Safety management in mechanical heart valve replacement and oral anticoagulant therapy

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Chapter 6

Failure Mode & Effect Analysis and Fault Tree Analysis in the use of the CoaguChek® Prothrombin Time Monitor

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Submitted
Chapter 6

6.1 ABSTRACT

Oral anticoagulation requires INR and dosage control. The availability of a portable device, called the CoaguChek® system, allows patient self-monitoring. In this study, this self-monitoring system is described. Then a risk analysis by means of Failure Mode & Effect Analysis and Fault Tree Analysis were applied. This systemic risk analysis revealed system weaknesses with respect to education, compliance, and technical reliability. This type of risk analysis used by the prescribing physicians can assist in recognizing increased risks of failure in the individual case as well as in analysing adverse events.
6.2 INTRODUCTION

6.2.1 Oral anticoagulant therapy

Oral anticoagulation by means of coumarin derivatives (vitamin-K antagonists) is an effective modality for the treatment and prevention of thromboembolic events in patients with prosthetic heart valves, deep-vein thrombosis, pulmonary embolism, peripheral vascular disease, after myocardial infarction, and during chronic atrial fibrillation (1). The biological effect of coumarin derivatives (measured by means of the prothrombin time (PT)) is extremely variable, which can be aggravated by various drugs, inconstant vitamin-K intake, and illnesses (vomiting, diarrhea, and febrile infection). PT fluctuations can also be due to inadequate patient counselling and poor patient compliance with respect to medication intake (2). Incorrect dosage, with either too much or too little of the medication, increases the risk of hemorrhagic or thromboembolic complications, respectively, necessitating frequent laboratory visits for venepunctures and dose adjustments.

Recently, a portable device, called the CoaguChek® system, has been granted CE certification, which means that an instrument for instant PT checks from one drop of capillary whole blood is now commercially available. The CoaguChek® system is supposed to have advantages that could lead to patient self-testing and self-adjustment of the coumarin dose:

1. tests can be done with a minimal amount of capillary whole blood, thereby avoiding venepunctures
2. tests can be done anywhere, thereby avoiding laboratory visits
3. tests can be done anytime, thereby improving dosage control
4. test results become instantly available, thereby avoiding delays in dose adjustments

6.2.2 The CoaguChek® system

The CoaguChek® system (manufactured by Roche Diagnostics, Germany) consists of the CoaguChek® monitor, CoaguChek® test strips, a lot-specific code chip and the CoaguChek® control solution. The Softclix® lancing device is used for blood collection. The CoaguChek® test strip is calibrated against HepatoQuick by the manufacturer. The calibration curve is stored for each strip number in the corresponding code chip.

Application of the CoaguChek® system involves the following action:

1. turn on the CoaguChek® meter
2. opt for either an INR blood test or a quality control procedure
3. insert a test strip
4. collect blood by means of a finger prick
5. apply blood onto the test strip
6. register the test result (the CoaguChek® monitor can store in its memory only the 30 most recent test results along with time and date)
7. determine and register the medication dose

It takes two minutes for the test result to become available. The CoaguChek® monitor measures the time from the blood’s first contact with the thromboplastin in the test strip until completion of coagulation. The results are displayed in the selected unit of measurement (INR, % Quick, or PT-calculated seconds). A quality control solution, called CoaguChek® PT Controls, is available to check the technical performance of the CoaguChek® system. After the capsule has been broken, followed by mixing of the calcium chloride solution and lyophilised citrated rabbit plasma for two minutes, the solution is ready for application onto the test strip. The CoaguChek® test result can then be compared with the predefined PT value of the control solution.

6.2.3 Aim of the study

This study was conducted in addition to a randomised crossover study comparing self-management of oral anticoagulation with management by a specialized anticoagulation clinic. The reason for doing this additional study was that although measures to prevent technical failure and human error had been taken, difficulties during the use of the CoaguChek® system by patients were observed, and evaluation of type and incidence of hazardous risks was considered necessary. A questionnaire on self-management was sent to patients in order to delineate the anecdotal problems they had encountered when using the CoaguChek® system (see appendix A). In this paper, we describe two different methods of risk analysis and the impact of the results on patient self-management of oral anticoagulation by means of the CoaguChek® system.

6.3 THE BASIC SYSTEM

Patients with an indication for long-term oral anticoagulation can determine the correct medication dose on their own by using the CoaguChek® prothrombin time (PT) monitor. After proper education and training in the use of the CoaguChek® system and adjustment of the dose, patients are able to decide when to do a PT check and how to modify the dose. When a result falls outside the predefined ranges, the patient must contact the controlling body, which will interpret the situation and test result and provide feedback. The result can be sent to the controlling body by (E-)mail or telephone (in the future, results can possibly be passed on automatically via a connection between the CoaguChek® system and the laboratory.
computer). Four main categories or subsystems are thus involved (see figure 1).

