Statistical Analysis of Predictors of Myocardial Infarction After Total Hip Replacement in Patients Over 60 Years

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***Abstract*— Myocardial infarction (MI), as well as delirium and cognitive dysfunction (D&CD) are common complications in elderly patients who underwent hip replacement (HR). Our study was aimed at determining the predictors to evaluate the risk for the development of MI and D&CD during the hospitalization period.**

The factors increasing the risk of MI in postoperative period are considered to be a low level of inter- and postoperative hemoglobin (Hb), late hemotransfusion (HT), poor comorbid status. Besides, in the group of patients who obtained regional anesthesia, MI occurred significantly more frequently compared to the group of patients with general anesthesia. We build a logistic regression equation for quantitative assessment of the effect of every mentioned factor. The factors increasing the risk of D&CD in postoperative period were low Hb and late HT. In particular, trigger level of hemoglobin for the development of D&CD was 100 g/L.

***Index Terms*—Biostatistic, predictors of myocardial infarction, arthroplasty.**

I. Introduction

ACCORDING to the WHO, in 2000 the number of patients with hip fracture comprised 1,672,000 throughout the world, including 311,000 in the USA and 620,000 in Europe [1]. With growing the proportion of elderly population, it is supposed that a total number of hip fracture will have made up 6.26 – 6.3 million by 2050 [2]–[4]. As a rule, such fractures require surgical treatment. As the risk for hip fracture increases with age, the main part of patients is elderly people who have in general poor comorbid status.

Previous study indicated that the overall mortality during hospitalization 4% [5] – 5% [6] and within one year after fracture 12.7% [5] – 33% [7]. The factors that predict mortality were American Society of Anesthesiologists rating of operative risk 3 or 4, and the development of one or more in-hospital postoperative complications. These results indicate that efforts at reducing one-year mortality after hip fracture should be directed at the prevention of postoperative complications.

Other studies showed the prevailing cause of early in-hospital death was MI, acute cardiac failure and pulmonary embolism [9]. Within 30 days after operation the incidence of MI comprised from 0.4% [8] to 2.2% [9]. The frequency of MI increased markedly with older age and was higher for male patients compared with female patients. The median time to myocardial infarction was 1 day; 83% events occurred within 3 days; and 93% occurred within 14 days after the operation [8]. Postoperative MI is a significant cause of morbidity and mortality in the noncardiac operative population because of the high prevalence of risk factors for coronary artery disease [9]–[12].

Delirium (D) is indeed the most common complication after hip fracture. The reported incidence of postoperative delirium in older adults undergoing surgery for hip fracture ranged from 16% to 62% with an average rate of 35% [13]. Another studies showed the incidence of postoperative delirium in the range of 10% to 22% [14]–[16]. The occurrence of D increases the time of patient's hospitalization, causes decompensation of concominant diseases and appears to be an important predictor of cognitive dysfunction with high risk for dementia. Acute postoperative cognitive dysfunction (POCD) was associated with the development of a major medical complication in 35% of all patients [14].

Postoperative predictors of acute D are considered to be acute pain, anemia, the use of urinary catheter, water and electrolyte imbalance, massive transfusions, intense interoperative blood loss [14], [17].

Patients with POCD at hospital discharge were more likely to die in the first three months after surgery. Likewise, patients who had POCD at both hospital discharge and three months after surgery were more likely to die in the first year after surgery. Patients with POCD are at an increased risk of death in the first year after surgery [18].

Our study was aimed at determining the predictors to evaluate the risk for the development of MI and D&CD during the hospitalization period.

There is no certain opinion of what method of anesthesia is the most suitable. In the review [19] general and regional anesthesia were compared. It was revealed insufficient evidence available from trials comparing regional versus general anesthesia to rule out clinically important differences. Regional anesthesia may reduce acute

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postoperative confusion but no conclusions can be drawn for mortality or other outcomes.

General anesthesia offers the advantages of greater control over duration, depth of anesthesia, and hemodynamic parameters, as well as complete control over the patient's airway and ventilation. It is preferred when there are contraindications to regional anesthesia, such as impaired coagulation or poor patient cooperation. Course of anesthesia, particularly interoperative hemodynamics, largely depends on current medications and techniques; this is true for general as well as regional anesthesia [21].

