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# Factors associated with in-hospital mortality in patients after acute cerebrovascular accident (according to the REGION-M register)

Zagrebelny A. V.[1], Lukina Yu. V.[1], Kutishenko N. P.[1], Lukyanov M. M.[1], Dmitrieva N. A.[1], Voronina V. P.[1], Okshina E. Yu.[1], Lerman O. V.[1], Blagodatskikh S. V.[1], Nekoshnova E. S.[1], Budaeva I. V.[1], Boytsov S. A.[2], Drapkina O. M.[1], Martsevich S. Yu.[1] on behalf of the REGION-M# workgroup

[1]National Medical Research Center for Preventive Medicine. Moscow; [2]National Medical Research Center of Cardiology. Moscow, Russia

**Aim.** To determine the main factors associated with in-hospital mortality in patients after acute cerebrovascular accident based on the medical history data.

**Material and methods.** The study used the data of retrospective hospital part of the REGION-M register, which included all patients hospitalized in one Moscow city clinical hospital from January 1, 2012 to March 30, 2017 with stroke and transient ischemic attack. We analyzed the presence of following parameters' information in case histories of patients who died in hospital and those who were discharged: risk factors (RF), socio-demographic factors, history of cardiovascular and concomitant diseases. The association of factors recorded at hospital admission with mortality rate was studied, and multivariate logistic regression was constructed. A combination of factors significantly associated with in-hospital mortality was determined.

**Results.** Of 900 patients (365 (40,6%) men and 535 (59,4%) women) included in the REGION-M register, 216 (24,0%) died in the hospital. Assessment of the RF information presence showed that the smoking data was disclosed in 54,3% of case histories, family history — 1,1%, education level — 8,6%, alcohol consumption — 7,4%, disability — 79,1%, hypercholesterolemia — 6,4%. However, there were no significant differences on the completeness of the data collection on the listed RF between deceased and discharged patients. Factors such as gender, age, and outcome were described in all case histories. Univariate analysis of factors significantly associated with patients' mortality marked out age and history of cardiovascular diseases (coronary artery disease (CAD), atrial fibrillation (AF), venous thrombosis) and/or concomitant diseases (diabetes, anemia). Multivariate logistic regression identified factors associated with increased in-hospital mortality as follows: CAD, AF, diabetes, venous thrombosis.

**Conclusion.** Hospital-based physicians pay little attention to the recording of cardiovascular RF and socio-demographic parameters in patients with stroke, regardless of the condition severity and outcome. In-hospital mortality is associated with age, CAD, AF, diabetes, and venous thrombosis.

**Key words:** stroke, register, risk factors, in-hospital mortality.

**Relationships and Activities.** The study was financially supported by a Pfizer grant, which did not affect the study management, analysis of the results and conclusions made.

#Region-M register workgroup: Akimova A. V., Arutyunov G. P., Belova E. N., Blagodatskikh S. V., Boytsov S. A., Budaeva I. V., Vernokhaeva A. N., Viskov R. V., Voronina V. P., Gladilkina M. P., Deev A. D., Dmitrieva N. A., Drapkina O. M., Zagrebelny A. V., Kvitivadze G. K., Kudryashov E. N., Kokareva I. V., Kudryashov E. V., Kutishenko N. P., Lerman O. V., Lukina Yu. V., Lukyanov M. M., Martsevich S. Yu., Matveeva A. D., Matskevich L. A., Mitichkin A. E., Nikitina G. I., Nekoshnova E. S., Ovsepyan M. A., Okshina E. Yu., Palamarchuk V. N., Parsadanyan N. E., Porezanova M. V., Stakhovskaya L. V., Stolboushkina E. A., Hapaeva M. A., Chernyshova M. I., Shamalov N. A.

