Preoperative Hemoglobin Dynamics in Patients with Trochanteric Fractures

A multivariate analysis

TEODOR STEFAN GHEORGHEVICI[1], BOGDAN VELICEASA[1]*, BOGDAN PUHA[1], STEFAN TOADER[2]*, IOANA DANA ALEXA[3], OVIDIU ALEXA[1]

[1] Grigore T. Popa University of Medicine and Pharmacy, Orthopaedics and Trauma Department,16 Universitatii Str, 700115, Iasi, Romania

[2] Grigore T. Popa University of Medicine and Pharmacy, Pathophysiology Department,16 Universitatii Str, 700115, Iasi, Romania

[3] Grigore T. Popa University of Medicine and Pharmacy, Geriatrics Department,16 Universitatii Str, 700115, Iasi, Romania

Preoperative anemia is a common finding among geriatric patients with trochanteric fractures. We assessed the dynamics of hemoglobin and the factors that influence it. A total of 780 patients with trochanteric fractures were selected. Distribution by gender showed a slightly higher proportion of female patients (64.1%). The preoperative interval ranged from a few hours to 19 days. Hospital admission period varied from 1 to 49 days. Hemoglobin ranged from 4.80 to 17.40 g/dl; 43.1% of patients had individual values below the baseline. Individually, the hemoglobin value varied from a decrease of 9.33 g/dL to an increase of 11.97 g/dL, but the total study group recorded an average decrease of 0.96 ± 1.75 g/dL. Hemoglobin had a downward trend directly correlated with the preoperative interval period. Decrease in hemoglobin was correlated with the percentage of blood lymphocytes, PLT/WBC ratio, prothrombin activity and APTT ratio. A low level of hemoglobin variation was associated with a shorter preoperative interval, reduced prothrombin time, prothrombin activity > 100, INR > 1.50 and APTT > 30.

Key Words: hemoglobin, dynamamics, trochanteric fractures.

Despite the anesthetic and surgical advances in recent years, the mortality of geriatric patients with extracapsular hip fractures remains high [1].

Numerous factors have been incriminated in increasing mortality. Among these, preoperative anemia is a common symptom among geriatric patients who have suffered from this type of fractures [2] being caused mainly by hemodilution due to hydroelectrolytic rebalancing process, but also through blood loss from the fracture site [3]. Numerous authors attempted to highlight the correlation between preoperative anemia and mortality [4,5].

Timing of surgery is one of the desiderata of successful treatment of proximal femoral fractures. Multiple studies [6,7] attempted to outline the optimal surgical treatment interval to reduce complications and to ensure a high quality of life and recovery, without achieving consensus. Several authors attempted to outline the optimal moment of surgical treatment by studying the evolution of functional status [6, 8] or postoperative mortality [7, 9]. However, we could not identify studies regarding the influence of preoperative interval on in-hospital mortality of these patients.

The objective of our study was to assess the dynamics of hemoglobin and the factors that influence it.

Experimental part

Material and methods

Between January 2013 and December 2015, 945 patients with trochanteric fractures were admitted in the Orthopaedics and Traumatology Clinic of the St. Spiridon Emergency Clinical Hospital, Iasi. From this group a total of 780 patients were selected. Exclusion criteria were: politraumatized patients, chronic oral anticoagulant treatment, chronic kidney disease, chronic hepatopathy, oncological diseases, septic or mechanical complications of initial surgical treatment and incomplete data in the registry. From the studied group, 654 patients underwent surgical treatment: reduction and osteosisthesis with Dinamic Hip Screw (DHS), Dinamic Condilian Screw (DCS), Gamma nail, Ender nail, Femoral nail, Proximal Femoral Nail (PFN) and 126 patients followed functional treatment.

Demographic characteristics, treatment type, fracture type, mortality, preoperative interval duration and variation of: Hemoglobin (Hb), Hematocrit (Ht), Thrombocytes (PLT), Lymphocytes (Ly), Ly%, Leukocytes (WBC), Erythrocytes (RBC), Prothrombin time (PT), International Normalised Ratio (INR), activated partial thromboplastin time (APTT) were analyzed.

Data were obtained from the Hospital Integrated Information System and patients medical records, and analyzed using the IBM software SPSS Version 18 (SPSS Inc., Chicago, IL, USA). Data were centralized into SPSS 18.0 databases. For statistical analysis we used both descriptive and analytical methods at 95% CI significance. For quantitative variables, at the 95% significance limit, we applied t-Student test and F test. We also used *Pearson* (r) correlation coefficient.

