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Context-Sensitive Clinical Alert Packages Written in Arden Syntax

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Abstract

An increasing body of raw patient data is generated on each day of a patient's stay at a hospital. It is of paramount importance that critical patient information be extracted from these large data volumes and presented to the patient's clinical caregivers as early as possible. Contemporary clinical alert systems attempt to provide this service with moderate success. The efficacy of the systems is limited by the fact that they are too general to fit specific patient populations or healthcare institutions. In this study we present an extendable alerting framework implemented in Arden Syntax, which can be configured to the needs and preferences of healthcare institutions and individual patient caregivers. We illustrate the potential of this alerting framework via an alert package that analyzes hematological laboratory results with data from intensive care units at the Vienna General Hospital, Austria. The results show the effectiveness of this alert package and its ability to generate key alerts while avoiding over-alerting.

Keywords:

Decision Support Systems, Clinical; Laboratory Critical Values; Infection Control

Introduction

Given the increasing body of raw clinical data being provided in electronic medical record (EMR) systems, a quality control mechanism is needed to ensure that potentially critical patient information is extracted from these large data volumes and offered to the appropriate patient caregivers in a timely manner. Clinical alerts are a part of such information; they make the patients' caregivers aware of immediate pathological, unusual, or occasionally life-threatening circumstances concerning the patient.

Electronic storage of patient data creates opportunities for computerized monitoring of patients and subsequently computerized generation of clinical alerts. Over the years, a substantial number of monitoring systems have been developed for a variety of healthcare settings, especially in the fields of infection control and adverse event detection [1-5]. The benefits of such systems are manifold: they offer complete and timely information on patients who require the immediate attention of caregivers, errors can be prevented, patient safety is enhanced, and institutional quality standards for patient care are upheld or improved.

A drawback of these systems is that their embedded detection rules or classification methods are usually based on guidelines for "standard" cases. As such, the generated monitoring results and alerts may be valid only for patients without additional underlying conditions. For example, de Bruin et al. describe an automated surveillance system for monitoring healthcare-associated infections [6]. In their study, a false-positive infection episode was detected due to a large number of leukocytes. However, the underlying cause of the leukocyte abnormality was not an infection but the patient's leukemia.

Modification of existing systems is not a viable option. There is usually little room for system or module customization; the systems are provided "as-is". This limits their use in healthcare environments other than the one(s) they were developed for. Individual institutions or even departments within an institution may employ different guidelines or different interpretations of the same guideline. A configurable and extendable framework of alert systems was developed by the use of established standards for the creation and integration of clinical decision support systems (CDSSs). The framework can be used directly at the point of care, and is tailored to the needs and preferences of healthcare institutions, departments, or even individual caregivers.

In this paper we present a preliminary version of such a framework for clinical alerts. Using Arden Syntax [7], an HL7 International [8] standard for computerized representation and processing of medical knowledge, we created an alert framework that supports configuration according to departmental or institutional requirements, such as the configuration of critical value limits, optimization of alert frequency to prevent over-alerting, and adaptable alert timing. Using patient data obtained from the Vienna General Hospital (VGH), Austria, we describe the potentialities of this alerting framework through an implemented alert package for the analysis of hematological laboratory test results. By way of an example, time- and context-sensitive clinical alerts were constructed for two infection parameters: *C-reactive protein (CRP) concentration* and *leukocyte count*. The alert package provides alerts for "standard" situations, as well as a variety of nonstandard contexts, such as underlying leukemia or preexisting infection episodes. Furthermore, alerts can be configured to the preferred frequency, thus avoiding excessive alerting.

Table 1 – Definitions of clinical alerts in an alert package for the analysis of hematological laboratory test results, including the respective alert description and context

Alert variable	ID	Message	Context	Rule
CRP concentration				
	C1	Slightly increased CRP	Previous value in the normal range or no previous value	20 mg/l ≤ CRP concentration < 50 mg/l
	C2	Moderately increased CRP	Previous value in the normal range or no previous value	50 mg/l ≤ CRP concentration < 100 mg/l
	C3	Significantly increased CRP	Previous value in the normal range or no previous value	CRP concentration ≥ 100 mg/l
	C4	Further increase of CRP	No leukemia, 4^{th} day of infection and beyond, value available between 12 and 36 hours prior to the current value.	CRP concentration ≥ 20 mg/l **and** $\frac{\text{CRP concentration} - \text{yesterday's CRP concentration}}{\text{yesterday's CRP concentration}} \geq 0.20$
Leukocyte count				
	L1	Leukocyte value indicates leukopenia	-	0.5 G/l < leukocyte count ≤ 3 G/l
	L2	Leukocyte value indicates leukocytosis. Admission diagnosis: leukemia	Leukemia	Leukocyte count ≥ 12 G/l
	L3	Significant increase of leukocytes	-	$\frac{\text{Leukocyte count} - \text{previous leukocyte count}}{\text{previous leukocyte count}} \geq 0.4$
	L4	Significant decrease of leukocytes	-	$\frac{\text{Leukocyte count} - \text{previous leukocyte count}}{\text{previous leukocyte count}} \leq -0.4$
	L5	Increased leukocytes compared to previous finding	No leukemia, no previous infection, previous value in the normal range.	Leukocyte count ≥ 12 G/l
	L6	Persistent leukocytosis	No leukemia, 4^{th} day of infection and beyond, value available between 12 and 36 hours prior to the current value	Leukocyte count ≥ 12 G/l **and** $\frac{\text{leukocyte count} - \text{yesterday's leukocyte count}}{\text{yesterday's leukocyte count}} \geq -0.10$