Zagrebelny A. V. ORCID: 0000-0003-1493-4544, Lukina Yu. V. ORCID: 0000-0001-8252-3099, Kutishenko N. P. ORCID: 0000-0001-6395-2584, Lukyanov M. M. ORCID: 0000-0002-5784-4525, Dmitrieva N. A. ORCID: 0000-0001-8119-9645, Voronina V. P. ORCID: 0000-0001-5603-7038, Okshina E. Yu. ORCID: 0000-0001-7891-3721, Lerman O. V. ORCID: 0000-0002-3299-1078, Blagodatskikh S. V. ORCID: 0000-0001-8445-0153, Nekoshnova E. S. ORCID: 0000-0003-0294-9618, Budaeva I. V. ORCID: 0000-0002-4789-5863, Boytsov S. A. ORCID: 0000-0001-6998-8406, Drapkina O. M. ORCID: 0000-0002-4453-8430, Martsevich S. Yu. ORCID: 0000-0002-7717-4362.

*Corresponding author:
azagrebelny@mail.ru, azagrebelny@gnicpm.ru

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## Introduction

Among cardiovascular diseases (CVD) and their complications, for several decades, stroke has been one of the leading deaths causes in the adult population in many countries [1].

Registries are now widely used to study the clinical and demographic characteristics of patients after stroke, its risk factors (RF) and factors affecting the clinical course of disease, the development of complications, death, and to assess the quality of treatment at various management stages.

The registry is a type of observational study carried out in accordance with certain rules for the inclusion of patients, collection, storage and processing of data, which helps in solving a number of research and practical issues of modern health care [2, 3]. One of the largest stroke registries today is the Get With The Guidelines-Stroke (GWTG-Stroke) program created in 2003 with the participation of the American Heart Association/American Stroke Association, which by 2016 had included >4 million patients with stroke [4, 5]. In various regions of the Russian Federation, registries of patients with stroke are also maintained [6-9]. However, not all registries assessed the prognostic value of various factors, as well as long-term prospective follow-up was rarely carried out. More often, the significance of various factors on the stroke development was studied in the registers.

It should be emphasized that the mortality rate in stroke is extremely high both in the acute phase and in the long-term follow-up of patients. According to Russian registries, in-hospital mortality with stroke is ~20% or more, while in foreign registries it varies from 5% to 16%, and in recent years this parameter has decreased [10, 11]. During the first year after stroke, almost every second patient dies, and after 5-8 years, the mortality rate reaches 60-80% [12-14]. Despite the high mortality rate, the significance of various factors influencing the death risk of such patients may vary at different stages of the disease course and differ in different regions.

The aim was to identify the main factors associated with hospital mortality in stroke patients in the retrospective hospital part of the REGION-M registry and which is included in the REGION registry [15].

## Material and methods

The design and protocol of the REGION study, carried out in the Moscow and Ryazan, were described in detail in the earlier publications [15, 16].

The REGION-M registry, conducted in Moscow, consisted of 2 stages of patient follow-up: retrospective in-hospital and prospective out-of-hospital.

This article analyzes the results of the in-hospital retrospective part of the REGION-M registry, which included all patients hospitalized in I. M. Inozemtsev City Clinical Hospital of Moscow from January 1, 2012 to March 30, 2017 with stroke and transient ischemic attack. Patients discharged from the hospital were included in the second, prospective, inpatient part of the registry.

The registry protocol was approved by the Independent Ethics Committee of the National Medical Research Center for Preventive Medicine.

The main attention was paid to the analysis of medical history. The registry records contained the patient's passport data, information about the disease onset and the characteristics of hospitalization, as well as data on physical examination and diagnostic tests. A large section of records was devoted to collecting information about the prior CVDs, their RFs, complications, surgical interventions, and data on concomitant diseases. A special section of the records was devoted to information on the results of diagnostic tests performed in the hospital. We collected data on drug therapy taken by patients before hospitalization, in the hospital and recommended to the patient at discharge. Data on the surgeries performed during hospitalization was also collected.

