
Acute pulmonary edema	1	–
Acute respiratory infection	1	–
Disseminated prostate cancer	–	1
Car accident	–	1
Multiorgan failure	–	1
Total deaths	15	6

* DVT = deep venous thrombosis; TIA = transient ischemic attack.
† One patient had 3 TIA episodes but was considered once in the analyses of risk (Table 3).
‡ Considered directly related to anticoagulant treatment.

Table 5. **Previous Clinical Trials on Patient Self-Management of Oral Anticoagulant Therapy***

Study, Year (Reference)	Design†	Mean Follow-up, *mo*	Study Groups	Patients Analyzed, *n*	Mean Age, *y*	Frequency of Testing
Gadisseur et al., 2003 (17)	Multicenter RCT (*n* = 2)	6	PSM	47	54	Weekly
			ACC	161	62	Monthly
Fitzmaurice et al., 2002 (9)	Multicenter RCT (*n* = 6)	6	PSM	23	63	2 wk
			UC	26	69	Monthly
Sidhu and O'Kane, 2001 (11)	Single-center RCT	24	PSM	34	61	1 wk
			UC and ACC	49	61	Monthly
Körtke and Körfer, 2001 (10)	Single-center RCT	38	PSM	305	62	10 d
			UC	295	62	45 d
Watzke et al., 2000 (14)	Single-center controlled trial	6	PSM	49	54	Weekly
			ACC§	53	52	1–2 mo
Cromheecke et al., 2000 (15)	Single-center RCT	3	PSM	45	42	1–2 wk
			ACC	44	42	1–2 wk
Sawicki, 1999 (13)	Multicenter RCT (*n* = 5)	6	PSM	90	55	Weekly
			UC	89	55	2 wk
Ansell et al., 1995 (16)	Single-center controlled trial, highly selected patients¶	44	PSM	20	44	2 wk
			ACC‖	20	48	2 wk
ACOA, 2004 (current study)	Single-center RCT	12	PSM	368	65	Weekly
			ACC	369	66	Monthly

* Trials on patient self-testing, such as those reported by White et al. (18), Horstkotte et al. (27), and Beyth et al. (12), are not included in this table. Other very small studies and studies that were not RCTs have not been considered. ACC = anticoagulation clinic; ACOA = Alternative Control of Oral Anticoagulant Treatment; INR = international normalized ratio; PSM = patient self-management; RCT = randomized, controlled trial; UC= usual care by family physician.
† Numbers in parentheses are numbers of centers.
‡ "Mixed" included mechanical heart valve, venous thromboembolism, atrial fibrillation, and others. "Heart valve" included only patients with mechanical valve replacement.
§ Matched by sex and age.
‖ Matched by sex, age, reason for anticoagulation, and duration of treatment.
¶ Based on adherence, stability of previous test results within target ranges, and willingness to participate.

quency of testing in the self-management group (27). This improvement in the proportion of tests or amount of time within target range could lead to a decrease in the incidence of complications. Such a decrease has been reported in 2 previous randomized, controlled trials that compared patient self-management (10) or patient self-testing (12) with care by general practitioners. Körtke and Körfer (10) found a complication incidence of 4.7% of patient-years in a control group and 2.9% of patient-years in a group of self-managed patients, along with an improvement in percentage of in-range INRs (61% vs. 78%).

Beyth and associates (12) studied a very old sample (mean age, 75 years) and reported complication incidence rates of 25% of patient-years and 14.7% of patient-years in the control group and in the self-testing group, respectively. These results coincided with an improvement in time within target range in the intervention group versus the control group (56% vs. 33%). What is surprising in Beyth and associates' results is that both comparison groups tested INR with the same frequency (monthly). These results and ours cast doubt on the simple explanation of the correlation among test frequency, improvement in control of INR, and decrease in major complications. We obtained a better clinical outcome without improving INR control, and Beyth and associates improved outcome without increasing test frequency. When used in an older sample (closer to that seen in clinical practice), patient self-management was equivalent or slightly superior (a difference of 3% in the number of in-range test results) to management by specialized physicians in our anticoagulation clinic, despite performance of 4 times more INR tests per patient (weekly vs. monthly). Surprisingly, in terms of clinical outcomes, patient self-management achieved better results than conventional management, reducing the risk for major complications by approximately 70% and exhibiting a trend toward reduced mortality. Our results call into serious question the usefulness of evaluating the safety of oral anticoagulation by using percentage of in-range INR tests or time within target range. The decrease in the risk for complications may be explained by the empowerment of the patient (8, 28), the impact of the self-management strategy on adherence, and the improvement on self-awareness of health status when patients are responsible for making clinical decisions themselves (29–31).

