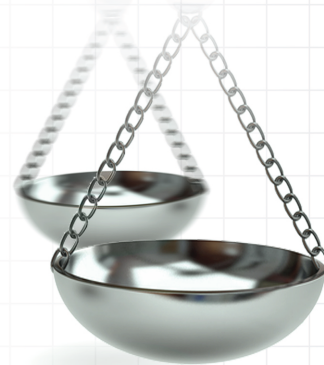




# Impact of an oral anticoagulation self-monitoring and self-management program in patients with mechanical heart valve prosthesis

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**Objective:** To analyze impact of implementation of an oral anticoagulation self-monitoring and self-management program among patients with mechanical valve prosthesis. **Materials & methods:** Observational and retrospective study performed in Hospital Moises Broggi, Barcelona, Spain. The program started on June 2019. The study compared 6-month period before and after the implementation of the program. **Results:** The study included 44 patients. There was a numerical increase of time in therapeutic range from  $53.6 \pm 21.3\%$  to  $57.1 \pm 15.7\%$  ( $p = 0.30$ ). Proportion of patients with international normalized ratio (INR)  $> 5$  significantly decreased from 3.9 to 2.0% ( $p = 0.04$ ). No significant differences were observed in thromboembolic or bleeding complications. Visits to emergency department decreased from (29.5 to 22.7%;  $p = 0.41$ ). **Conclusion:** Oral anticoagulation self-monitoring and self-management program seems an appropriate approach that could provide additional benefits in selected patients with mechanical valve prosthesis.

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**Keywords:** anticoagulation • bleeding • mechanical prosthesis • self-management • self-monitoring • thrombosis • vitamin K antagonists

After the introduction of direct oral anticoagulants in clinical practice, the use of vitamin K antagonists (VKA) have progressively decreased [1]. However, direct oral anticoagulants are contraindicated in patients with mechanical heart valve prosthesis, severe renal insufficiency or antiphospholipid syndrome [2,3].

VKA have a narrow therapeutic window and a highly variable metabolism, requiring periodic monitoring of anticoagulant activity and several dose adjustments to provide the best beneficial risk profile [4]. However, achieving a good anticoagulation control is difficult, even in specialized centers [5], making necessary the search of alternatives that improve not only anticoagulation control, but also facilitate the management of these patients and reduce healthcare overload [4,5].

Self-monitoring and self-management program implies that the patient takes responsibility about the control of its anticoagulation treatment with a portable coagulometer that allows a more frequent international normalized ratio (INR) monitoring and dose adjustment as required, leading to a better anticoagulation control [6]. In this context, oral anticoagulation self-monitoring and self-management could be an alternative, as it has demonstrated some benefits over the traditional method, including an improvement of quality of life (QoL) and a reduction of work absenteeism, unnecessary displacements or treatment-associated complications [6–9]. In addition, different meta-analyses have shown that compared with the traditional management, self-monitoring and self-management can improve the quality of the oral anticoagulation therapy, leading to a reduction of thromboembolic complications [6,10]. However, oral anticoagulation self-monitoring and self-management may be applied only to selected

patients [11]. In fact, it has been estimated that around 10–80% of anticoagulated patients could fulfill eligibility criteria for this approach [12,13].

On the other hand, patients with mechanical heart valve prosthesis require an excellent anticoagulation control, as these patients have a higher risk of thromboembolic and bleeding complications than nonvalvular atrial fibrillation patients [14]. In fact, it has been reported that better anticoagulation control improves survival among patients with mechanical heart valve prosthesis [9].

In this context, the management of anticoagulation with VKA after mechanical valve replacement may be improved with self-monitoring [15–17].

The aim of this study was to analyze the initial impact of the implementation of an oral anticoagulation self-monitoring and self-management program among patients with mechanical valve prosthesis in the Hospital de Sant Joan Despi Moisès Broggi.

## Materials & methods

Observational and retrospective study in which patients with mechanical heart valve prosthesis included in the oral anticoagulation self-monitoring and self-management program of the Hospital Moisès Broggi de Sant Joan Despi were analyzed. The Hospital Moisès Broggi (Sant Joan Despi and Hospitalet de Llobregat) is a regional hospital (level 2) with a total of 360 beds, located at the south metropolitan area of Barcelona, Spain.