A feature of the retrospective registry is inability to clarify information. However, the authors considered that no information about a disease is one thing, while no data on the RF is another. Therefore, if in-patient records did not contain information about previous CVDs and concomitant diseases, these diseases were considered absent. If there was no information about any RFs, then it was considered that there was no information about it.

Information from the registry records was entered into a specially developed electronic database.

The analysis of the obtained indicators of patients who died in hospital and were discharged was carried out.

In the presented article, for the analysis, we selected the factors registered at the prehospital stage and studied their contribution to mortality rate with the creation of a multiple logistic regression model.

Statistical processing of the obtained data was performed using the IBM SPSS Statistics 23 software (IBM Corp., USA).

At the first stage, using the descriptive statistics, the main characteristics of patients included in the registry were presented: patients who died during hospitalization and patients discharged from the hospital. Absolute values and percentages for qualitative traits were determined. Quantitative indicators were analyzed for distribution normality. Mean values and standard deviations for normally distributed quantitative traits were calculated. Median and interquartile range for non-normally distributed traits were calculated.

At the second stage, the completeness of data collection was assessed. If the prevalence of studied trait was <80%, it was not included in further analysis, since this could lead to false results.

At the third stage, using the Pearson's chi-squared test or Fisher's exact test (for 2×2 contingency tables), factors were identified that were significantly associated with in-hospital mortality.

At the fourth stage, a logistic regression model was created to determine a combination of factors with adjustment for sex and age that have a significant effect on in-hospital mortality. Data are presented as odds ratios with 95% confidence intervals.

## Results

The REGION-M registry included 900 patients after stroke: 365 (40,6%) men and 535 (59,4%) women. The mean age of patients was 70,6±14,0 years. The age of women was significantly higher than in men (73,3±13,9 vs 66,5±13,2 years, respectively ($p<0,001$)) (Figure 1). In the hospital, 216 (24,0%) patients died, and 684 (76,0%) patients were discharged.

The mean age of the deceased patients was 76,8±11,5 years, while of those discharged from the hospital — 68,6±14,2 years ($p<0,001$). Among the deceased patients, there were 133 (24,9%) women and 83 (22,7%) men (mean age, 80,1±9,1 years and 71,4±12,8, respectively ($p<0,001$)). Among the patients