*Figure 1: The four main categories or subsystems, which function together as a system* (14).

Based on this system, failure modes per subsystem and possible measures to prevent failure can be described (failure mode & effect analysis). In addition, the probability of occurrence of adverse events can be estimated (fault tree analysis).

### 6.4 ANALYSIS BY MEANS OF FAILURE MODE AND EFFECT ANALYSIS

Failure mode and effect analysis (FMEA) is an inductive, bottom-up process (12,13). By means of FMEA one can identify the failure modes of components in a system and estimate how critical they are for the functioning of the system as a whole. In table 1 different failure-modes in relation to their subsystems are shown. The consequences of the possible failure modes are assessed (e.g., what happens in case of wrong decisions or a mixing-up of data?) and both frequency and severity of failure are evaluated. A matrix can be developed to identify risk and tolerance in order to allow effective risk control (figure 2). Possible measures per component can than be then estimated.

*Figure 2: Risk analysis matrix uses both the probability and the severity of a potential failure.*
### Table 1: Failure-modes and possible measures in relation to their subsystems.

<table>
<thead>
<tr>
<th>Subsystem</th>
<th>Components</th>
<th>Subcomponents</th>
<th>Failure Mode</th>
<th>Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient</strong></td>
<td>patient education/training</td>
<td>test/dosage/medication information over test, dosage, and medication</td>
<td>no/wrong test result, wrong dose, no/wrong medication</td>
<td>clear and repeating training program, instruction of family members, backup/helpdesk</td>
</tr>
<tr>
<td><strong>Device</strong></td>
<td>CoaguChek® teststrip/codechip</td>
<td>technical function, energy supply, calibration, environmental conditions, expiry date</td>
<td>no/wrong test result</td>
<td>'easy to use' hard- and software, sufficient power supply, technical backup, correct storage of equipment, regular quality control</td>
</tr>
<tr>
<td><strong>Data infrastructure</strong></td>
<td>CoaguChek® patient (E-)mail/fax/phone controlling body</td>
<td>data registration and transportation</td>
<td>no/wrong data registration, no/wrong data transport</td>
<td>double-check data and transport, compatible software and backup system</td>
</tr>
<tr>
<td><strong>Controlling body</strong></td>
<td>personnel equipment</td>
<td>data handling, data interpretation, and advice</td>
<td>wrong data handling, wrong interpretation, no/wrong advice</td>
<td>compatible hard- and software, training programs and update for (competent) personnel</td>
</tr>
</tbody>
</table>

### 6.5 RISK ANALYSIS BY MEANS OF FAULT TREE ANALYSIS

Fault tree analysis (FTA) is a deductive, top-down approach. Allowing identification of the global chance of occurrence of potential adverse consequences of a danger (top events) (e.g., death, complications of treatment, and missed or delayed diagnosis), in which the same conditions and quantitative estimations are used as in FMEA. Device or system design then can be improved in order to reduce or eliminate conditions that can cause undesirable or unacceptable consequences (4).

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The main potential top events (TE) in case of failure of the CoaguChek® system are hemorrhagic or thromboembolic complications. The risk of these complications is expected to be lowest when the PT is inside predefined target limits and increases when the PT is out of target limits.

(Sub)events that can lead to the top event are:
1. no/wrong test result
2. wrong dose
3. no/wrong medication
1. no/wrong advice

As mentioned earlier, the patient self-management system can be divided into four subsystems for FMEA. This division does not match that of the four events leading to the top event described above, which explains the different nature of FMEA and FTA. However, use of both methods leads to extra information and enables generation of FTA.

To calculate the probability of the top event (P(TE)), information is required about the incidence of failure of the components involved in the event. However, information about the nature of a component or the risk of subsystem failure is often not easily available. It requires active action to retrieve information or to consult independent experts to generate useful estimations. Information could be obtained by sending questionnaires to the patients and the personnel of the controlling body for information on the subsystems, and by creating a system for the reporting of component failures.

The probability of the top event can then be calculated by adding to the probability of the top event in the ‘ideal’ situation (P₀(TE)), which means a PT inside the predefined target ranges, the probabilities of occurrence of the four (sub)events described above:

\[ P(TE) = P₀(TE) + \{P(1) + P(2) + P(3) + P(4)\} \]

Attention must also be paid to the dominance of the different components, because failure of some components lead faster to the top event than others. Based on the information on the incidence and dominance of failure of the different components, measures can be taken to reduce the occurrence of the top event.