There is no common opinion of what tactics of HT to use in elderly patients with hip fracture. In the study [33] it was ascertained that liberal tactics compared with restrictive didn't decrease mortality and inability to walk independently (7.6% и 6.6% respectively, abs risk diff = 1%, CI= -1.9 – 4.0); As noticed, with liberal tactics MI occurred in about 2.3%, and with restrictive – in 3.8% (OR=0.6, CI= 0.3 – 1.19). Thus, it was recommended not to perform perioperative HT in patients with hip fracture and no symptoms of anemia, and Hg level no less than 80g/L, even in elderly patients with cardiovascular risk and diseases.

Authors noticed a relation between high mortality rate and severe outcomes with interoperative transfusion stressed upon no evidence that exactly HT but not intense blood loss caused by surgical reasons led to that result [23]. In the recent study [22] pre- and severe postoperative anemia required replacement therapy was noticed to be the predictor of in-hospital mortality and death within a year, prolonged hospitalization and delirium.

As it was shown in the study [24], patients with higher postoperative Hg could walk long distance themselves (70 g/L 56 steps, 120 g/L 92 steps, $p<0.01$). The predicted distance walked at discharge in feet (95% CI) increased with higher Hb levels; 7 g/dL, 56 feet [42-70]; 8 g/dL, 61 feet [54-68]; 9 g/dL, 67 feet [64-70]; 10 g/dL, 74 feet [72-77]; 11 g/dL, 83 feet [80-85]; 12 g/dL, 92 feet [87-96].

In the study [25], in group with liberal compared to restrictive strategy, cardiovascular complications occurred more seldom (2% and 10% respectively, $p = 0.05$) as well as lethal outcomes (0% and 8% respectively, $p = 0.02$).

II. Materials and Methods

A. Data source

We conducted a retrospective analysis of 268 patients with hip fracture admitted to hospital within the first 24 hours. Data were taken from the archives of three clinical trauma hospitals of Yekaterinburg through 2005 – 2010. We analyzed medical records, operation protocols, HT, anesthesiology charts and telephone interviews with the patients.

Postoperative MI was made on the basis of cheat pain, unreasonable arterial hypotension, and ECG changes according to American Heart Association [20], D&CD were based on the conclusion of a neurologist or psychiatrist.

B. Study population and outcomes

Exclusion criteria were age under 60 years, combined trauma, pathological fractures, dementia, revision endoprosthesis and patients with developed pseudoarthrosis.

C. Statistical analysis

Multivariate logistic regression model for postoperative acute myocardial infarction was build. Forward stepwise selection was used to select risk factors from the list of potential confounders: health status according to K.A. Eagle index, anesthesia type, Hg level after operation, and timely HT, type of operation, duration, length of operation etc. Nonparametric tests of Mann-Whitney and Kruskel-Wallis were used for compare means. Methods of rank correlation were used for processing data in nominal and ordinal scales. Statistical significance was set at $P=0.05$.

Data management and statistical analyses were performed using SPSS version 16.

III. Results

Demographic and clinical characteristics of patients are shown in table 1. Table 2 indicates severe outcomes.

TABLE I
DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF PATIENTS

Characteristics	No. of patients	%
Age		
60-69	75	28
70-79	132	49.3
80-89	59	22
90 and over	2	0.7
Gender		
Males	30	11.2
Females	238	88.8
Concominant diseases		
Diabetes	27	10.1
Angina I-II class	56	20.9
Hypertension	173	64.6
Heart failure NYHA class I or II	152	56.7
Asthma	10	3.7
Duodenal and gastric ulcer	23	8.6
History of stroke	68	25.4
History of stroke	12	4.5
Urinary infections	35	13.1
Score according to Eagle index		
0	47	17.5
I	93	34.7
II	74	27.6
III	48	17.9
IV	6	2.2
Score according to ASA		
II	23	8.6
III	218	81.3
IV	25	9.3

Patients were divided into groups according to anesthesia type; general – 110 patients, spinal – 100, epidural – 14, spino-epidural – 44.