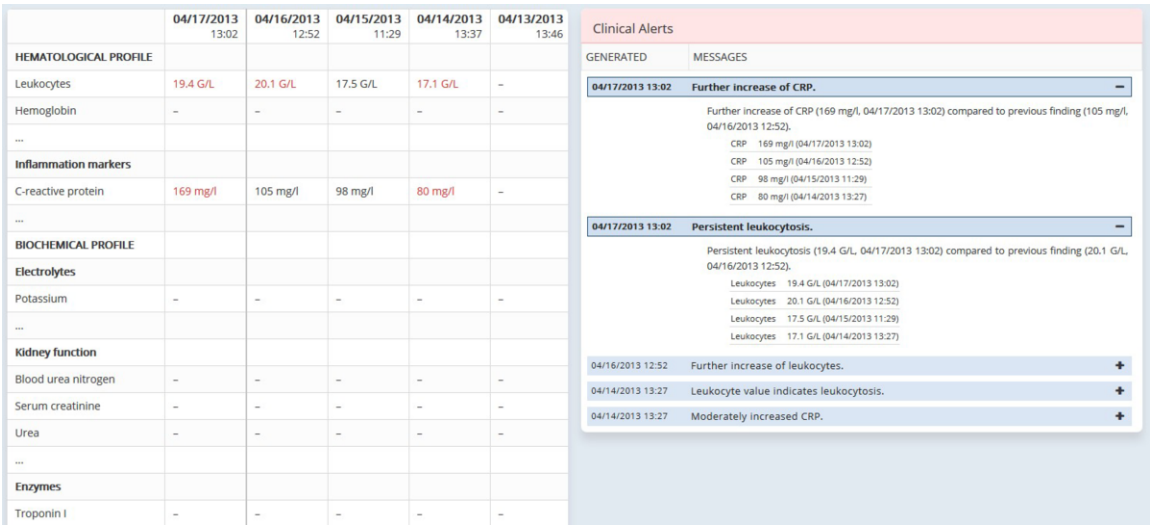

Figure 1 – The HTML5 web application frontend. On the left side, the patient's laboratory values for C-reactive protein (CRP) and leukocytes are displayed for the present day and three preceding days; values in red are associated with a clinical alert. On the right side, clinical alerts are displayed together with a short description. On clicking the alert, a more detailed alert message is shown along with an overview of the laboratory values related to the alert over the past few days. Alerts shown in bold type are those for the present day.

Methods

Outcome and variables

The primary outcome measures were the frequency and nature of the alerts generated by the alert package for each of the aforementioned clinical variables.

We used patient demographics (age, sex, length of stay) to describe the patient population. Laboratory data for the clinical variables *CRP concentration* (mg/l), and *leukocyte count* (G/l) were used for the generation of alerts. We report on the number of generated alerts for each alert rule.

Study design, setting, and participants

A retrospective single-center cohort study was performed on prospectively collected and validated data at VGH, a 1,933- bed tertiary-care and teaching hospital, and was approved by the ethics committee of the Medical University of Vienna. All adult patients (i.e., age ≥ 18 years) admitted to a VGH intensive care unit (ICU) for at least 24 hours between 1 January and 31 December 2013 were eligible for the study. Patients for whom laboratory values for both clinical variables (CRP concentration and leukocyte count) were not available were excluded from the study.

Data management and sample size

Demographic patient data as well as laboratory test results were retrieved from the Philips IntelliSpace Critical Care and Anesthesia information system, which is in operation at almost every ICU of the VGH.

The interrogation of data sources using the previously mentioned selection criteria yielded a total of 266 patient stays comprising 2,830 patient days.

Knowledge base and data processing

The alert package discussed in this paper is part of a framework consisting of automated, context-sensitive and customizable alert packages targeting a variety of issues in clinical routine. They were created by repeated discussions with experienced clinical experts and by eliciting their feedback on a variety of use cases in which alerts were generated for different clinical situations. Based on these discussions and feedback, alert rules were implemented by clinical knowledge engineers that, based on laboratory test results for the aforementioned clinical parameters, generate one or multiple (different) alerts. We discuss ten alerts that were defined in the knowledge base: four for CRP levels and six for leukocyte count. These alerts, together with their context and corresponding rules, are shown in Table 1.

The alerts were implemented in a knowledge base with Arden Syntax. The latter is a programming language for the collection, description, and exchange of medical knowledge in a computer-executable format. For this project we used Arden Syntax version 2.10 [7]. An Arden Syntax knowledge base comprises a set of programming units known as medical logic modules (MLMs) [9]. In all 17 MLMs were constructed; 14 MLMs for data import and preprocessing, and three MLMs for alert generation for a variety of contexts.