We estimate that a minimum of 50% of our population could safely use patient self-management to control anticoagulant therapy. This conclusion is based on the results of our recruitment (737 of 1233 patients agreed to participate) and the success of the training (300 of 368 patients learned to monitor themselves adequately). Relatively simple teaching programs are clearly useful in achieving good results. It must be emphasized that approximately 90% of the patients who participated in this study were not highly educated (that is, had only a primary-school education or were illiterate).

One weakness of our study is that it was an unblinded single-center trial. Also, it can be argued that the conventional management group did not receive training on self-management of oral anticoagulant therapy. However, our purpose was to compare patient self-management with the real-life situation in Spanish anticoagulation clinics, where patients taking oral anticoagulant therapy do not receive

Table 5. **Continued**

INR in Range, %	Time within Target Range, %	Major Hemorrhage	Thrombosis	Total Major Complications	Indications‡
66	69	2 cases	0 cases	2 cases	Mixed
59	63	1 case	0 cases	1 case	
66	74	0 cases	0 cases	0 cases	Mixed
72	77	1 case	0 cases	1 case	
68	76	0 cases	0 cases	0 cases	Heart valve
58	64	0 cases	1 case	1 case	
78	–	1.7% patient-years	1.2% patient-years	2.9% of patient-years	Heart valve
61	–	2.6% patient-years	2.1% patient-years	4.7% of patient-years	
84	–	1 case	1 case	2 cases	Mixed
74	–	0 cases	0 cases	0 cases	
55	–	0 cases	0 cases	0 cases	Mixed
49	–	0 cases	2 cases	2 cases	
53	–	1 case	1 case	2 cases	Mixed
43	–	1 case	2 cases	3 cases	
89	–	0 cases	0 cases	0 cases	Mixed
68	–	0 cases	0 cases	0 cases	
59	64	1.1%	1.1%	2.2%	Mixed
56	65	1.9%	5.4%	7.3%	

special training. Another potential limitation of our study is the relatively high dropout rate in the patient self-management group.

Our study also had several strengths. It was centrally randomized and controlled, and the sample of recruited patients was unselected and was larger than samples in previous trials on the same topic. We studied patients with a mean age of 66 years who had heterogeneous indications for anticoagulant therapy. Our follow-up period was twice as long as that of previous comparable trials, and our data were analyzed by using both intention-to-treat and on-treatment approaches.

In conclusion, patient self-management of oral anticoagulant treatment decreased the incidence of major complications in comparison with conventional management performed by physicians specialists. Many patients are candidates for self-management, since old age and low educational level do not seem to be major obstacles. Ideally, self-management with the specialized support of an anticoagulation clinic should be used to manage oral anticoagulation for as many patients as possible. In Spain, the portable coagulometer we used in our study costs 730 euros ($947 U.S.) and each reagent strip costs 3.6 euros ($4.67 U.S.). Previous studies addressing important issues associated with patient self-management, such as quality of life (32) and cost-effectiveness (33), have yielded promising results. Nevertheless, further studies are warranted.

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Appendix 1: Objectives and General Characteristics of the Training Course for Patient Self-Management

Primary Objectives

The primary objectives of the training course were to teach patients receiving oral anticoagulation, responsible relatives, or both how to use portable coagulometers, how to interpret results of INR tests, and how to self-adjust doses of oral anticoagulants.

Secondary Objectives

The secondary objectives of the training course were to give the patients basic information on blood coagulation, anticoagulant drugs, drugs that interact with oral anticoagulants, and indications for anticoagulation, as well as information on how to recognize and treat associated complications (bleeding or thrombosis). Also, patients were taught the factors that are most likely to change the effect of oral anticoagulants, such as other drugs, foods, and alcoholic drinks.