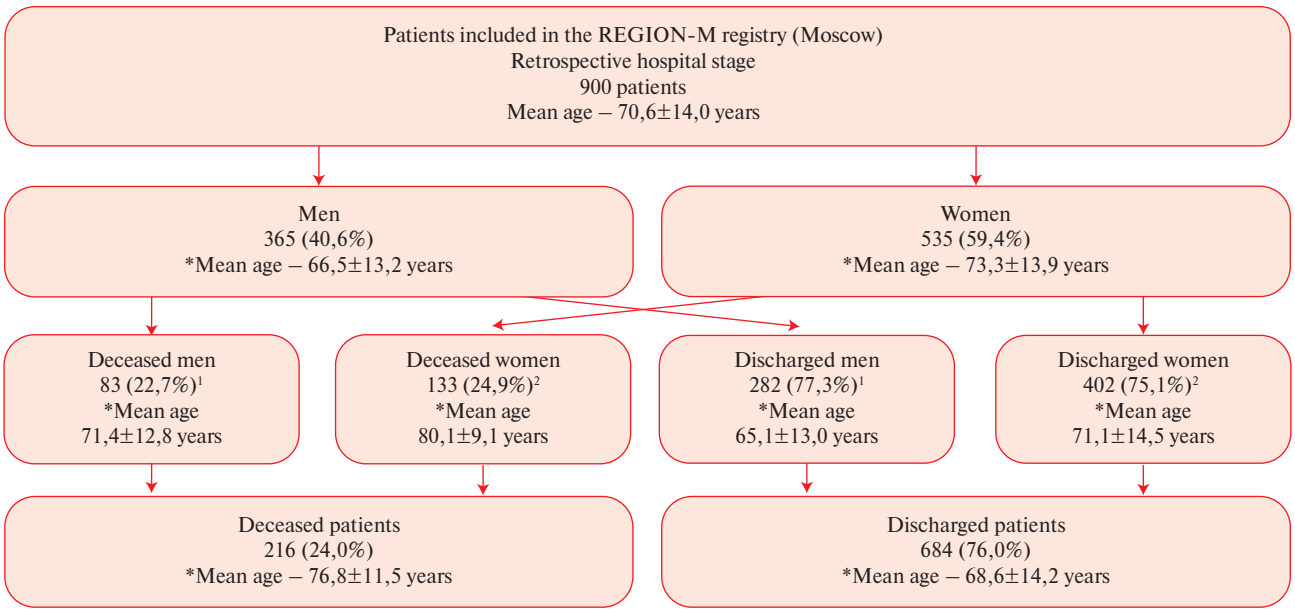



*Figure 1.* General characteristics of patients.
Note: * — p<0,001; [1] and [2] — indication of the group composition and comparison of the reliability of the difference in average age by sex.

**Table 1**

Frequency of indicating medical history data (n=900)

| Parameter | Survived (n=684) | Deceased (n=216) | Total (n=900) |
|---|---|---|---|
| Sex | 684 (100%) | 216 (100%) | 900 (100%) |
| Age | 684 (100%) | 216 (100%) | 900 (100%) |
| Smoking status | 394 (57,6%) | 95 (44,0%) | 489 (54,3%) |
| Family history of CVD | 7 (1,0%) | 3 (1,4%) | 10 (1,1%) |
| Education level | 56 (8,2%) | 21 (9,7%) | 77 (8,6%) |
| Hypercholesterolemia | 53 (7,7%) | 5 (2,3%) | 58 (6,4%) |
| Alcohol | 52 (7,6%) | 15 (6,9%) | 67 (7,4%) |
| Disability | 552 (80,7%) | 160 (74,1%) | 712 (79,1%) |

who were discharged, there were 402 (75,1%) women and 282 men (77,3%) (mean age, 71,1±14,5 years and 65,1±13,0 years, respectively (p<0,001)) (Figure 1).

Data on the completeness of information collection are presented in Table 1. Sex and age were indicated in all patients. Smoking status was noted in 489 (54,3%) patients, of which only 104 patients smoked (21,3%) and 385 did not. The presence of information about disability was in 79,1% of patients, about hypercholesterolemia — in 58 (6,4%) patients, about alcohol consumption — in 67 (7,4%) patients, about heredity — in 10 (1,1%) of patients. It is important to note that the prevalence of the studied factors practically did not differ between deceased and surviving patients (Table 1).

Due to the fact that the prevalence of the studied factors was complete only by sex and age, and data on other indicators did not exceed 80%, they were not included in further analysis.

Tables 2 and 3 present data on CVDs and comorbidities in history. Among CVDs, the most common were hypertension (HTN) in 856 (95,1%) patients and coronary artery disease (CAD) in 517 (57,4%) patients. Less commonly indicated were atrial fibrillation (AF) (29,8%), heart failure (HF) (18,2%), single myocardial infarction (MI) (19,7%), and stroke (25,7%). The presence of thrombosis was noted in 3,4%, heart defect — 3,0%, MI ⩾2 times — 2,2%, TIA — 2,5% of patients. The results demonstrated higher rates of in-hospital mortality in patients with stroke with a history of CVD and/or concomitant disease. In patients with a combination of CAD, prior MI and AF, in-hospital mortality was 30%. The mortality rate of patients with a history of stroke, HF, and HTN was slightly lower (~25%).

Every fifth patient had diabetes (n=181 (20,1%)) and obesity (n=193 (21,4%)). Moreover, approximately a third of patients (33,1%) with diabetes and every fifth (22,3%) patient with obesity died in the hospital (Table 3).