To select patients, a prescreening was performed among the entire population of patients in long-term anticoagulation treatment (for at least 3 months) older than 18 years. Those who were carriers of single or multiple mechanical valves were preselected. These patients were informed of this preselection, and of the existence of the program and its complete characteristics. Informed consent was obtained orally from the study participants before inclusion. During the selection phase, those patients who could not carry out a correct self-control at the discretion of the hemostasis evaluating staff were excluded. Exclusion criteria included: manifest inability to understand the operation of the INR determination systems or the dosage system and the unavailability of a mobile phone to download the control app or access the internet, as well as at the request of the patient. The study was conducted in compliance with the approval opinion received by Institutional Review Board.

The oral anticoagulation self-monitoring and self-management program started on 5 June 2019. Before the inclusion, patients were specifically educated and trained for this program. This self-control program was performed by the hemostasis service. The training course consisted of a 2-h module, which included basic skills on the use of a coagulometer, interpretation of INR values and VKA drug dosage. The patients had to demonstrate that they could follow the procedures adequately and the evaluation was carried out by the training staff during the course. The course was taught by a specialized nurse from the Haemostasis Service. All patients used the CoaguChek® S or CoaguChek XS portable coagulometer (Roche Diagnostics, Switzerland) equipped with Coaguchek PT test strips. The dosing schedule established a weekly INR determination frequency together with dose modification instructions based on the determined INR value. The patient had to enter the INR value in the TAONet® app or website. TAONet was the application that managed all the information of the oral anticoagulant therapy control system. It required access by individualized and secret password for each patient. The data that the patient could view included: parentage data, center responsible for control, reason for the anticoagulation indication, coagulometer serial number, previous INR (up to 5) and previous dosing schedules, target therapeutic range, list of levels of dosage, dosage proposed by the algorithm (highlighted and clearly visible), screen for communicating comments to the center and screen for patient response.

Once the result was entered into the system, the patient received the daily dosage for 1 week on their mobile phone or through the computer program to view and/or print it. INR and dosage data were viewed on TAONet by the haemostasis service staff on a weekly basis. This allowed the healthcare professional to control the decisions made by the patient at all times and to contact him/her if extreme values, inconsistencies in the dosage or poor control were detected. The daily dosage of vitamin K antagonist (VKA) treatment scheme proposed to the patient was included in the hospital's computer program (electronic health record) so that any professional could consult the different self-control treatment daily dosage schemes. In addition, part of the hemostasis team reviewed all determinations and contacted by phone the patients who presented extreme INRs (defined as  $\text{INR} > 5$  or  $\text{INR} < 1.6$ ). In these cases, the correct application of the procedure was evaluated and the established corrective actions were carried out, including advice for the correct dosage, repetition of the training course or withdrawal from the program in case of noncompliance.

Only those patients that completed the training course and reached the objectives of the course (i.e., the adequate management of the coagulometer, lancets and test strips; good interpretation of the results; appropriate decisions about the adjustment of treatment; and a correct introduction of the data into the system), and also performed the follow-up were considered capable for entering in the weekly self-monitoring and self-management program. In addition, if patients had incidents or handling doubts, they were instructed to contact by phone and/or also access the web: <https://autotao.csi.cat/tao>. All patients received a guide for the CoaguChek home coagulometer and a manual for the TAONet mobile application. All patients signed a contract for the transfer of all the material supplied.

For this study, the 6-month period before the implementation of the self-monitoring and self-management program was compared with the first 6-month period after the implementation. In the traditional oral anticoagulation program, a nurse performed the INR determinations to the patients according to clinical practice (usually once a month, and more frequently when required), and the physician revised the values and modified the treatment as needed. In the oral anticoagulation self-monitoring and self-management program, patients had to perform themselves an INR control every week and modified the dose of the anticoagulant treatment. Although the results were revised by the physician, no specific action was taken in the self-monitoring and self-management program.

Baseline clinical characteristics, including biodemographic data (age, sex, bodyweight, height, BMI), cardiovascular risk factors (hypertension, dyslipidemia, diabetes, current smoking), the history of cardiovascular disease (atrial fibrillation, coronary heart disease, heart failure, prior stroke, peripheral artery disease, chronic kidney disease), the type of mechanical heart valve prosthesis implanted (aortic, mitral or both), other conditions (cancer, chronic liver disease) and the number of medications were recorded.

Time in therapeutic range was calculated according to the Rosendaal method [18]. It was considered as appropriate an INR range of 2.5–3.5 in the case of mitral mechanical prosthesis and 2.0–3.0 in the case of aortic mechanical prosthesis [19]. Oral anticoagulation parameters, including the number of INR determinations, the time in therapeutic range and the proportion of patients with INR <1.5 or >5 were compared between both periods (before and after the implementation of the self-monitoring and self-monitoring program). In addition, thromboembolic and bleeding complications, as well as hospitalizations and visits to the emergency department were also compared between both periods.