This course was designed within the context of the ACOA clinical trial. It must be applied to patients who are randomly assigned to a self-management program. The program must be understandable and executable by any regular patient who is receiving long-term treatment and is not mentally or physically disabled, independent of age and educational level. It is based on the German model but was adapted to correspond to Spanish behavioral characteristics (13, 34–36). The didactic tools used in the course were created by the investigators and are not commercially available.

Organization of Sessions

Sessions were held at a hospital and were taught by a trained nurse. Patients were divided into small groups of 5 to 8 and had the option of being accompanied by a relative. Two sessions were held on 2 consecutive days. Each session was intended to last for 2 to 3 hours (total time for the regular course, 4 to 6 hours). An optional extra session was held 7 days later.

After the course, the patient began self-management with a short trial period (2 to 3 weeks), during which he or she could consult with a health professional over the telephone. At the end of this period, the nurse evaluated patients' progress and examined them to approve the beginning of clinical follow-up in the trial.

Didactic Tools

The following tools were used during the course.

1. The last regular INR control sheet. This was given to patients after each INR measurement in our anticoagulation clinic. The sheet included such information as name, diagnosis, intended INR target range, last 10 INR tests with dates and doses of oral anticoagulant, current INR result, dosage until next appointment, and date for next appointment.
2. CoaguChek S kit (coagulometer, fingerstick, reactive strips).
3. Sanitary material for finger puncture (antiseptic, cotton wool, bandage).
4. Diary for self-management of oral anticoagulant treatment.
5. Folder with exercises to practice management of doses.
6. Pens or pencils.
7. Posters with schemes on blood coagulation.
8. Screen and projector for transparencies.
9. Blackboard and chalk.

Session 1

Session 1 lasted approximately 2 hours. The main objectives of this session were to teach self-testing of INR control and impart the basic principles of coagulation and oral anticoagulants. During the introduction, the relationship of the program to the clinical trial and the objectives of the clinical trial were summarized. The nurse clearly described the main objectives of the training course, summarized the topics and the course structure (using transparencies), and explained the basic concepts of blood coagulation (using posters and transparencies). The basic concepts were as follows: function of coagulation; physiologic utility; abnormal (excessive) clot formation; diseases caused by excessive clot formation; drugs used to treat these diseases (oral anticoagulants and heparins); coagulation factors, vitamin K–dependent factors, and anti–vitamin K drugs; and risk for overdosing on anticoagulants (bleeding episodes).

Traditional control of oral anticoagulant treatment and the new strategy, patient self-management, were compared. The nurse described the potential advantages of patient self-management: increased frequency of testing at home, increased accuracy of control, possible decreased risk for bleeding and thrombosis, increased quality of life, and reduced work burden at the anticoagulation clinics.

The nurse then described the content of the CoaguChek kit. The patients were shown how to use the fingerstick and were told about the coagulometer and its management. The nurse provided a step-by-step description of the self-testing procedure (**Appendix 2**) by using transparencies and demonstration. Patients were given practical advice on how to obtain a good drop of blood (for example, clean and dry hands, warm skin). Each patient repeated the procedure using a kit, and the nurse checked each patient's performance. The INR result was noted in each patient's diary (**Appendix 3**, **Appendix Tables 1** and **2**). To conclude the session, the patients were given more information about the theory of the process, such as the concept of INR (**Appendix 4**), the definition of the target range, and the way different diseases can imply different target ranges.

Session 2

Session 2 also lasted approximately 2 hours. The main objectives of this session were to teach patients how to adjust doses after obtaining an INR result and to stress the importance of the diary. After a review of the first session, patients repeated the step-by-step self-testing procedure and used cards to obtain the correct dose (Appendix 4, **Appendix Tables 3** and **4**). Each patient was given specific cards depending on his or her target range and his or her current doses. Next, the nurse presented examples of theoretical cases and determined different doses as required by different situations (Appendix 5).

Patients were then given individual examinations on adjustment of doses. Each patient had to adjust his or her dose for

Appendix Table 1. **Example of Diary Sheets Used To Record 1 Year of Follow-up***

	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday	Comments
Date								
INR								
Dose level								
Date								
INR								
Dose level								
Date								
INR								
Dose level								
Date								
INR								
Dose level								

* Each diary contained 12 sheets (4 weeks per sheet). INR = international normalized ratio.

different INR results (within target, above target, and below target). The patients who passed this examination (no mistakes in any proposed INR) received a CoaguChek kit and a card with a study contact telephone number. Patients started the probe period during the next few weeks, before the final examination. During this time, they performed an INR test weekly and adjusted doses according to the dosing cards. Support was available by telephone if necessary. The questions the patients asked helped the researchers to evaluate the degree of learning for each patient and to decide whether he or she needed a third training session.