Results and discussions

Distribution by gender showed a slightly higher proportion of female patients (64.1%), the gender ratio being F/M 1.8/1. Distribution by age group revealed a peak in the age group 80-89 years both for female (48%) and male (32.1%) patients. The mean age in relation to patients'gender was significantly lower in male 70.89 ± 15.87 years, with variations from 34 to 99 years, and in the female gender the mean value was 78.94 ± 10.09 years, with variations in the range of 22-97 years ($p = 0.001$). The distribution by place of origin showed a slightly higher percentage of rural patients (57.6%), the ratio of rural to urban patients being 1.4/1.

* email: velbogdan@yahoo.com; toaderstefan@gmail.com

Parameters	N	Average	Standard Deviation	Standard Error	Reliable Interval		Min	Max	p
					- 95%CI	+95%CI			
Total	654	4.92	2.76	0.11	4.71	5.13	0	19	
Diagnosis									0.336
Basicervical fr.	69	4.71	2.82	0.34	4.03	5.39	0	16	
Trochanteric fr.	1	2.00	.	.	.	.	2	2	
Pertrochanteric fr.	464	5.02	2.70	0.13	4.78	5.27	0	19	
Complex trochanteric fr.	66	4.95	3.22	0.40	4.16	5.75	0	16	
Trochantero-diaphysaire fr.	40	4.60	2.72	0.43	3.73	5.47	0	14	
Intertrochanteric fr.	14	3.64	1.60	0.43	2.72	4.57	0	6	
Sex									0.421
Female	415	4.99	2.63	0.13	4.73	5.24	0	15	
Male	239	4.81	2.96	0.19	4.43	5.19	0	19	
Age group									0.774
< 70 years	148	4.86	3.00	0.25	4.38	5.35	0	19	
≥ 70 years	506	4.94	2.68	0.12	4.70	5.17	0	16	

Table 1
STATISTICAL INDICATORS OF THE PREOPERATIVE INTERVAL BASED ON CLINICAL DATA

Parameters	N	Average	Standard Deviation	Standard Error	Reliable Interval		Min	Max	p
					- 95%CI	+95%CI			
Total	780	10.92	4.97	0.18	10.57	11.27	1	49	
Diagnosis									
Basicervical fr.	87	10.16	4.68	0.50	9.16	11.16	1	27	
Trochanteric fr.	29	3.55	3.28	0.61	2.30	4.80	1	14	
Pertrochanteric fr.	533	11.42	4.93	0.21	11.00	11.84	1	49	**0.001**
Complex trochanteric fr.	75	11.17	5.11	0.59	10.00	12.35	1	34	
Trochantero-diaphysaire fr.	42	11.17	2.77	0.43	10.30	12.03	6	19	
Intertrochanteric fr.	14	9.79	2.52	0.67	8.33	11.24	4	14	
Sex									
Female	500	10.89	4.69	0.21	10.48	11.31	1	36	0.835
Male	280	10.97	5.45	0.33	10.33	11.61	1	49	
Age group									
< 70 years	180	10.75	6.43	0.48	9.80	11.70	1	49	0.597
≥ 70 years	600	10.97	4.45	0.18	10.62	11.33	1	37	
Treatment									
Functional	126	6.24	4.80	0.43	5.39	7.08	1	21	
DCS	53	12.00	4.88	0.67	10.66	13.34	1	34	
DHS	549	11.87	4.54	0.19	11.49	12.26	1	49	**0.001**
Ender nail	5	9.80	2.77	1.24	6.35	13.25	5	12	
Gamma nail	41	10.85	2.58	0.40	10.04	11.67	7	19	
PFN/femoral nail	6	14.00	5.29	2.16	8.45	19.55	7	20	

Table 2
STATISTICAL INDICATORS OF THE ADMISSION PERIOD BASED ON CLINICAL DATA

In our study group, patients with pertrochanteric fractures (68.33%) prevailed. Correlated to gender, the percentage distribution based on diagnosis recorded significant differences (p = 0.001) for both sexes: pertrochanteric fractures were the most common (67.6% vs. 69.6%); in females there was an increased frequency of basicervical fracture (14.4% vs. 5.4%); a higher frequency of complex trochanteric fracture (10% vs. 9.4%) and trochanteric fracture (8.2% vs. 3.8%) was noted in males.

The preoperative interval ranged from a few hours to 19 days, with an average of 4.92 ± 2.76 days, slightly lower in patients with trochanteric fracture (2 ± 0 days), intertrochanteric fracture (3.64 ± 1.60 days), trochantero-diaphysaire fracture (4.60 ± 2.72 days) and basicervical fracture (4.71 ± 2.82 days) (p = 0.336) (table 1). The mean preoperative interval did not differ significantly between sexes or age groups.