Of 12 cases of MI, 11 – with elevation of ST segment, 1 – with Q wave, 9 – with shock, 3 without shock, 3 – fatal, 9 – nonfatal. The median time for IM development is the first 24 hours, 11 cases of MI occurred within the first 24 hours, 1 –

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within three days. Of 12 cases of delirium, 4 occurred within the first 24 hours, 8 – within the second day; of 25 cases of cognitive dysfunction, 10 occurred within the first 24 hours, 15 – within the second day.

TABLE II
POSTOPERATIVE OUTCOMES

Outcome	No.	%
Death	14	5.2
MI	12	4.5
Myocardial ischemia	9	3.4
D&CD	37	13.8
PE, fat (inter- and post-)	10	3.7
Gastrointestinal hemorrhage	7	2.6
Diarrhea	7	2.6
Interoperative hypotension followed by vasopressors administration	53	19.8
Urinary infections	26	9.7
Stroke	5	1.9

A. Myocardial infarction

Among the factors influencing the incidence of MI, we revealed the following: health status according to Eagle index, anesthesia type, Hg level after operation, and timely HT.

Table 3 presents distribution of patients in groups according to health status indicating the number of patients with MI and without MI in each group. Thus, in group with 0 score (47 patients) the incidence of MI accounted for 0%,

TABLE III
RISK FOR THE DEVELOPMENT OF MI DUE TO HEALTH STATUS

Heath status (Eagle index), points	Myocardial infarction, n	
	yes	no
0	0	47
1	1	92
2	3	71
3	6	42
4	2	4
Total	12	256

in the group with IV score (6 patients) – 33%. Health status has statistically significant influence on the incidence of MI ($p<0.001$, Kendell correlation coefficient = 0.196).

The distribution of patients according to the used anesthesia is presented in table 4; in every group there were shown patients with and without MI. In the group of patients who had general anesthesia (110 patients) the frequency of MI constituted 0.91%, compared to the group of patients

TABLE IV
RISK FOR THE DEVELOPMENT OF MI DUE TO TYPE OF ANESTHESIA

Anesthesia type	Myocardial infarction	
	yes	no
general	1	109
regional	11	147
Total	12	156

who had regional anesthesia (158 patients) – 6.9%. In the group of patients with regional anesthesia the risk for MI was significantly higher (Kendall correlation coefficient r=0.143 ($p=0.02$).

TABLE V
ANESTHESIA TYPES IN PATIENTS WITH DIFFERENT SCORES ACCORDING TO EAGLE SCALE

Health status (Eagle index), scores	Anesthesia type	
	general	regional
0	26	21
1	40	53
2	26	38
3	16	32
4	2	4
Total	110	158

Importantly, in groups with different health status the proportion of patients undergone general and regional anesthesia differed significantly (Table 5). For example, in the group with 0 score according to Eagle scale, the ratio of patients who had general and regional anesthesia made up 26 to 21; that was 2.5 times higher than in group with score III according to Eagle scale with the ratio 16 to 32.

However, correlation between anesthesia type and the incidence of MI can't be suggested ambiguous. In other words, the fact that in patients with regional anesthesia frequency of MI was significantly higher than in patients with general anesthesia can't be explained only because general anesthesia was more often used in health group 0 and regional – in health groups 2 or 3, thereafter patients with regional anesthesia initially had higher risk for MI due to their somatic / cardiovascular diseases.

Table 6 indicates two-factor distribution of patients according to health group and used anesthesia; each group contains patients with and without MI. For example, in group of patients with Eagle score II and regional anesthesia (48 patients) the incidence of MI was 4.2%.

For MI and anesthesia type with excluded influence of health status, partial coefficient correlation of Kendall made up 0.137 ($p=0.026$).

An important factor of the development of MI in in-hospital postoperative period is inter- and postoperative level of hemoglobin. In group with MI postoperative hemoglobin was 83±2.2 (95% CI = 78 – 88), in group without MI – 96±1 (95% CI = 94 – 98).