### Statistical analysis

For the descriptive analysis, continuous variables were described using the mean and standard deviation and categorical variables by their absolute (n) and relative frequencies (%). Events before and after the implementation of the program were compared by the incidence rates. To evaluate time in therapeutic range, extreme INR values (<1.5 and >5) were separated from the rest. Then, the Chi-squared test was performed to compare proportions before and after the implementation of the program. The Rosendaal method was used to estimate the proportion of controls and time in days in which INR was in therapeutic range, defined as 2.5–3.5 for mitral mechanical prosthesis and 2.0–3.0 for aortic mechanical prosthesis. The Student's *t*-test or the Wilcoxon test for paired data, according to the distribution of the sample, were used to compare the mean in therapeutic range in the overall study population, before and after the implementation of the program. Data were analyzed with the statistical programs SPSS v.25 for Windows and EPIDAT 3.1.

### Results

A total of 50 patients were initially recruited in the self-monitoring and self-management program. However, 4 (8%) patients did not reach a complete learning of the program and 2 (4%) patients left the program during the follow-up. As a result, a total of 44 patients were finally included for the analysis. Mean age was  $61.8 \pm 11.1$  years and 50% of patients were women. An aortic mechanical prosthesis had been implanted in 50.0% of patients, a mitral mechanical prosthesis in 36.4% of patients and aortic and mitral mechanical prostheses in the remaining 13.6% of patients. Cardiovascular risk factors and cardiovascular disease were common, being hypertension (54.5%), atrial fibrillation (43.2%), coronary artery disease (25.0%) and heart failure (25.0%) the most frequent ones (Table 1).

With regard to anticoagulation control, 466 INR determinations were performed before the implementation of the self-monitoring and self-management program and 1170 determinations during the self-monitoring and self-management period. There was a trend toward an increase of time in therapeutic range from  $53.6 \pm 21.3\%$  to  $57.1 \pm 15.7\%$  ( $p = 0.30$ ) between both periods. However, total INR determinations in therapeutic range

**Table 1. Baseline clinical characteristics of the study population.**

| Biodemographic data                                     | Population (n = 44; 100%) |
|---------------------------------------------------------|---------------------------|
| Age, years                                              | 61.8 ± 11.1               |
| Sex (women), n (%)                                      | 22 (50.0)                 |
| Bodyweight, kg                                          | 77.6 ± 16.1               |
| Height, cm                                              | 167.2 ± 10                |
| BMI, kg/m <sup>2</sup>                                  | 27.3 ± 5.3                |
| Cardiovascular risk factors                             |                           |
| – Hypertension, n (%)                                   | 24 (54.5)                 |
| – Dyslipidemia, n (%)                                   | 23 (52.3)                 |
| – Diabetes, n (%)                                       | 10 (22.7)                 |
| – Smoking, n (%)                                        | 6 (13.6)                  |
| Cardiovascular disease                                  |                           |
| – Atrial fibrillation, n (%)                            | 19 (43.2)                 |
| – Coronary heart disease, n (%)                         | 11 (25.0)                 |
| – Heart failure, n (%)                                  | 11 (25.0)                 |
| – Prior stroke, n (%)                                   | 6 (13.6)                  |
| – Peripheral artery disease, n (%)                      | 5 (11.4)                  |
| – Chronic kidney disease, n (%)                         | 3 (6.8)                   |
| Mechanical heart valve prosthesis                       |                           |
| – Aortic valve                                          | 22 (50.0)                 |
| – Mitral valve                                          | 16 (36.4)                 |
| – Aortic and mitral valves                              | 6 (13.6)                  |
| Other conditions                                        |                           |
| – Cancer, n (%)                                         | 4 (9.1)                   |
| – Chronic liver disease, n (%)                          | 1 (2.3)                   |
| Medications                                             |                           |
| – 1–3, n (%)                                            | 13 (29.5)                 |
| – 4–7, n (%)                                            | 21 (47.7)                 |
| – 8–12, n (%)                                           | 10 (22.7)                 |
| Antiplatelets, n (%)                                    | 1 (2.3)                   |
| Mean time on VKA before inclusion in the program, years | 5.5                       |

VKA: Vitamin K antagonists.