Chronic lung diseases were indicated in 120 (13,3%) out of 900 patients, cancer — in 90 (10%),

**Table 2**

Data on CVDs

| CVD | Total (% of n=900) | Deceased n=216 (% **) | Discharged n=684 (% ***) | p ($\chi^2$) |
|---|---|---|---|---|
| Stroke | 216 (25,7%) | 59 (27,3%) | 157 (23,0%) | 0,191 |
| TIA | 21 (2,5%) | 3 (1,4%) | 18 (2,6%) | 0,292* |
| CAD | 517 (57,4%) | 166 (76,9%) | 351 (51,3%) | <0,0001 |
| Single MI | 177 (19,7%) | 58 (26,9%) | 119 (17,4%) | 0,002 |
| MI ⩾2 times | 20 (2,2%) | 6 (2,8%) | 14 (2,0%) | 0,525* |
| HF | 164 (18,2%) | 39 (18,1%) | 125 (18,3%) | 0,942 |
| HTN | 856 (95,1%) | 209 (96,8%) | 647 (94,6%) | 0,406 |
| AF | 268 (29,8%) | 94 (43,5%) | 174 (25,4%) | <0,0001 |
| Heart defect | 27 (3,0%) | 11 (5,1%) | 16 (2,3%) | 0,075 |
| Thrombosis | 31 (3,4%) | 16 (7,4%) | 15 (2,2%) | <0,0001 |

Note: * — Fisher's exact test, ** — % of deceased patients, *** — % of discharged patients.

**Table 3**

Data on comorbidities

| Concomitant disease | Total (% of n=900) | Deceased n=216 (% **) | Discharged n=684 (% ***) | p ($\chi^2$) |
|---|---|---|---|---|
| IGT | 81 (9,0%) | 14 (6,5%) | 67 (9,8%) | 0,138 |
| Diabetes | 181 (20,1%) | 60 (27,8%) | 121 (17,7%) | 0,001 |
| Anemia | 74 (8,2%) | 28 (13,0%) | 46 (6,7%) | 0,004 |
| Obesity | 193 (21,4%) | 43 (19,9%) | 150 (21,9%) | 0,528 |
| Cancer | 90 (10,0%) | 26 (12,0%) | 64 (9,4%) | 0,252 |
| Chronic kidney disease | 80 (8,9%) | 21 (9,7%) | 59 (8,6%) | 0,744 |
| Massive bleeding | 3 (0,3%) | 1 (0,5%) | 2 (0,3%) | 0,705* |
| Chronic lung disease | 120 (13,3%) | 30 (13,9%) | 90 (13,2%) | 0,783 |

Note: * — Fisher's exact test, ** — % of deceased patients, *** — % of discharged patients.

impaired glucose tolerance (IGT) — in 81 (9,0%), chronic kidney disease — in 80 (8,9%), anemia — in 74 (8,2%). In 3 (0,3%) patients, there was prior massive bleeding. The mortality rate among patients with the listed comorbidities was also high: from 17,3% in patients with IGT to 37,8% in patients with a history of anemia.

According to statistical analysis, the presence of CAD, prior MI, AF, venous thrombosis, diabetes and anemia was associated with a higher in-hospital mortality (p<0,05) (Tables 2 and 3).

Figure 2 shows the fourth stage of statistical processing with the creation of a multivariate logistic regression model adjusted for sex and age. Factors such as age, history of CAD, AF, diabetes, venous thrombosis increase in-hospital mortality. The presence of HF in patients was associated with mortality decrease (p<0,008).