Patients who made at least 1 mistake or had difficulty managing the coagulometer received a third training session. Those who still had difficulties after the third training session were invited to bring a companion. The companion also learned the self-management technique, took an examination, and signed a document assuming the responsibility of the testing and dosing for the patient. If the patient could not bring a companion, he or she was declared incapable of self-management and was excluded from the program.

Final Examination

For the final examination, an interview with the training nurse was scheduled. Each patient came to the unit with his or her CoaguChek kit and diary. The training nurse used 4 criteria to approve the patients' inclusion in the trial follow-up.

1. Accurate diary records during the probe period.
2. Satisfactory performance of self-testing procedure.
3. Correct diary recording of INR result, doses, and time for next test.
4. Correct answer to question about hypothetical INR results.

Appendix 2: Self-Testing Procedure

A CoaguChek coagulometer with power adapter and batteries, reactive strips (CoaguChek PT test), and fingerstick and lancets (Softclix II, Roche Diagnostics) were needed for the self-testing procedure. The batteries allowed for approximately 60 measurements. The coagulometer turned off automatically in 4 minutes if not used. Each box of reactive strips had a coding chip

Appendix Table 2. **Example of Diary Entries for a Woman with a Mechanical Aortic Valve and a Target International Normalized Ratio Range of 2.0 to 3.0***

	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday	Comments
Date	April 1, 2002							Level 15
INR	2.9							
Dose level	¼	½	½	¼	½	½	¼	
Date	April 8, 2002					April 13, 2002		Level 13
INR	5.7					2.4		
Dose level	0	¼	¼	½	¼	¼	½	
Date						April 20, 2002		Level 14
INR						1.8		
Dose level	¼	¼	½	¼	¼	½	¼	
Date						April 27, 2002		Level 14
INR						2.4		
Dose level	½	¼	½	¼	½	¼	½	

* Dose level is given as fraction of tablets. INR = international normalized ratio.

Appendix Table 3. **Information on Front Sides of Sample Dose Cards***

Test Result	What To Do	Next Test
INR target range, 2.0–3.0		
1–1.3	Repeat test; increase 2 levels	4 d
1.4–1.8	Increase 1 level	5 d
1.9–3.2	Maintain	7 d
3.3–4.9	Decrease 1 level	7 d
5–7	Repeat test; stop taking acenocoumarol for 1 day, then decrease 2 levels	5 d
INR target range, 2.5–3.5		
1–1.5	Repeat test; increase 2 levels	4 d
1.6–2.3	Increase 1 level	5 d
2.4–3.6	Maintain	7 d
3.7–4.9	Decrease 1 level	7 d
5–7	Repeat test; stop taking acenocoumarol for 1 day, then decrease 2 levels	5 d
INR target range, 3.0–4.5		
1–1.5	Repeat test; increase 3 levels and add LMWH (enoxaparin, 40 mg/d)	4 d
1.6–2.3	Repeat test; increase 2 levels	5 d
2.4–2.8	Increase 1 level	7 d
2.9–4.6	Maintain	7 d
4.7–5.5	Decrease 1 level	7 d
5.6–7.0	Repeat test; decrease 2 levels	5 d

* INR = international normalized ratio; LMWH = low-molecular-weight heparin.

that functioned only for the strips from that box. This coding chip had to be placed in the coagulometer each time a new box of reactive strips was started. The coding chip had to be placed while the coagulometer was turned off.

The steps for self-testing were as follows.