**Table 2. Anticoagulation control.**

|                                 | Before self-monitoring and self-management program (n = 44) | Self-monitoring and self-management program (n = 44) | p-value |
|---------------------------------|-------------------------------------------------------------|------------------------------------------------------|---------|
| Total INR determinations        | 466                                                         | 1,170                                                | –       |
| INR in therapeutic range, n (%) | 442 (94.8)                                                  | 1,141 (97.5)                                         | 0.01    |
| TTR, % (95% CI)                 | 53.6 ± 21.3(47.2–60.1)                                      | 57.1 ± 15.7 (52.3–61.9)                              | 0.29    |
| INR <1.5, n (%)                 | 6 (1.3)                                                     | 6 (0.5)                                              | 0.18    |
| INR >5, n (%)                   | 18 (3.9)                                                    | 23 (2.0)                                             | 0.04    |

INR: International normalized ratio; TTR: Time in therapeutic range.

significantly increased after the implementation of the program (94.8 vs 97.5%;  $p = 0.01$ ) and the proportion of patients with INR >5 significantly decreased (3.9 vs 2.0%;  $p = 0.04$ ; [Table 2](#)).

Outcomes during the follow-up were reported in [Table 3](#). Overall, thromboembolic and bleeding complications were low during both 6-month periods. Whereas, no significant differences were observed in thromboembolic or bleeding complications between both periods, there was a trend to a decrease in the proportion of visits to the emergency department after the implementation of the self-monitoring and self-management program (29.5 vs 22.7%;  $p = 0.41$ ).

Table 3. Outcomes during the follow-up.

|                             | Before self-monitoring and self-management program (n = 44) | Self-monitoring and self-management program (n = 44) | p-value |
|-----------------------------|-------------------------------------------------------------|------------------------------------------------------|---------|
| Bleeding, n (%)             | 1 (2.3)                                                     | 1 (2.3)                                              | 1       |
| Stroke, n (%)               | 1 (2.3)                                                     | 0                                                    | 0.32    |
| Embolism, n (%)             | 0                                                           | 0                                                    | 1       |
| Hospitalization, n (%)      | 2 (4.5)                                                     | 3 (6.8)                                              | 0.66    |
| Emergency department, n (%) | 13 (29.5)                                                   | 10 (22.7)                                            | 0.41    |

## Discussion

This study showed that developing an oral anticoagulation self-monitoring and self-management program in a second level hospital is feasible and may improve anticoagulation control with low rates of thromboembolic and bleeding complications among patients with mechanical heart valve prosthesis.

A total of 44 patients (mean age 61.8 years; 50% women) with mechanical heart valve prosthesis (50.0% mitral, 36.4% aortic, 13.6% mitral and aortic) were included in the study. In contrast to previous studies that have analyzed the impact of self-monitoring and self-management on patients taking VKAs in which a low proportion had mechanical heart valve prostheses (between 19 and 50%) [7,20,21], in our study all patients had mechanical heart valve prostheses. As a result, the data reported focused on a population that has not been well studied.

In our study, 8% of patients did not reach a complete learning of the program and 4% of patients left the program during the follow-up. Different studies have shown that a high proportion of patients cannot complete self-monitoring and self-management programs. Thus, a study performed in 126 patients showed that after 2-years of follow-up, only 61% of patients completed the program [7]. In a 3-year prospective quasi-experimental study with a control group performed in Spain, only 26.13% of the overall study population accepted to participate in the program. Of these, 4.5% of patients required additional learning support and 4.2% did not complete the follow-up [8]. Other studies have reported a high variability in successful rates to complete the program [22–25]. The success of self-monitoring and self-management method depends on consistent, regular and frequent testing [26]. As a result, self-monitoring and self-management is not feasible for all patients, and require the identification of selected patients with a high motivation. In addition, although self-management increases the autonomy of the patients, it is recommended that the physician or another healthcare provider monitor the results obtained by the patient and can adjust the anticoagulant dose in case of poor INR control. In our study, communication between the patients and the healthcare providers through phone and website was very useful as it rapidly allowed evaluating the actions taken by the patients in order to avoid unnecessary risks. Only a low number of problems were reported and this method increased the autonomy and confidence of patients with the program.

Suboptimal anticoagulation control with VKA is associated with an increased risk of outcomes [27]. Of note, it has been reported that in patients with atrial fibrillation, self-managed oral anticoagulant is associated with a significantly lower risk of all-cause and ischemic stroke compared with direct oral anticoagulants [28]. Similarly, poor INR control is also common in patients with mechanical heart valve prosthesis and this is also associated with a higher risk of events [14,29,30]. By contrast, a high warfarin treatment quality improves outcomes among patients with mechanical heart valve prosthesis [31]. In addition, adherence and persistence to oral anticoagulation remains challenging nowadays [20,32], even in patients with mechanical heart valve prosthesis [33]. As a result, it is mandatory to develop strategies to improve anticoagulation control to reduce outcomes in this population [34].