Mann-Whitney test showed statistically significant difference ($p=0.002$) in the level of postoperative hemoglobin: in the group of patients who developed postoperative MI, on average the level of postoperative hemoglobin was 13g/L lower than in patients without postoperative MI.

High frequency of postoperative (2 and more days) blood transfusion (HT) (31%) was conditioned by two factors: restrictive tactics for interoperative HT and volume of drainage blood loss from 0 to 1200 ml (254±11ml). Making decision of HT at the second day or later after operation conditioned by not significant drainage blood loss but only restrictive tactics, we viewed as late and untimely. Logistic regression analysis revealed that late HT was the factor of the development of MI in the nearest postoperative period ($p=0.025$).

As health group (according to Eagle scale), type of anesthesia, and presence of blood transfusion are categorical variables but hemoglobin level refers to interval scale, we made logistic regression equation:

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TABLE VI
THE INCIDENCE OF MYOCARDIAL INFARCTION DUE TO EAGLE SCORE AND ANESTHESIA TYPE

Anesthesia type		Health status (Eagle index), scores					Total
		0	I	II	III	IV	
General	Myocardial infarction	0	0	1	0	0	1
	No Myocardial infarction	26	40	25	16	2	109
Regional	Myocardial infarction	0	1	2	7	1	11
	No Myocardial infarction	21	52	46	25	3	147

P = exp(z)/(1+exp(z)), where P – probability of MI, z – fictitious variable calculated with formula

z = 8.557 + 0*[Transfusion = Present] – 2.034*[Transfusion = Absent] – 0.065 *Hg +

– 22,414*[Eagle=0] – 6.441*[Eagle=1] – 4.8*[Eagle=2] – 3.35 *[Eagle=3] + 0*[Eagle=4] –

+ 0*[Anesthesia = Regional] – 3.459*[Anesthesia = General].

How to work with categorical variables: variable takes on a value 0 if data in square brackets are false or 1 if it is true. For example, patient with health group 2 according to Eagle scale, undergone HT, got general anesthesia, Hg=70 g/L, then the probability of MI

z = 8.557 + 0*1 – 4.8*1 – 0.065*70 – 3.459*1 = –4.252, therefore

P = exp(–4.252)/(1+exp(–4.252)) = 1.4%.

B. Delirium

In the previous reviews, influence of anemia on the incidence of the development of D&CD has been widely discussed. To exclude the influence of anemia and determine only the influence of transfusion strategy on the frequency of the development of D&CD, we divided the group into three subgroups according to postoperative Hg level (Table 7). Patients with interoperative lethal outcomes were excluded. The frequency of transfusions for each group was the following: I – 68.3%, II – 40%, III – 40%.

Kraskell-Wallis test showed significant effect of transfusion strategy on frequency of the development of D&CD in the group II (p=0.002). Using liberal strategy, the frequency of D&CD was significantly lower than in restrictive or absent transfusion (Table 8).

It is noticed that drainage blood loss in group I was significantly higher compared to group II: 307 and 218 ml respectively (p<0.01).

IV. DISCUSSION

Patients with severe cardiovascular pathology are at high risk in hip arthroplasty. Risk of developing postoperative complication and death increases with age. Factors related to patient's cardiac pathology and their age are aggregated by estimated performance Eagle index. Patients with high Eagle score experience postoperative cardiovascular and acute mental disorders much more often; there are similar findings in research [18]. A history of cardiac-related conditions, including arrhythmia, CAD, MI, CHF, or valvular disease, was associated with a significantly increased risk of adverse cardiovascular events postoperatively [27]. In the review [26] they collected data on different types of operations in the proximal part of the femur; there was no considerable decrease in MI frequency in use of neuroaxial anesthesia vs general anesthesia. As different types of surgical intervention in the proximal part of the femur vary considerably in the amount of blood lost during the operation, and level of traumatism experienced by the patient the results in smaller groups represent practical interest. For the examined group of patients with hip arthroplasty MI develops statistically more often in the group with regional anesthesia (p=0.02). High-impact prospective studies are necessary to confirm these findings and establish firm clinical guidelines.