Hospital admission period varied from 1 to 49 days, with an average of 10.92 ± 4.97 days, significantly lower in patients with trochanteric fractures (3.55 ± 3.28 days). The median admission period was significantly lower in patients treated with ender nails (9.80 ± 2.77 days), but higher compared to the mean for functional treatment (6.24 ± 4.80 days) (table 2).

Parameters	N	Average	Standard Deviation	Standard Error	Reliable Interval		Min	Max	p
					- 95%CI	+95%CI			
Total	654	-0.96	1.75	0.07	-1.10	-0.83	-9.33	11.97	
Sex									
Female	415	-0.77	1.78	0.09	-0.94	-0.59	-9.33	11.97	**0.001**
Male	239	-1.31	1.63	0.11	-1.52	-1.10	-6.40	4.50	
Age group									
< 70 years	148	-1.19	1.63	0.13	-1.46	-0.93	-6.00	4.30	0.068
≥ 70 years	506	-0.90	1.77	0.08	-1.05	-0.74	-9.33	11.97	
Diagnosis									
Basicervical fr.	69	-0.75	1.63	0.20	-1.14	-0.36	-9.33	3.20	
Trochanteric fr.	1	0,00	.	.	.	.	0.00	0.00	
Pertrochanteric fr.	464	-0.96	1.76	0.08	-1.12	-0.80	-6.40	11.97	0.400
Complex trochanteric fr.	66	-0.92	1.52	0.19	-1.30	-0.55	-5.80	2.90	
Trochantero-diaphysaire fr.	40	-1.49	2.15	0.34	-2.18	-0.80	-6.00	3.60	
Intertrochanteric fr.	14	-0.82	1.49	0.40	-1.68	0.04	-3.50	0.60	

Table 3
STATISTICAL INDICATORS OF ÄHB BASED ON CLINICAL DATA

Hemoglobin ranged from 4.80 to 17.40 g/dL; 43.1% of patients had individual values below the baseline (F: 11-15 g/dL; M: 13-16 g/dL). The mean level was significantly lower in females (11.44 vs. 12.27 g/dL, p = 0.001) in the age group over 70 years (12.27 vs. 11.58 g/dL, p = 0.001) and in patients with the following diagnoses: complex trochanteric fractures, pertrochanteric and trochantero-diaphysaire fractures (p = 0.001). Preoperatively, the mean hemoglobin level decreased significantly from 11.74 ± 1.87 g/dL at admission to 10.81 ± 1.72 g/dL (p = 0.001). Individually, hemoglobin value varied from a decrease of 9.33 g/dL to an increase of 11.97 g/dL, but the total study group recorded an average decrease of 0.96 ± 1.75 g/dL. Gender-correlated, the mean decrease was significantly lower in femalescompared to males (-0.77 vs. -1.31 g/dL; p = 0.001) and slightly lower in the age group over 70 years compared to ages above this limit (-0.90 vs. -1.19 g/dL, p = 0.068). The highest decrease in the mean level of hemoglobin was seen in patients with trochantero-diaphiasaire fractures (-1.49) and the lowest in the patient with trochanteric fractures (0.0), but the differences were not statistically significant depending on diagnosis (p = 0.400). Depending on the type of surgery, the highest decrease in ΔHb was observed in patients with PFN/femoral nail (-1.42), and the lowest was recorded in patients with DSH (-0.91), but the differences were not statistically significant (p = 0.404) (table 3).

The correlation between the preoperative interval and the ΔHb was direct, which reasserts that 38.2% of patients had a higher level of the preoperative interval associated with a higher ΔHb level, a statistically significant correlation (r = +0.382, p = 0.037). ΔHb significantly correlated with the following parameters observed at admission (table 4).

Decrease in hemoglobin was significantly lower in the operated patients (-0.96 vs. -2.76 and -1.66, p = 0.001). The level of hemoglobin at admition and the admition period were in a weak indirect correlation but statistically significant, indicating that in 18.2% of patients the higher values of the admition period were associated with a preoperatively lower hemoglobin (r = -0.182; p = 0.022).

Analyzing the evolution of hemoglobin in the preoperative and INR ranges, it was noted that a lower level of ΔHb was associated with a shorter preoperative interval and INR values above 1.50. Analyzing the evolution of hemoglobin by preoperative interval and APTT, it was noted that a lower level of ΔHb was associated with a shorter preoperative interval and APTT values above 30.

