

The Software Development and Design Based Approach in Assessing the Probability of Essential Hypertension Disease

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Abstract

Background and objectives: Software design and development for cardiovascular genetics laboratories.

Materials and methods: Integrated development environment-Delphi 7.0, Pascal language. In this program were laid down results of a retrospective analysis of hypertensive patients hospitalized in the Department of Arterial Hypertension (AH) of the Republican Specialized Center of Cardiology (RSCC) for the period from 2011 to 2013 y., passed the clinical and genetic testing according to the plan of Research Project ADCC-15.13.1. The study included 100 healthy volunteers and 800 patients with I-II grade of essential hypertension EH, all of them were Uzbek males in the mean age of 48.3 ± 8.1 yrs. The study was approved by the medical ethical committee of the center of cardiology, Tashkent Uzbekistan. Informed consent was obtained from each individual recruited.

Results: We have attempted to develop «CDS» application for the genetics cardiology department. For support parameters, we took the results of SNP-genotyping cardiovascular markers, biochemical, clinical parameters, as well as nutritional status. We have developed «GeneSecure» platform with «CDS» for IBM Pentium, Windows OS.

Conclusion: The polygenic nature of EH and incomplete update patient records significantly reduce diagnostic effect of the CDS. However, in some cases, the CDS are not always able to clearly determine the synergistic and intergenomic effect of analyzed genes. These issues occur when the volume of new data exceeds the amount of filer memory, leading to the appearance of these areas, which are very difficult to manage.

Keywords: Electronic Medical Records (EMR); Clinical Decision Support (CDS); Single Nucleotide Polymorphisms (SNP); DNA Database; Essential Hypertension (EH)

Introduction

It is known that the gene impact on the development of essential hypertension (EH) can range from low to high risk. In this regard, it is logical to suppose that the use of a genetic test is an important aspect of modern predictive medicine. However, cardiologist and clinical genetics consultation for the analysis of these large data is not enough today. A potential solution to this problem might be «CDS» application that can synchronize the genetic and clinical information in the context of essential hypertension pathology. At present there are 2,500 clinical genetic tests available to physicians [1,2]. Therefore be unreasonable to expect that the physician is able to remember each genetic test for each state in conjunction with the main clinical features of the patient [3]. Today, these conservative operations can take the clinical decision support system «CDS». These advanced systems usually operate within the electronic medical records «EMR», DNA databases and «CDS» dispatcher [4]. The demand for such systems is gradually increasing in hospitals and medical centers, especially in the cardiac profile. It is known that the gene impact on the development of essential hypertension (EH) can range from low to high risk. In this regard, it is logical to suppose that the use of a genetic test is an important aspect of modern predictive medicine [5]. However, cardiologist and clinical genetics consultation for the analysis of these large data is not enough today. A potential solution to this problem might be «CDS» application that can synchronize the genetic and clinical information in the context of essential hypertension pathology.

The aim of the present study was to develop the software design for cardiovascular genetics laboratories.

Materials and Methods

In this program were laid down results of a retrospective analysis

of hypertensive patients hospitalized in the Department of Arterial Hypertension (AH) of the Republican Specialized Center of Cardiology (RSCC) for the period from 2011 to 2013, passed the clinical and genetic testing according to the plan of Research Project ADCC-15.13.1. The study included 100 healthy volunteers and 800 patients with I-II grade of EH, all of them were Uzbek males in the mean age of 4.3 ± 8.1 yrs. The study was approved by the medical ethical committee of the center of cardiology, Tashkent Uzbekistan. Informed consent was obtained from each individual recruited.

The software development and design

Integrated development environment-Delphi 7.0, Pascal language. For support parameters, we took the results of SNP-genotyping cardiovascular markers, biochemical, clinical parameters, as well as nutritional status.

Genetic cardiovascular risk prediction

Continuous variables were expressed as mean \pm standard deviation and categorical variables as percentages. Differences in continuous variables between cases and controls were examined using the

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Systems	Genes	Negative genotypes	DC
ENDOTHEL	B2BKR / +9/-9	9+/-9	0.6
	eNOS / 4a/4b	4a/4b	2.1
SNS	ADRB3 / Trp64Arg	T/T	3.6
	β2-AR / Gln27Glu	Glu27Glu	2.4
RAAS	ACE / I/D	D/D	1
	CYP11B2 / C344T	T/T	1.8

Table 1: Genetic panel.

disease duration of 5.4 ± 4.41 years (LVMI 159.8 ± 35.55). The highest blood pressure was recorded on a level of 220/130 mm Hg (0.5% of the sample). The highest level of total cholesterol, total cholesterol recorded in 2 patients at the level of 327 mmol/l at the age of 52 years. Only 13% of patients from the whole sample had a weight within the normal range (BMI 23.43 ± 1.17). Registration of the genotyping results has identified an association RAAS system genes (*CYP11B2*/S344T; *ACE*/I/D) with the risk of violations of water-salt metabolism, ENDOTHEL system genes (B2BKR/+9/-9; eNOS /4a/4b) with the risk of endothelial dysfunction, SNS system genes (ADRB3/Trp64Arg; B2-AR/Gln27Glu) with insulin resistance development risk.

As a result of «CDS» system testing revealed significant deficiencies. First of all it concerned the lack of coordination between the EMR, the DNA database and «CDS» dispatcher due to the autonomy of some clinical modules architecture. Another problem has been related with the understanding and use of the tool. Is not uncommon the «CDS» conclusion does not coincide with the findings of the clinician. Perhaps the reason for this controversy is the effect of syntropy and differences between the standards of norms of laboratory parameters, or forms of treatment standards in the care process.

Conclusion

Thus, the carrier state of TT-damaging genotype of *CYP11B2* gene and DD-genotype of *ACE* gene have been identified in 39% and 25% cases, respectively. The CDS showed a tendency to a violation of water-salt metabolism in patients with TT- genotype of *CYP11B2* gene and DD- genotype of the gene *ACE* gene via multivariate analysis. This displacement may be observed due to renal dysfunction caused by *CYP11B2* and *ACE* genes regulation, the mechanism of Na^+ - exchange through diuresis.

The detected connection of 4a/4b-genotype (eNOS gene) and 9+/-9 (B2BKR gene) with the development of endothelial dysfunction in 24% and 8% cases respectively, is most likely due to coupling of the polymorphic marker and site mutation leading to a change of NO production by endothelial cells.

Also the CDS has identified Glu/Glu - homozygous connection of β2-AR gene and high body mass index (BMI) with impaired glucose

tolerance and systolic blood pressure in obese patients. The identified association of T/T-genotype of *ADRB3* gene and Glu/Glu-genotype of β2-AR gene with the developing insulin resistance risk in 50% and 8% cases respectively confirmed that these genes mediate the physiologic effects of adrenaline.

However, in some cases, the CDS are not always able to clearly determine the synergistic and intergenomic effect of analyzed genes. These issues occur when the volume of new data exceeds the amount of filer memory, leading to the appearance of these areas, which are very difficult to manage. The polygenic nature of EH and incomplete update patient records significantly reduce diagnostic effect of the CDS.

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