Control charts in anticoagulant treatment

Susana Rafaela Martins
Algoritmi R& D Centre
University of Minho, Braga, Portugal - maleafar@gmail.com

Pedro Nuno Ferreira Pinto de Oliveira
EPIUnit, ICBAS, Universidade do Porto, Porto, Portugal - pnoliveira@icbas.up.pt

Lino Costa
Algoritmi R& D Centre, Department of Production and Systems
University of Minho, Braga, Portugal - lac@dps.uminho.pt

Abstract

Atrial fibrillation is the common cardiac arrhythmias of these days particularly in elderly adults. Fibrillation is characterized by an abnormal operation in heart, in case the uncoordinated atria contractions result on accumulation of blood on headset and it will form a clot. This clot can move to other organs and limbs and it can trigger other medical problems. Thus, fibrillation affects the patient's life. Currently the anticoagulant treatment using warfarin is the fully validated treatment to prevent the health problems mentioned above. Oral anticoagulant therapy is the most used treatment, because through the ingestion of medication the blood will become more fluid and consequently it reduces the possibility of blood clots. A patient who undertakes this treatment should be periodically monitored to ensure maximum effectiveness of the drug and ensure that it is under control. Sometimes it is not easy to understand that anticoagulant treatment is under control, therefore control charts are an important tool to assess whether or not the coagulation is controlled. The control charts are able to detect possible changes in industrial processes, but they are used in several areas, particularly in the health services. The application of control charts in health has increased substantially and recently there have been several studies using process control techniques, in particular to support the monitoring of patients. There are several types of charts: Shewhart, EWMA and CUSUM. Shewhart charts are traditionally used to control the average of individual observations. Shewhart control charts are simple and very easy to apply and interpret for monitoring the process in real time allowing the rapid detection of changes in the process. However, some authors argue that there are better charts to detect process variations. EWMA and CUSUM charts are an alternative to Shewhart because they are more sensitive to small variations and use the information contained in all sampling, therefore they are more appropriate to study individual observations. The goal of this study is to use control charts to monitor anticoagulant treatment and choose the best chart to help this monitoring. In this work, Shewhart, EWMA, and CUSUM are applied to case studies with data collected from a public hospital. The advantages and drawbacks of each type of control chart are discussed.

Keywords: Control Charts; Anticoagulant treatment.

Acknowledgments: This work has been supported by FCT (Fundação para a Ciência e Tecnologia) in the scope of project PEst-OE/CEC/UI0319/2013.

1. Introduction

Atrial fibrillation (AF) is a common cardiac arrhythmias particularly in elderly adults. Fibrillation is characterized by short interruptions or acceleration of cardiac rhythm. These uncoordinated contractions will cause accumulation of blood and formation of clot because atrium is not completely empty. This clot can move in the body and lodge in any organ and cause health problems, such as myocardial infarction, pulmonary embolism, obstruction of the vessels of the legs, among others. That affects the patient's life, causes you the hemodynamic compromise, decreases quality life, increases health care costs, and increases risk of death. Currently, anticoagulant treatment with warfarin is fully validated to prevent those health problems.
Oral anticoagulant therapy is the most widely used and allows blood to be more fluid and consequently reduces possibility of blood clots. To ensure effectiveness of this treatment, the international normalized ratio (INR) is periodically controlled. The frequency of controls tends to vary according to the coagulation levels [7]. Therefore, it is important to develop and use a system that takes into account the patient history to monitor results control and optimize treatment in medication dosage terms. The main goal of this work is monitoring a treatment and identify abnormal situations using control charts.

2. Atrial fibrillation

Atrial fibrillation (AF) is a defective in circulatory system characterized by a cardiac arrhythmia that causes interruptions or acceleration of heartbeat. AF is most common in elderly adults and their frequency and mortality turn this arrhythmia in the important health problem. In technical terms, the AF is an extra ventricular tachyarrhythmia characterized by uncoordinated atrial activity [7]. Atrium is not totally empty due to the return or accumulation of blood and it can form a clot, or thrombus. Additional to this discomfort, the clot can move to any part of body and can cause acute myocardial infarction, pulmonary embolism, obstruction of the vessels of the legs and stroke [9]. Moreover, AF causes hemodynamic impairment, decreased cardiac performance, decreased quality life and functional status, increase risk of death and health care costs [7]. Patients with this pathology have to do an anticoagulant treatment. The anticoagulant treatment aims to thin the blood and facilitate blood circulation, preventing the formation of clots. This treatment with drug administration, usually by oral form influence vitamin K cycle and will inactivate the enzymes responsible for blood clotting. Naturally it is necessary to control this anti vitamin change by measuring INR. INR is measured with a drop of blood collecting in a small finger prick. If INR values are not within the parameterized limit values (between 2 and 3) the dosage is changed. It is important to refer that if a patient has a INR lower than limit he has a greater risk of stroke, if he has a INR upper the limit, it is increased bleeding risk [7] [9]. Monitoring and control patient using the support of process control techniques, including control charts is very important to assure his quality health.