The association between increase in preoperative interval and decrease in hemoglobin is well known, but the mechanisms of its occurrence are not yet understood. Trochanteric fractures are commonly associated with

Parameters at admission	Pearson Correlation	p
Hematocrit (Ht)	-0.391	**0.001**
Limfocytes #	-0.059	0.128
Limfocytes %	+0.301	**0.009**
Leukocytes (WBC)	+0.045	0.888
Erythrocytes (RBC)	+0.289	**0.001**
Thrombocytes	+0.077	0.149
PLT/WBC	+0.200	**0.010**
Prothrombin time	+0.006	0.887
Prothrombin activity	-0.201	**0.009**
INR	+0.199	**0.011**
APTT	+0.069	0.077
APTT ratio	+0.225	**0.001**

Table 4
ΔHB CORRELATION WITH LABORATORY PARAMETERS DETERMINED AT ADMISSION

important blood loss requiring blood transfusions to restore the body's homeostasis. These transfusions involve important risks such as transmission of microbial and viral infections, immunological reactions, volume overload, renal insufficiency, impairment of patient's mental state, increased mortality, rehabilitation and high costs [10]. Post-operative blood pressure increases the risk by 1.5 times for thromboembolic events [11]. Geriatric patients frequently experience anemia at admission, requiring re-balancing for safe surgery. According to Bhaskar [4], the incidence of anemia in the geriatric population is around 17%, and among patients with hip fractures between 40 and 72%. Other authors [12] reported an incidence between 38.5% and 46%. This is correlated with gender, age of patients and type of fracture.

Numerous studies identified a correlation between the presence of anemia, increased mortality and diminishing postoperative functional outcomes in patients with proximal femoral fractures [3, 4, 13, 14]. Identifying the ideal operator time from the perspective of limiting preoperative blood loss should be a constant concern to ensure therapeutic success for patients with trochanteric fractures.

The epidemiological characteristics of patients included in the study were similar to those in the general population.

The preoperative interval ranged from a few hours to 19 days, averaging 4.92 ± 2.76 days. Compared to literature data, it was lower compared to the South American population [15] and similar to the United States and Western Europe. Intertrochanteric fractures (3.64 ± 1.60 days), trochatero-diaphysaire (4.60 ± 2.72 days) and basicervical fractures (4.71 ± 2.82 days) ($p = 0.336$) showed mean values without significant differences between sexes or age groups. In a comparative study of extra and intracapsular fractures, Morris et al. (16), identified 39.4% vs. of 22.5% patients ($p < 0.001$) requiring blood transfusions, more frequent among patients requiring intramedullary fixation vs. DHS (67.4 vs. 32.0%, $p < 0.001$).

Admission period ranged from 1 to 49 days, with an average of 10.92 ± 4.97 days, being lower in case of osteosynthesis with Ender or Gamma rods and higher in the case of DHS or DCS, explained by the difference in size of wounds and blood loss during surgery. We found a poor correlation between Hb value at admission and admission period ($p = 0.022$). In the present study, we defined anemia as a decrease in hemoglobin values below 11.8 g/dL, the mean value used by authors being 12 g/dL, consistent with the definition of the World Health Organization [2]. The hemoglobin at admission ranged from 4.80 to 17.40 g/dL. 43.1% of patients had individual values below the baseline (F: 11-15 g/dL; M: 13-16 g/dL). The mean level was significantly lower in females (11.44 vs. 12.27 g/dL, $p = 0.001$) in the age group over 70 years (12.27 vs. 11.58 g/dL, $p = 0.001$) confirming the study of Bhaskar [4].

The duration of the preoperative interval was positively correlated with ΔHb, but the correlation was moderate and was present in 38.2% of patients ($r = +0.382$, $p = 0.037$). Decrease in mean Hb values could be explained not only by the degree of fracture comminution and the preoperative interval but also by the change in patient coagulation status. It is known that hip fractures in the elderly have a direct impact on coagulation. Okamura et al. [17] identified high levels of D-dimers and fibrin degradation products during the perioperative period. Chen et al. [18] identified increased preoperative serum levels of fibrinogen and D-dimers of geriatric patients with hip fractures. They identified a moderate PT and INR decrease and an increase in APTT, close to the control value. In our study group, a reduced level of ΔHb was associated with a shorter preoperative interval and lower values of prothrombin time, prothrombin activity > 100, INR > 1.50 and APTT > 30, confirming the coagulation cascade damage theory. D-dimers values were not routinely determined, so they could not be analyzed.

The study presents a number of limitations. First, it uses the data from a single trauma center, ideally it would be a multicenter study. Secondly, a more elaborate quantification of admission Hb values by collecting samples at fixed time intrrvals would have been helpful. Despite these limitations, Hb values at admission were consistent with those in the literature.