1. Turn on the coagulometer.

2. Wait for the appearance of the icon "INSERT STRIP" on the screen.

3. Open the strip blister and save for discarding the used strip.

4. Insert the reactive strip completely in the coagulometer following the direction of the arrow.

5. On the screen, the icon "PLEASE WAIT" will appear until the strip reaches the adequate temperature for the reaction.

6. Then, the icon "APPLY THE SAMPLE" will appear on the screen.

7. Puncture the finger with Softclix II and obtain an adequate drop of blood.

8. You will have 90 seconds to apply the blood drop to the appropriate zone.

9. The coagulometer will start the measurement automatically. The icon "PERFORMING TEST" will appear on the screen.

10. You must record the INR result in your diary.

Note: If the blood drop is too small or is not well placed on the reactive strip, or if too much time elapses before applying the blood sample, an "ERROR" icon will appear on the screen. In this case, the complete procedure must be repeated from the beginning. The second blood sample must be obtained from a different finger.

Appendix 3: Diary

The first page contained the patient's personal data (name, address, birth date, and home telephone number). The second

Appendix Table 4. **Information on Reverse Sides of Sample Dose Cards for Levels 1 through 54***

Level	Guideline†
1	0, 0, ⅛
2	0, ⅛
3	0, ⅛, ⅛
4	0, ⅛, ⅛, ⅛, ⅛
5	⅛
6	⅛, ⅛, ⅛, ¼
7	⅛, ⅛, ¼
8	⅛, ¼
9	⅛, ¼, ¼
10	⅛, ¼, ¼, ¼
11	¼
12	¼, ¼, ¼, ½
13	¼, ¼, ½
14	¼, ½
15	¼, ½, ½
16	¼, ½, ½, ½
17	½
18	½, ½, ½, ¾
19	½, ½, ¾
20	½, ¾
21	½, ¾, ¾
22	½, ¾, ¾, ¾
23	¾
24	¾, ¾, ¾, 1
25	¾, ¾, 1
26	¾, 1
27	¾, 1, 1
28	¾, 1, 1, 1
29	1
30	1, 1, 1, 1 + ¼
31	1, 1, 1 + ¼
32	1, 1 + ¼
33	1, 1 + ¼, 1 + ¼
34	1, 1 + ¼, 1 + ¼, 1 + ¼
35	1 + ¼
36	1 + ¼, 1 + ¼, 1 + ¼, 1 + ½
37	1 + ¼, 1 + ¼, 1 + ½
38	1 + ¼, 1 + ½
39	1 + ¼, 1 + ½, 1 + ½
40	1 + ¼, 1 + ½, 1 + ½, 1 + ½
41	1 + ½
42	1 + ½, 1 + ½, 1 + ½, 1 + ¾
43	1 + ½, 1 + ½, 1 + ¾
44	1 + ½, 1 + ¾
45	1 + ½, 1 + ¾, 1 + ¾
46	1 + ½, 1 + ¾, 1 + ¾, 1 + ¾
47	1 + ¾
48	1 + ¾, 1 + ¾, 1 + ¾, 2
49	1 + ¾, 1 + ¾, 2
50	1 + ¾, 2
51	1 + ¾, 2, 2
52	1 + ¾, 2, 2, 2
53	2
54	2, 2, 2, 2 + ¼

* To decrease dose, read from left to right; to increase dose, read from right to left.
† Guidelines are in fractions of tablets.

page gave the hospital name and a contact telephone number. The last page contained the number of the clinical record, the kind of oral anticoagulant used (warfarin or acenocoumarol), the individual target range, the date on which long-term oral anticoagulation was started, and diagnostic information.

The diary also included a table (**Appendix Table 1**) to record 1 year of follow-up (12 sheets, with 4 weeks per sheet). A sample diary can be seen in **Appendix Table 2**.

Appendix 4: Adjustment of Doses and Instructions to Patients

What Is the INR?

It is a measure of your anticoagulation level. This measurement is accepted internationally and allows comparison of results among different laboratories and coagulometers. A healthy person not taking oral anticoagulants will have an INR very close to 1.0. An INR of 2.0 indicates that it took twice as long for your blood to clot than it would if you were not receiving anticoagulation and were healthy. If the INR is 3.0, your clotting time will be 3 times longer than that of normal people. The INR result that you measure by the portable coagulometer is exactly the same as that measured at a laboratory in a hospital.

Dose Adjustment

The main goal is to maintain your INR within target range. The target range is the range of INR values where the treatment is most safe and indicates the lowest risk for bleeding and the lowest risk for thrombosis. It depends on your disease. The target range is fixed for different groups of patients (for example, patients with a mitral valve usually have an INR range of 2.5 to 3.5). However, the anticoagulant doses required to achieve INRs within the target range vary depending on the individual.

