Retrospective analysis of clinical decision support system use in patients with hypertension and atrial fibrillation (INTELLECT)

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Aim. To evaluate the relationship between the clinical decision support system use (CDSS) and adherence to clinical guidelines.

Material and methods. Medical records of 300 patients with atrial fibrillation and hypertension from the electronic medical database of the Almazov National Medical Research Center were analyzed. Demographic and clinical data, as well as information on anticoagulant, antiarrhythmic and antihypertensive prescriptions were analyzed. The primary endpoint was adherence of prescribed treatment to current clinical guidelines for each of the three therapies. Firstly, a group of independent clinical experts assessed primary endpoint for retrospective prescriptions. Secondly, new prescriptions were simulated by another group of clinical experts using CDSS and blinded to previous therapy. Primary endpoint at the second step was analysed by independent experts. We compared adherence to relevant clinical guidelines with and without use of CDSS. Additionally, we analyzed predictors of failing to meet the current recommendations in the retrospective records.

Results. Out of 300 patients, only 291 (97%) had all characteristics and were included in the analysis. In 26 patients (18%), all three treatment strategies were in accord with current clinical guidelines. Anticoagulant therapy was adherent to the guidelines in 92% of cases. Experts who used CDSS were 15% (95% confidence interval [CI], 10-21%) more likely to prescribe novel oral anticoagulants and 14% (95% CI, 10-19%) less likely to prescribe warfarin compared to baseline. Antiarrhythmic therapy was adherent to the guidelines in 69% of cases. When the CDSS platform was applied, experts were 14% (95% CI 4-19%) more likely to prefer antiarrhythmic drug (AAD) monotherapy and 32% (95% CI 26-37%) more often prescribed radiofrequency ablation (RFA) of left atrium. At baseline, antihypertensive therapy combinations were adherent clinical guidelines in 28% of cases. The use of the CDSS platform by experts was significantly associated with an increase in the frequency of prescribing dual and triple antihypertensive therapy.

Conclusion. CDSS use is associated with improved adherence to current clinical guidelines. Prospective randomized trials are needed to evaluate the CDSS effectiveness in the prevention of cardiovascular events.

Keywords: artificial intelligence, atrial fibrillation, hypertension, clinical guidelines, clinical decision support system.

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Trial ID: NCT04564118 (www.clinicaltrials.gov).

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Atrial fibrillation (AF) and hypertension (HTN) are socially significant diseases and are often combined with each other. HTN occurs in 60–80% of patients with AF. In patients with HTN and AF, the risk of cardiovascular diseases, such as stroke and myocardial infarction, is several times higher [1].

Clinical guidelines attempts to integrate up-to-date information about treatments and allows a physician to help guide decisions about which drug group or treatment is appropriate for a patient. A number of studies have shown that decision-making algorithms, according to clinical guidelines, help to reduce the number of adverse events in patients and improve the effectiveness of treatment [2-8].

There is a large time gap between the daily update of patient care data and the current guidelines, which are updated every 3-6 years.

Currently, there are no convenient algorithms for clinical guidelines for physicians, nurses, pharmacists that could improve the prognosis of patients and help healthcare in general. In some countries, for example, in the USA, clinical decision support systems (CDSSs) are being developed and actively introduced into clinical practice, which can improve the quality of care for the population and reduce healthcare costs.

Modern CDSSs have evidence-based proven efficacy, which has been demonstrated in a number of publications [2-8].

The MedicBK is a CDSS computer program that allows the analysis of published clinical data and suggests therapy options in accordance with the latest guidelines, data from the latest clinical studies, and individual patient characteristics.

The aim was to assess the compliance of the prescribed therapy with current published data [9, 10], as well as to assess the relationship between MedicBK use and the compliance of treatment with clinical guidelines.

Material and methods

The study included data from 300 patients over 18 years of age with nonvalvular AF and HTN who underwent out- or inpatient treatment at the Almazov National Medical Research Center in the period from 2019 to 2020. The protocol is registered at www.clinicaltrials.gov: NCT04564118.

The study did not include patients with secondary HTN, AF due to thyroid disease, acute coronary syndrome within prior 6 months, active liver disease, glomerular filtration rate <30 ml/min.