Side-effects of regional anesthesia are widely covered in literature. Only one study is indicated [19] where statistically significant difference was not found in systolic pressure drop and 11 studies where it was established that hypotension occurs more often after regional anesthesia. [29] shows a reliable increase in ST depression. A significant increase in the overall number of ST segment depressions was reported for those in the spinal anesthesia group. In the group of patients we examined interoperative hypotension was

TABLE VII
DISTRIBUTION OF PATIENTS DUE TO HG LEVEL

Group No.	Postop. Hg, g/L	Patients No.	Transfusion strategy		
			Liberal	Restrictive	Absent
I	< 90	104	34	37	33
II	90 - 110	112	27	17	68
III	> 110	45	18	0	27

TABLE VIII
INCIDENCE OF D&CD IN GROUPS WITH DIFFERENT TRANSFUSION STRATEGIES

Group No.	Patients No.	Patients No with D&CD due to transfusion strategy			p-value
		Liberal	Restrictive	Absent	
I	104	10 (29.4%)	9 (24.3%)	4 (12.1%)	0.219
II	112	0	6 (35.3%)	7 (10.3%)	0.002
III	45	0	0	1 (3.7%)	0.414

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corrected with adrenomimetics (mesaton, dopamine); in regional anesthesia adrenomimetic support was required much more often OR=4.98, (4.18–5.78).

Inter- and postoperative level of hemoglobin is an important MI and D&CD predictor. Patients with severe cardiac complications are resistant to normovolemic hemodilution without risk of developing myocardial ischemia with hemoglobin level lower than 103g/liter [30]. Blood transfusion is associated with a lower short-term mortality rate among elderly patients with acute myocardial infarction, if the hematocrit on admission is 30.0 per cent or lower and may be effective in patients with a hematocrit as high as 33.0 per cent on admission [28]. The effect of anemia was examined in many studies, the review [31] shows significant influence of anemia to the postoperative complications and mortality. Patients with or at risk of coronary artery disease do tolerate moderate acute normovolemic hemodilution (ANH) provided that normovolemia is maintained they need to be carefully monitored and treated immediately when signs of inadequate myocardial oxygenation develop; it has been shown that early signs of ANH-induced myocardial ischemia can be easily treated by minimal transfusion [32]. Anemia is a predictor of developing early acute postoperative psychotic disorders [17]. Early HT allows creating a certain "safety margin". In the examined group, withdrawal of early transfusion and waiting for its drop up to critical level created a risk of developing uncontrolled anemia which leads to development of MI and acute D&CD. Our research showed that if elderly patients' organism has been exposed to severe anemia, transfusion strategies are not equally efficient in protecting patients against acute psychotic disorders. In the same time if postoperative hemoglobin level was managed at the level of 100g/liter, hemotransfusion is efficient in protecting patients against acute psychotic disorders. Thus, hemoglobin level of 100g/l is a transfusion trigger which prevents from developing acute psychotic disorders in elderly patients with hip fracture in hip arthroplasty; liberal hemotransfusion strategy decreases the risk of developing D&CD.

In order to predict cardiovascular complications mathematical models of myocardium are elaborated [34], [35]. It is much cheaper and safer to use mathematical models for the myocardial infarction risk estimation than make decisions based on empirical data only.

V. Conclusion

For the examined group of patients with hip replacement we obtained the following results.

MI statistically more often developed in the group with regional anesthesia. However, the choice of anesthesia (general or regional) for hip arthroplasty is made by an anesthesiologist and based on patient's comorbidities, clinical experience of an anesthesiologist and potential complications of regional anesthesia. High-impact prospective studies are necessary to confirm these findings and establish firm clinical guidelines.

High score according to Eagle index was a considerable predictor of MI.

Inter- and postoperative Hg level was an important predictor of MI and D&CD.

A transfusion trigger preventing the development of acute psychotic dysfunction in elderly patients with hip fracture after hip replacement was hemoglobin level of 100 g/L.

Liberal blood transfusion strategy improved the results in the examined patients.

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