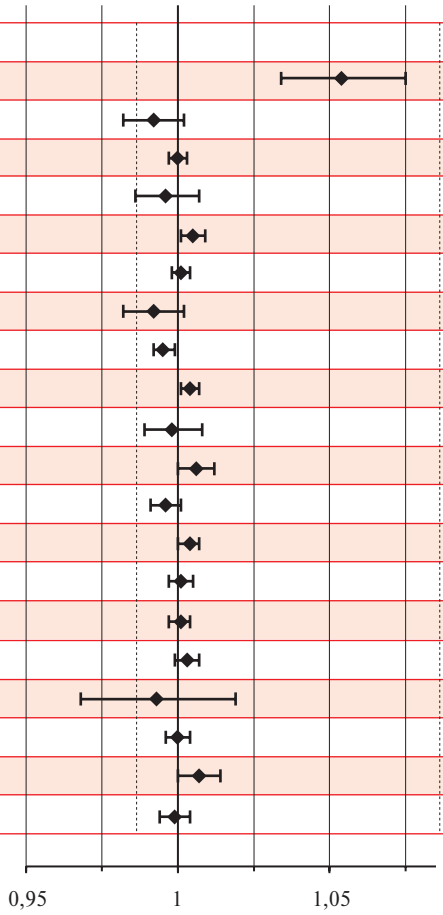
## Discussion

According to REGION-M registry, in-hospital mortality remains extremely high: almost every fourth patient hospitalized with stroke dies in the hospital (24,0%). The mortality rate in the groups of men and women differed insignificantly (22,7% vs 24,9%, respectively), however, the mean age of deceased patients was ~9 years higher (p<0,001) in women compared to men. The mean age of the deceased men and women was significantly higher (p<0,001) compared with the mean age of discharged patients (Figure 1).

The obtained indicators coincide with another in- and out-of-hospital registry of patients with stroke (LIS-2), according to which in-hospital mortality was 21,6% [5]. The sex and age ratios of patients who died and were discharged from the hospital were approximately the same as in REGION-M [5]. Women accounts for most of both deceased patients (65,7%) and all those admitted to the hospital (61,6%).

In another Russian registry of inpatients with stroke, conducted in the Smolensk Oblast [6], approximately the same results were obtained: the predominance of women among both admitted and discharged (~60%) patients. Moreover, the mean age of deceased women was >8 years higher than the mean age of deceased men.

In comparison with foreign studies, it was found that in-hospital mortality in stroke patients in Russia is higher: 21-24% vs 5,2-5,6% [3, 12]. The authors of foreign registries emphasize that in the middle of




| Parameter | OR (CI 95%) | p |
|---|---|---|
| Age | 1,054 (1,034-1,075) | p<0,0001 |
| Sex | 0,992 (0,982-1,002) | p=0,117 |
| Stroke | 1,000 (0,997-1,003) | p=0,953 |
| TIA | 0,996 (0,986-1,007) | p=0,492 |
| CAD | 1,005 (1,001-1,009) | p=0,006 |
| Primary MI | 1,001 (0,998-1,004) | p=0,61 |
| Recurrent MI | 0,992 (0,982-1,002) | p=0,127 |
| HF | 0,995 (0,992-0,999) | p=0,008 |
| AF | 1,004 (1,001-1,007) | p=0,006 |
| HTN | 0,998 (0,989-1,008) | p=0,719 |
| Heart defect | 1,006 (1,000-1,012) | p=0,069 |
| IGT | 0,996 (0,991-1,001) | p=0,14 |
| Diabetes | 1,004 (1,000-1,007) | p=0,031 |
| Chronic lung disease | 1,001 (0,997-1,005) | p=0,654 |
| Obesity | 1,001 (0,997-1,004) | p=0,687 |
| Anemia | 1,003 (0,999-1,007) | p=0,16 |
| Massive bleeding | 0,993 (0,968-1,019) | p=0,589 |
| Cancer | 1,000 (0,996-1,004) | p=0,993 |
| Thrombosis | 1,008 (1,000-1,014) | p=0,038 |
| Chronic kidney disease | 0,999 (0,994-1,004) | p=0,675 |

*Figure 2.* Parameters associated with in-hospital mortality in patients with stroke.
Note: sex adjusted for age; other factors adjusted for sex and age.

the first decade of 21st century, in-hospital mortality in patients with stroke, even in developed countries, was 15-17%, and such a significant decrease in mortality was achieved only after creation of special stroke departments [6, 12]. It should be emphasized that in the Moscow hospital, on the basis of which REGION-M was carried out, a special center was also created. As shown in Russian studies, a set of measures implemented in stroke centers has significantly reduced the rate of stroke mortality in total mortality pattern from 19,2% in 2010 to 15,9% in 2016 [17].