After entering the main characteristics of patients into the CDSS database, 7 expert cardiologists from the Federal Almazov National Medical Research Center appointed therapy for these patients using this program. This CDSS allows selecting a therapy based on its efficacy and safety in accordance with the current clinical guidelines for management of HTN and AF, as well as up-to-date data from the latest publications. During analysis, experts assessed the compliance of the proposed therapy for AF and HTN with clinical guidelines [11, 12]. Each of the included patients was simulated with CDSS treatment assignment. The primary endpoint was the assessment of the compliance of prescribed therapy in medical records with the current guidelines on AF and HTN, as well as a comparison of the previous prescriptions with the therapy selected using CDSS.

Operational concept of CDSS. CDSS based on data from modern clinical studies, which are subjected to statistical processing. The choice of CDSS characteristics is due to a set of features that have proven their influence on cardiovascular events and are included in various risk stratification scores. On the other hand, the CDSS takes into account the signs that are absolute contraindications for some drugs. The indirect comparison using network meta-analysis is used as the main tool for assessing the effectiveness and safety of therapy. The network meta-analysis results are presented as an intervention effectiveness/safety measure for each pairwise comparison, followed by a forest plot. In addition, P-scores are calculated, demonstrating that a specific intervention has an advantage over all other interventions [13]. For visualization, the P-scores are presented as a scatterplot. The content was evaluated by experts of the Almazov National Medical Research Center and showed compliance with modern guidelines on AF and HTN. Detailed information on the CDSS methodology is available at http://mediebk.com.

Statistical processing. The sample was formed from a total of 2560 electronic health records (EHR) for 2019. To form the sample, we used the sample command for R language, which generated a sequence of 300 random numbers without replacement. The resulting sequence was applied to numbered list of patients in such a way that patients were randomly included in the sample.

Quantitative and qualitative variables are presented as mean±standard deviation and as absolute and (in parentheses) relative values, respectively. The McNemar’s test was used to compare the qualitative traits (type of therapy) between the register data and expert prescriptions, and in some cases the difference in absolute risks and related 95% confidence interval (CI) were calculated. If the latter rules out zero, the intergroup difference is considered significant.

All analyzes were performed using the R programming language (R Core Team (2020). R: A language and environment for statistical computing.
Results

Due to insufficient EHR data necessary for treatment decision-making, 9 patients were excluded from the analysis. The characteristics of 291 included patients are presented in Table 1. The study included men and women aged 32 to 90 years (mean age, 67.3±10.3 years).

| Parameter | n 291 |
|-----------|-------|
| Hospitalization | 66 (22.7%) |
| Outpatient visit | 225 (77.3%) |
| Men | 134 (46.0%) |
| Age, years | 67.3±10.3 |
| Height, cm | 169.8±10.0* |
| Weight, kg | 87.5±18.6† |
| Prior antihypertensive therapy | 220 (75.6%) |
| Uncomplicated hypertension | 191 (65.6%) |
| Coronary artery disease | 124 (42.6%) |
| Prior percutaneous coronary intervention | 4 (5.2%) |
| Hypercholesterolemia | 176 (60.4%) |
| Bradycardia | 90 (30.9%) |
| Atrioventricular block | 33 (11.3%) |
| Hypertrophic cardiomyopathy | 94 (32.3%) |
| Heart failure | 188 (64.6%) |
| Cerebrovascular disease | 55 (18.9%) |
| Diabetes | 62 (21.3%) |
| Chronic kidney disease | 72 (24.7%) |
| Hyperkalemia | 35 (12.0%) |
| Hypokalemia | 31 (10.6%) |
| Gout | 11 (3.8%) |
| Severe COPD | 12 (4.1%) |
| Bilateral renal artery stenosis | 2 (0.7%) |
| Prior major bleeding | 0 (0.0%) |
| Liver disease | 32 (11.0%) |
| Prior angioedema | 13 (4.4%) |
| Constipation | 5 (1.7%) |
| Smoking | 33 (11.3%) |
| Alcohol abuse† | 6 (2.7%) |
| Regular exercise | 8 (2.7%) |

Note: * — no data in 62 (21.3%) patients, † — no data in 64 (22.0%) patients.