Figure 3 shows the top of the fault tree analysis. The fault tree can be made as detailed as necessary. The subsystems can be divided in components. The components can be divided in subcomponents etc.
6.6 COMMENTS

The CoaguChek® monitor seems to be an adequate instrument to accurately determine PT values \(^{(6,8,9)}\). The manufacturer has taken several quality assurance measures with respect to the device adjuncts. The manufacturer calibrates the CoaguChek® test strip. The calibration curve is stored for each strip number in the corresponding code chip. The technical performance of the CoaguChek® can be tested by means of the quality control solution. The solution contains a predefined prothrombin time value. Following the manual for quality control, there is a (predefined) target value and a control range. Recent studies have shown that the mean difference of CoaguChek® PT test results compared to standard laboratory methods is between 5 and 14 percent \(^{(7,8,16)}\). A target value of 4.6 INR units and a control range of 3.0-6.6 INR units (PT Control Lot No 241751) permits an unacceptable difference of more than 30 percent. Adjustment of the target range of the control solution will be necessary to make the quality control a valuable method in order to determine the technical performance of the device. However, FTA showed that adverse events can be caused not only by device failure but also by failure of many other components \(^{(14,15)}\). In addition, system analysis by means of FMEA and FTA reveals that subsystems and components are interdependent, and that failure of each of them can evoke a chain of events resulting in treatment failure.
The patient plays a crucial role in the system's success or failure. He is the initiator for control, communication and treatment, and accurate PT determination greatly depends on patient skills and education. Handling the CoaguChek® comprises multiple steps, which require the patient's full attention. From the outcome of the questionnaire about the CoaguChek® system, sent to 48 patients on self-management in the Netherlands (appendix A), we know that it is considered easy to use, but that the test strips are too sensitive to surrounding temperatures. In fact, the CoaguChek® system can only be used at temperatures between 18 and 32 degrees Celsius. It was also reported that too much blood was required for the CoaguChek® PT test strips. If less than 25 ml was applied, the CoaguChek® system could not measure the PT and the display showed 'sample error'. The manufacturer solved the problem by making a new test strip, the CoaguChek® PT test mini, which requires only 10 ml of blood. No sample errors occurred by using the mini strip. Another patient complaint is the confusing question 'Is this a control?' after the monitor has been switched on. This question refers to the quality control, but is often explained by patients as blood control or PT control. When blood rather than the control solution is applied and this question is answered with 'YES', the display will show 'sample error'. This problem might be solved by the use of software in the patient's native language. The CoaguChek® can operate in six different languages, however, so far the Dutch language is not available. These flaws did not lead to adverse events, but they were responsible for many of the cases of test failure. Success of device and patient self-management therefore also depends on risk redundancy and patient tolerance in terms of patient skills in coping with deviations from normal process action. It therefore remains beyond doubt that good and structured training must be given to device users and prescribers. Furthermore, regular retraining programs, counseling, and learning from an adverse event registry can prevent patients from making mistakes due to lack of knowledge or experience.

Making wrong dose adjustments or taking the wrong medication increases the risk for undertreatment or overdosing. However, the human body tolerates incorrect dose adjustments, irrespective of cause, very well. Although apparently not rare, they do not seem to lead invariably to adverse events (3,15). According to the risk analysis matrix (figure 1), the probability of occurrence of adverse events would be occasional and the severity minimal. However, such qualifications largely depend on the definition of defined target performance and the comparison of performance with that of other strategies for oral anticoagulation.

6.7 CONCLUSION

So far, the number of adverse events due to patient self-management of oral anticoagulation by means of the CoaguChek® PT test has been low. However, when one has to analyse an
adverse event from hindsight, it is difficult to discriminate between an adverse event due to the natural course of the underlying disease and that due to an avoidable treatment error.

Based on FMEA and FTA, one can

1. detect system flaws
2. provide a framework for process analysis and risk awareness
3. provide a reference to assess past incidents and safety performance (of both the system as a whole and its major components)
4. generate measures (often simple) to prevent potential failures

FMEA and FTA are transparent analyses, which can be done easily by a doctor functioning as a quality assurance manager, and assisted by workers on the floor. Besides, the addition of FMEA and FTA by prescribers and users would generate a more comprehensive understanding of risks and safety of a device (11). This would also offer the chance to set standards on how to measure and to compare outcome, either before the device is marketed or after an adverse event has been reported.

6.8 REFERENCES