3. Control Charts

Initially control charts appeared to detect possible changes in industrial processes. Today they are used in several areas of services in particular on health services. Application control charts in health has increased substantially. They are used in many hospital services because they contributed to an improvement of the economic and administrative management process and they improve the well-being of patients and follow-up clinician. Control charts have also been used to prevent hospital adverse conditions [4]. Recently have been several investigations using process control in health, in particular to monitoring patients. For example, Sonesson et al. (2003) realized a prospective study of statistical analysis in public health and they refer the importance of control techniques to statistical surveillance [10]. Grigg et al. (2003) also highlighted the control charts feature, in this case, using the adjusted risk in medical monitoring [5]. More recently, Correia et al. (2011) developed work in this area by applying control charts for monitoring chronic respiratory diseases [3] [2]. Control charts are important in continuous improvement processes they are use to detection of undesirable changes, but may also contribute to identification of improvements. Control charts construction is generally simple, it consists in the data sampling throughout, statistical analyze and select the best graphic

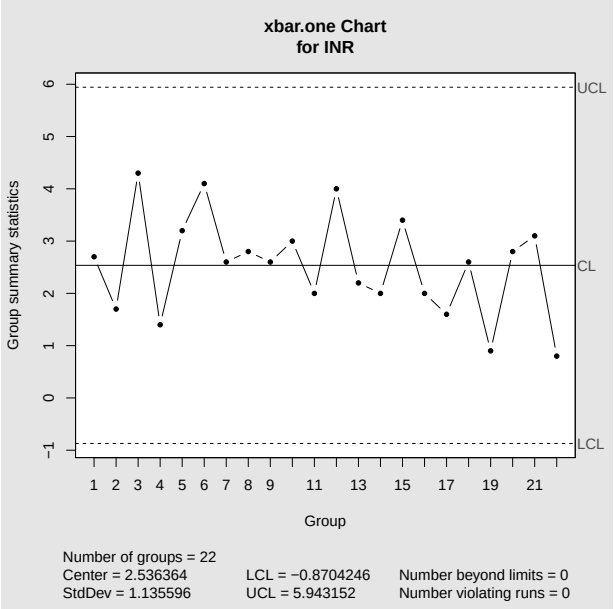
representation. These charts represent lines designated as control limits and it is expected data is between that limits if process is under control. If there are some points outside limits, it is required identify the cause, because process is out of control [4]. There are several types of charts, but the simplest are the Shewhart charts. Shewhart charts are traditionally used to control the average of individual observations or individual observations. To build these charts it is necessary that variables are normal, independent and identically distributed. Shewhart charts are easy to apply and to interpret in monitoring process on real time with real values and with rapid detection of these changes. However, some authors argue that there are better charts to detect process variations such as EWMA and CUSUM charts because they are more sensitive to small variations [3] [2]. EWMA and CUSUM charts are presented as an alternative to Shewhart charts because they use all observations obtained so far. The major advantages of these charts are that at each moment they use information contained in all sampling times, thus they are more sensitive to small deviations of process and less sensitive to normality. Therefore they are more appropriate to study individual observations. CUSUM charts have a high visual impact to illustrate the changes in the average value over the slope of the change of the points represented [4]. These charts monitor the process until something not conformed is found. The performance of these charts is evaluated by the time elapsed until detect a non-conforming element [5]. EWMA charts use a weight parameter, that it is greater in the latest observation and lowest in the others [4]. The choice of this parameter influences charts performance because the weight of each observation condition result [1]. EWMA and CUSUM charts are often similar in terms of performance particularly in the univariate case [6]. Gomes et al. (2010) consider EWMA a compromise between Shewhart and CUSUM charts because for large variations it is like the first one and for small variations it is similar to the second one. However, EWMA charts are difficult to read and interpret [4]. Anyway, the choice of control charts should be made based on the context [5]. Control charts are important to monitoring anticoagulant treatment because INR levels are the key to maintain this treatment controlled.