Abbreviation: COPD — chronic obstructive pulmonary disease.

A significant proportion of patients (77%) were treated on an outpatient basis. Most of them took antihypertensive therapy before seeking help.

The study design is shown in Figure 1.

Anticoagulant therapy did not meet the guidelines in 8% of patients, mainly due to the appointment of low molecular weight heparins and antiplatelet agents. Experts who used CDSS were 15% (95% CI, 10-21%) more likely to prescribe new oral anticoagulants and 14% (95% CI, 10-19%) less likely to prescribe warfarin compared to the EHR data.

Antiarrhythmic therapy did not meet the guidelines in 31% of cases. Experts who used CDSS 14% (95% CI, 4-19%) more often preferred antiarrhythmic monotherapy and 32% (95% CI 26-37%) more often prescribed pulmonary vein ablation (Table 2).

According to EHR data, combined antihypertensive therapy did not formally meet clinical guidelines in 72.5% of cases (Table 3). The most common inappropriate prescription was monotherapy. Perhaps this was due to patients’ preferences due to fear of polypharmacy. At the same time, the CDSS use by experts was significantly associated with an increase in prescription rate of dual and triple therapy: the experts worked with a patient model without taking into account psychosocial factors.

Only in 18% of the 291 included patients, all three therapies complied with current clinical guidelines (Tables 2 and 3). Specifically, three out of four antihypertensive therapy prescriptions did not meet recommendations.

Abbreviations: HTN — arterial hypertension, AF — atrial fibrillation, CDSS — clinical decision support system, DSS — decision support system, EHR — electronic health record.
### Table 2

**Anticoagulant and antiarrhythmic therapy**

| Therapy                                | EHR appointments, N (%) | Experts + CDSS, N (%) |
|----------------------------------------|-------------------------|-----------------------|
|                                        | Total                  | Adequate              | Total                  | Adequate              |
| Anticoagulant                          | 291 (100.0%)           | 268 (92.1%)           | 291 (100.0%)           | 291 (100.0%)†         |
| Novel oral anticoagulants              | 224 (79.7%)            | 224 (79.7%)           | 277 (95.2%)*           | 277 (95.2%)           |
| Rivaroxaban                            | 96 (34.1%)             | 96 (34.1%)            | 8 (2.7%)*              | 8 (2.7%)              |
| Apixaban                               | 109 (38.8%)            | 109 (38.8%)           | 202 (69.4%)*           | 202 (69.4%)           |
| Dabigatran                             | 19 (6.7%)              | 19 (6.7%)             | 67 (23.8%)*            | 67 (23.8%)            |
| Warfarin                               | 47 (16.1%)             | 43 (15.3%)            | 5 (1.7%)*              | 5 (1.7%)*             |
| Therapy is not indicated               | 10 (3.6%)              | 0 (0.0%)              | 4 (1.3%)               | 4 (1.3%)              |
| Left atrial appendage occlusion        | 0 (0.0%)               | 0 (0.0%)              | 8 (2.7%)*              | 8 (2.7%)              |
| Other therapy                          | 10 (3.4%)              | 0 (0.0%)              | 0 (0.0%)               | 0 (0.0%)              |
| Antiarrhythmic†                        | 291 (100.0%)           | 201 (69.1%)           | 291 (100.0%)§          | 291 (100.0%)§         |

**Rhythm control**

| Therapy                                | EHR appointments, N (%) | Experts + CDSS, N (%) |
|----------------------------------------|-------------------------|-----------------------|
|                                        | Total                  | Adequate              | Total                  | Adequate              |
| Antiarhythmic drugs                    | 71 (24.4%)             | 66 (22.6%)            | 112 (38.4%)*           | 112 (38.4%)           |
| Pulmonary vein RFA                     | 2 (0.7%)               | 0 (0.0%)              | 93 (32.0%)*            | 93 (32.0%)            |
| Therapy is not indicated               | 3 (1.0%)               | 0 (0.0%)              | 0 (0.0%)               | 0 (0.0%)              |
| Other therapy                          | 6 (2.1%)               | 6 (2.1%)              | 0 (0.0%)               | 0 (0.0%)              |