When the INR is below the target range (for example, 1.7), there is an increase in thrombosis risk. When the INR is above the target range (for example, 4.6), there is an increase in bleeding risk. The risks increase in proportion to the deviation from the target range. For example, an INR of 8.3 implies a higher risk for bleeding than an INR of 7.2.

The drug used in our clinic is acenocoumarol (Sintrom, Novartis Farmaceutica, Barcelona, Spain). Each pill contains 4 mg, so daily doses are given in quarter-pill increments. For example, one quarter of a pill equals 1 mg, one half of a pill equals 2 mg, three quarters of a pill equals 3 mg, and 1 pill equals 4 mg.

Dose Cards

The dose cards (**Appendix Tables 3** and **4**) provide simple guidelines to help choose the correct doses. The cards have 2 printed sides. The first side depends on your target range, and the other side depends on your usual dose of anticoagulant. The cards include important rules.

1. If the INR is higher than 7, you must repeat the test. If the result is the same, call the anticoagulation clinic.

2. If you are bleeding overtly, test your INR and go to the hospital emergency department.

3. If you must increase the anticoagulant dose, follow the arrow on the card (read the guideline from right to left).

4. If you must decrease the anticoagulant dose, follow the arrow on the card (read the guideline from left to right).

The patient's last dose before starting self-management was listed on the guideline card. The dose was highlighted to emphasize the patient's current dose level.

Appendix 5: Dosing Exercises

Problem 1

Ms. Sánchez has a target INR range of 2.0 to 3.0. She is currently taking 16 mg of acenocoumarol per week: one-half tablet, one-half tablet, three quarters of a tablet, one-half tablet, one-half tablet, three quarters of a tablet, one-half tablet (level 19). Her INR result was 3.2. Which dose must she take? When must she repeat the test?

Solution: Ms. Sánchez should maintain level 19. The next test should be performed in 7 days.

Problem 2

Mr. Pérez has a target range of 2.5 to 3.5. His usual dose is level 26: three quarters of a tablet, 1 tablet, three quarters of a tablet, 1 tablet, three quarters of a tablet, 1 tablet, three quarters of a tablet. His INR result was 4.8. Which dose must he take? When must he repeat the test? If his target range were 3.0 to 4.5, what should he do?

Solution: Mr. Pérez should decrease his dose 1 level from level 26 to level 25, starting with three quarters of a pill. The next test should be performed in 7 days. Mr. Pérez would do exactly the same if his target range were 3.0 to 4.5.

Problem 3

Mr. Garcia has a target range of 2.5 to 3.5. His usual dose is 1 pill per day (level 29). On Tuesday, his INR result was 1.3. He remembered that he forgot to take his pill 1 day last week. What must he do? What is his new dose? When must he repeat the test?

Solution: Mr. Garcia should repeat the test and confirm the INR. He should note in the diary that he forgot to take a dose and should increase the dose 2 levels (from level 29 to level 31), starting with the higher fraction. He should test his INR again in 4 days.

After 4 days, Mr. Garcia's INR is 2.8. What must he do, considering that the previous low INR (1.3) was due to an omission of a dose?

Solution: Mr. Garcia should try to avoid further omissions of doses. He should continue with the usual dose of 1 pill per day (level 29) and should repeat the test in 7 days.

Problem 4

Mrs. Martinez has a target range of 2.0 to 3.0. She takes one-half pill per day. Her INR test result was 4.5. What must she do?

Solution: Mrs. Martinez should decrease her dose 1 level, from level 17 to level 16, starting with one quarter of a pill. The next test should be performed in 7 days.

Problem 5

Mr. Alonso has a target range of 3.5 to 4.5. His usual dose is one-half pill to three quarters of a pill, alternatively (level 20). Today, his INR test yielded a result of 1.4. What must he do?

Solution: First, Mr. Alonso must repeat the test and confirm the very low INR. If it is confirmed, he should increase the dose 3 levels to level 23, three quarters of a pill every day. In addition, he must inject prophylactic doses of low-molecular-weight heparin during the next 3 days (subcutaneous enoxaparin, 40 mg/d, until the next test). The next test should be performed in 4 days.

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