Since the hospital part of REGION-M was retrospective, the studied indicators from the medical records reflect the data actually noted by the doctors. It was impossible to clarify information, respectively, with a quantitative and qualitative analysis of these indicators. It is clear that not all of factors could be included in the logistic regression.

An example of insufficient diagnosis and/or insufficient data on the patient's anamnesis can be the analysis of hypercholesterolemia, which was not included in the logistic regression model, since the information on it was only in 58 out of 900 patients. At the same time, out of 900 patients with stroke, 216 patients had prior stroke, 177 patients — MI, 517 patients — CAD. Such indicators suggest the presence of a greater number of lipid metabolism disorders in patients with a history of severe cardiovascular disease.

The study showed that only sex, age, and outcome of the disease were indicated in all patients, since this information is required when filling out the medical records. The presence of other indicators is significantly lower, which may be partly due to the impossibility of a qualitative history collection by doctors in patients with stroke upon admission and/or due to insufficient attention to these RFs. The smallest number of patients included in REGION-M had data on heredity, alcohol consumption, hypercholesterolemia, and educational level. Smoking is indicated a little more than half of the patients. Information on disability was noted in 80% of patients. It can be seen that data on RFs did not always depend on the disease outcome (mortality), and hence on the patient's condition during hospitalization. For example, information on smoking status was available in 394 (57,6%) survived and 95 (44%) deceased patients, while the data on hypercholesterolemia was noted in 53 (7,7%) and 5 (2,3%) patients, respectively. For the

rest of RFs, the difference in deceased and discharged patients did not exceed 1% (Table 1).

REGION-M registry was the closest to the LIS-2 registry in terms of objectives and methods. According to the LIS-2 registry, there was also a significant amount of unknown data on studied factors and diseases. For example, a history of hypercholesterolemia was unknown in 67,5% of all patients, while the obesity status was not indicated in 36,3% of patients. The proportions of patients with diabetes in the LIS-2 and REGION-M registries differed insignificantly — 20,6% and 20,1%, AF — 26,8% and 29,8%, HTN — 86,8% and 95,1%, stroke — 20,7% and 25,7%. The proportion of patients with CAD (15,6%) and myocardial infarction (12,8%) in the LIS-2 registry were significantly less.

The univariate analysis revealed the following factors associated with hospital mortality: age, CAD, MI, AF, HF, venous thrombosis, diabetes and anemia. When the selected factors were included in the multivariate analysis, it was found that the age of patients, a history of AF, diabetes, CAD, and thrombosis were associated with an increase in in-hospital mortality (Figure 2). The presence of HF in patients was associated with a decrease in mortality.

The factors associated with a high in-hospital mortality in the REGION-M registry in some cases coincided with those in foreign registers (age, AF, diabetes). However, the revealed negative relationships between mortality and HF were not confirmed in foreign studies. Perhaps this indicates that the doctors in the REGION-M registry did not always correctly diagnose HF. It is also possible that the treatment of patients with HF was more complete.

In the LIS-2 registry, indicators influencing in-hospital mortality were the age of patients, stroke type, the severity of impaired consciousness upon admission, a history of HF and AF. When compared with REGION-M, the indicators were slightly different. This is probably due to some difference in the parameters associated with in-hospital mortality included in the multivariate logistic regression model.

## Conclusion

Hospital-based physicians pay little attention to the recording of cardiovascular RF and socio-demographic parameters in patients with stroke, regardless of the condition severity and outcome. In-hospital mortality is associated with age, CAD, AF, diabetes, and venous thrombosis.

**Relationships and Activities.** The study was financially supported by a Pfizer grant, which did not affect the study management, analysis of the results and conclusions made.

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