**Rate control**

| Therapy                                | EHR appointments, N (%) | Experts + CDSS, N (%) |
|----------------------------------------|-------------------------|-----------------------|
|                                        | Total                  | Adequate              | Total                  | Adequate              |
| Antiarhythmic drugs                    | 3 (1.0%)               | 3 (1.0%)              | 0 (0.0%)               | 0 (0.0%)              |
| Beta Blocker‡                          | 56 (19.2%)†            | 56 (19.2%)†           | 71 (24.4%)*            | 71 (24.4%)            |
| Atrialventricular nodal RFA            | 1 (0.4%)               | 0 (0.0%)              | 6 (2.0%)               | 6 (2.0%)              |
| Non-dihydropyridine calcium channel blocker | 2 (0.7%)             | 2 (0.7%)              | 4 (1.3%)               | 4 (1.3%)              |
| Beta-blocker + non-dihydropyridine calcium channel blocker | 1 (0.4%)               | 1 (0.4%)              | 1 (0.4%)               | 1 (0.4%)              |
| Digoxin                                | 1 (0.4%)               | 1 (0.4%)              | 3 (1.0%)               | 3 (1.0%)              |
| Beta-blocker + digoxin                 | 15 (5.1%)              | 15 (5.1%)             | 1 (0.4%)*              | 1 (0.4%)              |
| Therapy is not indicated               | 3 (1.0%)               | 0 (0.0%)              | 0 (0.0%)               | 0 (0.0%)              |
| Other therapy                          | 2 (0.7%)               | 2 (0.7%)              | 0 (0.0%)               | 0 (0.0%)              |

**Note:** * — p<0.05 (McNemar’s test between the total number of appointments in the register and the number of appointments by experts using CDSS); † — in 10 cases with a CHA2DS2-VASc score of 1 (for men) and 2 (for women), anticoagulant therapy was recommended, which does not contradict the guidelines, since the final decision remains with the doctor; ‡ — 74 patients received beta-blocker monotherapy with as a component of antihypertensive therapy; § — in 4 cases the experts prescribed allapalin, which is not supported by CDSS; † — in 3 cases, patients were prescribed combination therapy (left atrial appendage occlusion and warfarin).

**Abbreviations:** RFA — radiofrequency ablation, CDSS — clinical decision support system, EHR — electronic health record.

### Table 3

**Antihypertensive therapy**

| Therapy                                | EHR appointments, N (%) | Experts + CDSS, N (%) |
|----------------------------------------|-------------------------|-----------------------|
|                                        | Total                  | Adequate              | Total                  | Adequate              |
| Monotherapy                            | 75 (25.7%)             | 4 (1.3%)              | 0 (0.0%)               | 0 (0.0%)              |
| Dual therapy                           | 79 (27.1%)             | 36 (12.3%)            | 102 (35.0%)*           | 102 (35.0%)           |
| Triple therapy                         | 67 (23.0%)             | 21 (7.2%)             | 120 (41.2%)*           | 120 (41.2%)           |
| Triple boosted therapy                 | 59 (20.2%)             | 19 (6.5%)             | 69 (23.7%)             | 69 (23.7%)            |
| Therapy is not indicated               | 11 (3.8%)              | 0 (0.0%)              | 0 (0.0%)               | 0 (0.0%)              |
| Total                                  | 291 (100.0%)           | 80 (27.5%)            | 291 (100.0%)§          | 291 (100.0%)          |

**Note:** * — p<0.05 (McNemar’s test between the total number of appointments in the register and the number of appointments by experts using CDSS); † — in 25 cases, the therapy offered by CDSS had absolute contraindications, which is not taken into account by current clinical guidelines.

**Abbreviations:** CDSS — clinical decision support system, EHR — electronic health record.
Discussion
This work demonstrates the importance and significance of CDSS in selection of optimal treatment strategy for a specific patient according to clinical guidelines in order to reduce the risk of future cardiovascular events. Currently, the main documents regulating treatments by diseases are clinical guidelines [11, 12], created based on evidence-based clinical studies. Given the growing number of patients with various comorbidities and risk factors, the application of clinical trials results in everyday practice requires more time to make the right decision. In most cases, the guidelines describe the appointment of a drug group, while information on a specific drug should be read in the additional literature. The presented clinical study to assess the effect of CDSS on the choice of treatment for patients with HTN and AF is the first in Russia and suggests making a decision on the prescription of a specific drug based on clinical trials.