4. Results

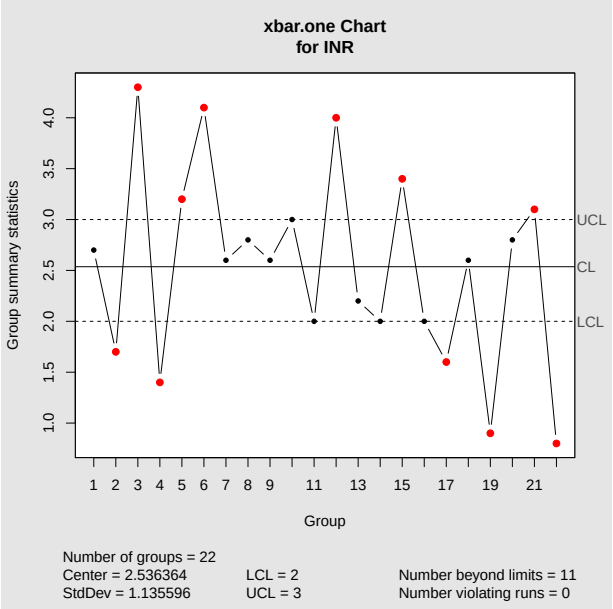
INR analysis of several patients would be very interesting and could help doctors to control them better. As a preliminary study, the data from a single patient will be analyzed with the different types of control charts. The patient was 78 years old and started doing this treatment because it was diagnosed an atrial fibrillation. Data is about one year of treatment with warfarin. In this study, it is analysed the INR data since it was the variable that the doctor considered to prescribe treatment. The control charts to analyze INR values were built using the qcc package provided by the R environment version 3.0.1 [8]. INR values of this patient were measured along about one year in 22 consultations. These values range between 0.8 and 4.3 with a mean of 2.5, a median of 2.6 and a standard deviation of 1.14. According to the Shapiro test data can be considered normal (p-value=0.81), they also have a random distribution because do not exist any pattern on points positions in the graph. Therefore, the assumptions for using Shewhart charts are satisfied. Two different Shewhart control charts are constructed: one with 3s control limits, typical Shewhart charts and one with INR acceptable limits for these patients (in medical terms).

Figure 1 show the Shewhart control charts for the INR patient's data. According to Figure 1a, it can be said that patient is controlled because data are randomly distributed since there is no pattern in the distribution and no points outside the control limits. Figure 1b shows the same distribution of the previous Figure 1a, but there are many points outside the INR acceptable limits. Thus, that patient are controlled but our INR levels are not controlled. We can say that this patient are controlled because our all INR limits are between lower control limit (LCL=-0.87) and upper control limit(UCL=5.94). But in medical terms this pattien are not controlled, because she have many INR levels that are out of recommended values.In figure1b we can see 5 points below lower recommended limit (Lower specification limit-LSC=2) and 6 points above upper recommended limit (Upper specification limit-USL=3). In other words INR levels are a behavior controlled but in medicals terms they are out of control. Therefore, it seems important to build CUSUM and EWMA charts.

Figure 2 present the CUSUM and EWMA control charts for the INR patient data. In both graphs the patient's INR values are controlled because they are within control limits. However, the CUSUM chart is not

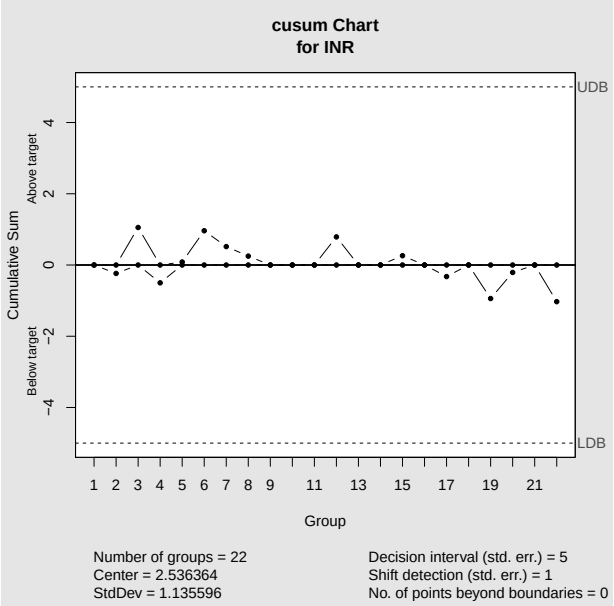


(a) Shewhart control chart with 3s control limits.