Different studies have shown that selected mechanical heart valve patients can manage oral anticoagulant therapy themselves [35]. The introduction of portable coagulometers, such as CoaguChek, INRatio and Prottime may facilitate the implementation of oral anticoagulation self-monitoring and self-management programs as an alternative to the traditional management. In our study, the CoaguChek XS handheld coagulation analyzer was used. This coagulometer has been validated and correlates strongly with conventional laboratory methods [36].

Our data showed that the implementation of the self-monitoring and self-management program was associated with a trend toward a higher anticoagulation control and with low outcome rates. A Cochrane review of 28 clinical trials showed that both, trials of self-management or self-monitoring significantly improved time in therapeutic range, and reduced the risk of thromboembolic events and self-management trials significantly decreased all-cause mortality, but not major bleeding risk [6]. A recent study showed in 126 patients that switching to a self-monitoring program translated into a significant improvement of time in therapeutic range, a reduction of extreme INR values

and a greater QoL after 2-years of follow-up. Moreover, thromboembolic and bleeding events were low [7]. In a 3-year prospective study, anticoagulation control, complications and QoL improved with the self-management program compared with usual care [8]. Consequently, our data are in line with the available evidence.

Another important issue is whether these programs are cost-effective, as costs could be a barrier for their implementation [11,37], particularly when considering specialized clinics [38] or those countries with a high quality of anticoagulation [39]. It should be considered not only the costs of training, portable coagulometers, lancets and test strips, but also the costs of thromboembolic and bleeding complications after the application of these programs [26,40]. As a result, self-monitoring and self-management seems a cost-effective approach, mainly in the case of a reduction of thromboembolic complications. In our study, no stroke or embolism was reported during the implementation of the self-monitoring and self-management program. In addition, there was a trend toward a reduction of visits to the emergency department. In Spain, it has been reported that the cost of patients admitted in stroke units reaches 27,711 € per patient/year, being social costs, particularly informal care, the main determinant [41]. Therefore, more efforts are needed to reduce stroke burden and self-monitoring and self-management could be cost-effective also in Spain.

Our study has some strengths and novelties. Thus, having a website that allows patients to consult in case of doubts or incidents has only being analyzed in most recent published studies. Furthermore, all patients were carriers of mechanical prostheses, a subgroup of patients less studied and with a greater risk of thromboembolism and hemorrhage than those who were only anticoagulated due to isolated atrial fibrillation. In general, our data were in line with the available evidence.

### Limitations of the study

Our study had several limitations. First of all, it is a single-center observational study with a retrospective analysis. Our work had a slightly lower number of patients than previous studies, and the evaluation of the QoL before and after the self-program was not assessed. In addition, this was a single center study and only patients that wanted to participate were recruited. Moreover, data were limited to the first 6 months of the implementation of the program. There were no specific criteria of selection for patients to participate in the self-monitoring program. Further, given the design of the sample, the intervention group only contained individuals who wanted to participate. This fact can lead to a bias. Most of the included patients had been under conventional control for a long time and, therefore, had more experience with VKA treatment. Moreover, these patients received additional training at the start of self-program, thus this could be a reason of their better outcomes.

However, the aim of this study was to report the initial experience with self-monitoring and self-management among patients with mechanical heart valve prosthesis. In general, our data were in line with the available evidence. It is very likely that with a higher number of patients and longer follow-up, significant differences would have been reached.

### Conclusion

Oral anticoagulation self-monitoring and self-management can be an option in selected patients with mechanical heart valve prosthesis in order to provide a better INR control and to reduce thromboembolic and bleeding complications.

#### Summary points

- Developing an oral anticoagulation self-monitoring and self-management program improves anticoagulation control with low rates of thromboembolic and bleeding complications among patients with mechanical heart valve prosthesis.
- The success of self-monitoring and self-management method depends on consistent, regular and frequent testing.
- Self-monitoring and self-management is not feasible for all patients.
- The program required the identification of selected patients with a high motivation.
- Self-management increases the autonomy of the patients.
- Physicians or another healthcare provider must monitor the results obtained by the patient and must adjust the anticoagulant dose in case of poor international normalized ratio control.
- Self-monitoring and self-management seem a cost-effective approach, mainly in the case of a reduction of thromboembolic complications.



### Author contributions

All authors contributed extensively to the work presented in this paper. All authors have contributed to the conception, design, or acquisition of data, or analysis and interpretation of data. All authors have participated in drafting, reviewing, and/or revising the manuscript and have approved its submission.

### Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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### Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

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