Comparative analysis demonstrated the compliance of anticoagulant, antiarrhythmic and antihypertensive therapy in 18% of cases. Most often, discrepancies with clinical guidelines were observed in antihypertensive therapy (72.5%). When making a decision on the appointment of antihypertensive therapy, CDSS offered more than 10-15 combinations that are difficult to remember and analyze during conventional office visit without using special software. CDSS use was associated with a significant increase in prescription rate of combined antihypertensive therapy, which may be due to the availability and objectivity of combination selection. When prescribing multiagent treatment regimens, absolute and relative contraindications for one of the drugs are not always taken into account, which is also difficult to foresee in patients with multimorbidity.

In the publications evaluating the effectiveness of antihypertensive therapy, along with assessing the accuracy of the doctor’s adherence to clinical recommendations, an emphasis is placed on increasing patient adherence to treatment [5, 14]. To minimize the risk of cardiovascular events, it is necessary to take into account and analyze all available risk factors in a specific patient, based on current clinical guidelines, which CDSS allows to do.

Comparative analysis of antiarrhythmic therapy before and after CDSS use revealed a discrepancy between the initially prescribed therapy and clinical guidelines in 31% of cases. It is known that neither drug therapy nor catheter ablation has a significant advantage in mortality rate of AF patients [15]. However, in patients who underwent pulmonary vein ablation, there is a long-term significant decrease in arrhythmia recurrence with a lower hospitalization rate and, as a consequence, significantly better quality of life [16]. The present study showed that in case of CDSS use, experts were 32% more likely to recommend pulmonary vein isolation, which can improve quality of life.

When deciding on the anticoagulant therapy in a patient with AF, a cardiologist can use fairly simple risk scores for thromboembolic events (CHA₂DS₂-VASc) and bleeding (HAS-BLED). However, observational studies showed that only ~60% of patients with AF receive anticoagulant therapy in accordance with clinical guidelines [12]. At the same time, the use of novel oral anticoagulants demonstrates the best efficacy and safety profile (lowest risk of thromboembolic events, major cardiovascular events, and all-cause mortality) [17, 18].

Analysis of three therapy directions (antihypertensive, anticoagulant and antiarrhythmic), the anticoagulant therapy showed the lowest incidence of non-compliance with clinical guidelines (8%). In the overwhelming majority of patients, this was due to the prescription of low molecular weight heparins during bridging anticoagulation before the pulmonary vein isolation. According to current guidelines, bridge therapy has no clinical benefits and is associated with an additional bleeding risk [9]. As for outpatient stroke prevention, the use of CDSS was accompanied by an increase in prescription rate of novel oral anticoagulants by 14%. This, in turn, decrease the risk of any adverse cardiovascular events. There were also significant differences in the choice of a specific anticoagulant agent in favor of more effective and safer drugs.

Thus, this study shows that CDSS greatly facilitates a physician’s work in choosing the optimal therapy that fully complies with clinical guidelines for a particular patient, which should ensure not only the clinical effect, but also, possibly, should reduce the risk of cardiovascular events.

Study limitations. This was a retrospective study, which did not allow assessing the causal relationship between the CDSS use and the endpoint. The study did not assess the CDSS impact on prognosis, since in the context of COVID-19 pandemic, it was difficult to arrange face-to-face patient visits to assess hard endpoints. Experts made decisions based on the given characteristics without taking into account the patient wishes and social factors. To assess the objective impact of CDSS on prognosis, it is necessary to conduct a study in an actual clinical practice.
Conclusion

The INTELLECT study revealed a formal discrepancy between the prescribed therapy and current clinical guidelines in 82% of cases. CDSS use is associated with improved adherence to current clinical guidelines. Prospective randomized trials are needed to evaluate the CDSS effectiveness in the prevention of cardiovascular events.

Relationships and Activities: none.

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