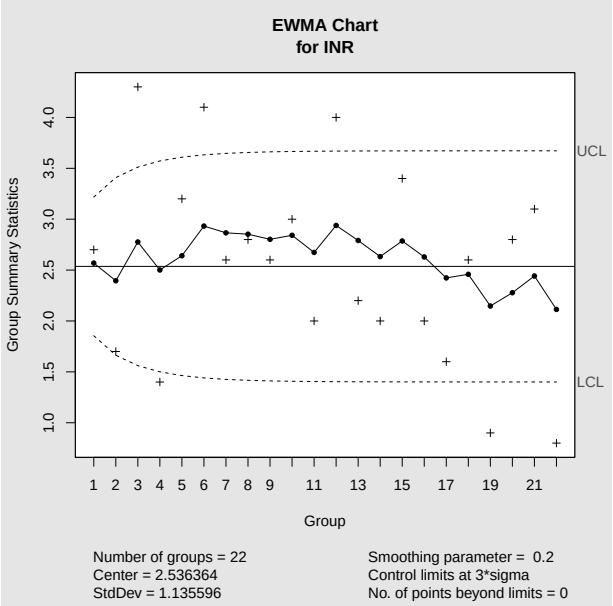


(b) Shewhart control chart with INR acceptable limits.

Figure 1: Shewhart control charts.



(a) CUSUM control chart.



(b) EWMA control chart.

Figure 2: CUSUM and EWMA control charts.

very powerful when data are not independent, which is the case because an observation is influenced by the previous ones. In the EWMA chart, all points appear within the control limits, but some patient's INR values are outside and, in practical terms, this can leave doubt in doctor interpretation because two informations seem contradictory. Besides it is more difficult to doctors to understand the plotted values in the chart and, generally, to interpret this chart. Shewhart charts seem be the most appropriate for this purpose.

5. Conclusions

In this paper, INR data from a patient is considered to build different types of control charts. Based on the results, Shewhart charts seem to be the best charts to monitor INR levels because they are most simple and use real values. Moreover, they are more natural to doctor interpret. As future work, it is intended to improve this study, considering a large number more patients to compare the different charts. Furthermore, it is also intended to study others variables, for example blood pressure and prothrombin time because they also have influence on blood circulation and consequently on INR levels.

References

[1] Polona K. Carson and Arthur B. Yeh. Exponentially weighted moving average (ewma) control charts for monitoring an analytical process. *Industrial & Engineering Chemistry Research*, 47(2):405–411, 2008.

[2] Florbela Correia, Rui Nêveda, and Pedro Oliveira. Chronic respiratory patient control by multivariate charts. *International Journal of Health Care Quality Assurance*, 24(8):621–643, 2011. PMID: 22204267.

[3] Florbela Correia and Pedro Oliveira. Control charts and chronic respiratory patients. *Biometrical Letters*, 47(1):69–81, 2010.

[4] Maria Ivete Gomes, Fernanda Figueiredo, and Maria Isabel Barão. *Controlo Estatístico de Qualidade*. Sociedade Portuguesa de Estatística, 2 edition, 2010.

[5] Olivia A Grigg, VT Farewell, and DJ Spiegelhalter. Use of risk-adjusted cusum and rsprtcharts for monitoring in medical contexts. *Statistical methods in medical research*, 12(2):147–170, 2003.

[6] Michael D. Joner, William H. Woodall, Marion R. Reynolds, and Ronald D. Fricker. A one-sided mewma chart for health surveillance. *Quality and Reliability Engineering International*, 24(5):503–518, 2008.

[7] J.C.O. Maralo. Novas opções terapeuticas de hipocoagulação na fibrilhação auricular. Master's thesis, Universidade do Porto, 2010.

[8] R Core Team. *R: A Language and Environment for Statistical Computing*. R Foundation for Statistical Computing, Vienna, Austria, 2014.

[9] EPE Serviço de Cardiologia do Hospital de Setúbal. Saiba mais hipocoagulação e fibrilhação auricular, 2010.

[10] Christian Sonesson and David Bock. A review and discussion of prospective statistical surveillance in public health. *Journal of the Royal Statistical Society: Series A (Statistics in Society)*, 166(1):5–21, 2003.