Implementation, management, testing, and execution of the MLMs were done using the ARDENSUITE clinical decision support technology platform, which comprises an integrated development and test environment (IDE), as well as the ARDENSUITE server to execute MLMs [10]. The ARDENSUITE server can be accessed through web-service protocols, i.e., representational state transfer (REST) [11] or simple object access protocol (SOAP) [12].

Data presentation

For data presentation, an HTML5 web application was created using the Ionic framework [13] (Figure 1). Upon selecting a patient in the web application, the necessary MLMs are accessed using JavaScript JQuery [14] commands through REST calls. The ARDENSUITE server extracts parameter values from the POST REST call and executes the called MLM(s) with these parameters. The alerts generated by these MLMs are then transmitted back to the web application through a JavaScript Object Notation (JSON) [15] object and displayed in the web application.

Results

Of the 266 patients included in the study, 115 were female (43%). The patients' mean age was 61 years, with an interquartile range (IQR) of 21 years. The mean duration of the hospital stay was 11 days, with an IQR of 11 days.

In all 5,492 data entries were registered for the two clinical variables: 2,697 entries (49%) for CRP levels and 2,795 for leukocyte counts. Values for both variables were available for 2,662 patient days (94%), only CRP levels were available for 35 patient days (1%), and only leukocyte counts for 135 patient days (5%).

During the study period a total of 2,382 alerts were generated for CRP levels and leukocyte count, amounting to an average of 0.89 alerts per patient day. The maximum number of alerts displayed on a single patient day was four; the most numerous alerts displayed for a single patient during his/her stay was 90, over a period of 81 days.

CRP levels were alerted on 459 occasions (19.3%), and leukocyte counts on 1,923 occasions. Table 2 shows the number of times each alert listed in Table 1 was generated.

Table 2 – Frequency of clinical alerts generated during the study period for each alert defined in Table 1.

Alert ID	#Generated
C1	133
C2	84
C3	79
C4	163
L1	95
L2	1,032
L3	214
L4	88
L5	161
L6	333
Total	**2,382**

Discussion

We present a configurable framework for clinical alerts implemented in Arden Syntax. Using the framework, healthcare institutions, departments, and patient caregivers can adapt alerts to make them more relevant and useful, and avoid over-alerting. Alert fatigue is a very serious problem in clinical routine. Various studies on alerting suggest that by far the large majority of alerts are ignored or overridden [16, 17]. Most patient caregivers (about 90%) do not respond to all alarms, but rather match their response rates to the expected probability of true alarms [18]. In view of these facts, it would be very important to use an alerting framework that can be configured to the preferences of a healthcare institution or caregiver. Last but not least, this would maximize the caregiver's perception of the usefulness of alerts.

Through cooperation with clinical experts, it became evident that there is no real objective metric to establish when an alert is justified or not. Rather, there are some guidelines to when an alert is useful, namely, when it can be acted upon by some kind of intervention. Furthermore, there are some expectations as to the number of generated alerts; most physicians do not expect more than one alert per person per patient day. With a maximum of four alerts per day and an average of 0.89 alerts per patient day, the alert package discussed here proved to be quite conservative in its alerting frequency.

Of all the alerts, L2 was generated significantly more often (in all 1,032 times; see Table 2) than the others. This may be partly explained by the fact that the alert rule is very straightforward and therefore more likely to be generated. However, the L2 alert was only meant for patients with leukemia, which makes it less likely than many others. MLMs and data consultation disclosed that the leukemia diagnosis of a patient was not included in the data transfers from VGH. Therefore, the check as to whether the patient had leukemia was not conducted by the MLM; a leukocyte count of $\geq$ 12 G/l was used as the sole criterion. This resulted in the alert being generated for all patients with a leukocyte count $\geq$ 12 G/l and not adhering to the specific context of L2, which also explains the large number.

The limitations of this study are worthy of mention. First, as this was a pilot feasibility study, we conducted a retrospective cohort study on prospectively collected data. As such, prospective behavior in this framework still needs to be studied. Furthermore, as the pilot study was conducted on a single-center basis, the generalizability of these results needs to be reviewed as well. A third limitation is the lack of other relevant patient data. Although there are alerts especially for patients with leukemia, the (admission) diagnosis for leukemia by itself is regrettably not part of the data volume to distinguish between infection-triggered leukocytosis and leukemia. Finally, we need to assess the ease and practicality of adapting MLMs to caregivers' preferences while adhering to institutional guidelines. Although the implemented alert package has been tested and adapted by clinical partners with diverse clinical backgrounds, a more extensive study with data outside the ICU setting and with multiple alert packages will be carried out for a better analysis of the framework.

Conclusion

We presented a configurable framework for automated alerting based on electronic patient data. We showed the feasibility and potentialities of the system with respect to its configuration for different contexts and the optimization of alert frequency.

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