Conclusions

Hemoglobin has a downward trend directly correlated with the preoperative interval period. Decrease in hemoglobin is correlated with the percentage of blood lymphocytes, PLT/WBC ratio, prothrombin activity and APTT ratio. A low level of hemoglobin variation is associated with a shorter preoperative interval, reduced prothrombin time, prothrombin activity > 100, INR > 1.50 and APTT > 30.

References

1.SMITH, T., PELPOLA, K., BALL. M., et all. Pre-operative indicators for mortality following hip fracture surgery: a systematic review and meta-analysis. Age Ageing, **43**(4), 2014, p. 464-471.

2.KOVAR, F.M., ENDLER, G., WAGNER, O.F., JAINDL, M., Basal haemoglobin levels as prognostic factor for early death in elderly patients with a hip fracture-A twenty-year observation study. Injury, **46**(6), 2015, p. 1018-1022.

3.KUMAR, D., MBAKO, A.N., RIDDICK, A., et al. On admission haemoglobin in patients with hip fracture. Injury, **42**(2), 2011, p. 167-170.

4.BHASKAR, D., PARKER, M.J., Haematological indices as surrogate markers of factors affecting mortality after hip fracture. Injury, **42**(2), 2011, p. 178-82.

5.BORGES, A., TORRES, J., SAO SIMAO, R., et al. Impact of preoperative analytical values on post-operative mortality rate of intertrochanteric fractures. Acta Med. Port., **27**(2), 2014, p. 218-222.

6.FU, M.C., BODDAPATI, V., GAUSDEN, E.B., et al. Surgery for a fracture of the hip within 24 hours of admission is independently associated with reduced short-term post-operative complications. Bone Joint J., **99-B**(9), 2017, p. 1216-1222.

7.MOJA, L., PIATTI, A., PECORARO, V., et al. Timing Matters in Hip Fracture Surgery: Patients Operated within 48 Hours Have Better Outcomes. A Meta-Analysis and Meta-Regression of over 190,000 Patients. PLoS One, **7**(10), 2012, p. e46175.

8.NOVACK V, JOTKOWITZ A, ETZION O, et al. Does delay in surgery after hip fracture lead to worse outcomes? A multicenter survey. Int. J. Qual. Health Care, **19**(3), 2007, p. 170.

9.MAJUMDAR, S.R., BEAUPRE, L.A., JOHNSTON, D.W., et al. Lack of association between mortality and timing of surgical fixation in elderly patients with hip fracture: Results of a retrospective population-based cohort study. Med. Care, **44**(6), 2006, p. 552-559.

10.SHANDER, A., HOFMANN, A., OZAWA, S., et al. Activity-based costs of blood transfusions insurgical patients at four hospitals. Transfusion, **50**(4), 2010, p. 753.

11.NILSSON, K.R., BERENHOLTZ, S.M., GARRETT-MAYER, E., et al. Association between venous thromboembolism and perioperative allogeneic transfusion. Arch. Surg., **142**, 2007, p. 126-132.

12.HALM, E.A., WANG, J.J., BOOCKVAR, K., et al. The effect of perioperative anemia on clinical and functional outcomes in patients with hip fracture. J. Orthop. Trauma, **18**(6), 2004, p. 369-374.

13.ZHANG, J.Q., XUE, F.S., MENG, F.M., LIU, G.P., Is basal haemoglobin level really a prognostic factor for early death of elderly patients undergoing hip fracture surgery? Injury, **46**(10), 2015, p. 2079-2080.
14.LUPESCU, D., GREABU, M., TOTAN, A., et al. Biochemical Markers with Predictive Value in Polytrauma Patients with Femoral Fractures. Rev. Chim. (Bucharest), **69**, no.10, 2018, p. 2762-2767.
15.DANIACHI, D., NETTO ADOS, S., KEISKE, N., et al. Epidemiology of fractures of the proximal third of the femur in elderly patients. OnoRev Bras. Ortop., **50**(4), 2015, p. 371-377.
16.MORRIS, R., RETHNAM, U., RUSS, B., TOPLISS, C., Assessing the impact of fracture pattern on transfusion requirements in hip fractures. Eur. J. Trauma Emerg. Surg., **43**(3), 2017, p. 337-342.
17.OKAMURA, K., NAKAGAWA, I., HIDAKA, S., et al. Perioperative changes of the coagulation markers in patients undergoing hip fracture surgery. Masui, **56**(11), 2007, p. 1353-1357.
18.CHEN, LIU., YING, SONG., JINGZHONG, ZHAO., et al. Elevated D-dimer and fibrinogen levels in serum of preoperative bone fracture patients. Springerplus, **5**, 2016, p. 161.

Manuscript received:11.03.2018