ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Correlation between the bleeding coagulation tests before vertebral surgery and the perioperative bleeding amount in geriatric patients using antiaggregants and anticoagulants

Bulent Yardimci[1], Meric Enercan[2], Azmi Hamzaoglu[3], Reyhan Diz Kucukkaya[4], Nomin Bold[5]

[1]Associate Professor, Department of Internal Medicine, Medical Faculty, Yeni Yuzyil University, Istanbul, Turkey, [2]Professor, Department of Orhopedics and Traumatology, Demiroglu Bilim University, Istanbul Spine Center, Florence Nightingale Hospital, Istanbul, Turkey, [3]Professor, Istanbul Spine Center, Florence Nightingale Hospital, Istanbul, Turkey, [4]Professor, Consultant, Department of Haematology, Istanbul Florence Nightingale Hospital, Istanbul, Turkey, [5]Medical Doctor, Department of Infectious Disease and Microbiology, Medical Faculty, Maltepe University, Istanbul, Turkey

Submission: 18-01-2023 Revision: 02-04-2023 Publication: 01-05-2023

ABSTRACT

Background: The world is witnessing an increase in its elderly population, which is reflected in the growing number of orthopedic surgeries being performed. With the increase in the number of major operations performed on the elderly, it has become crucial to manage bleeding effectively during vertebral surgery. The substantial use of antiaggregants and anticoagulants in elderly patients presents an increased risk of bleeding, resulting in increased morbidity and mortality rates if not well managed. Hence, it is essential to evaluate these patients thoroughly in the pre-operative period to minimize the risk of bleeding and improve patient outcomes. **Aims and Objectives:** The aims of this study were to research how effective the use of antiaggregants (AAs) and anticoagulants (oral anticoagulants [OAC] and low-molecular-weight heparin [LMWH]) is on operations and post-operative bleedings in surgery performed at our orthopedics clinic especially in the geriatric age group. **Materials and Methods:** This study was made retrospectively on 80 patients aged 65 years and over, who have undergone vertebral surgery on hospitalization at the Istanbul Florence Nightingale Hospital's Orthopedics Clinic between the months of January 2017 and December 2019. **Results:** The rate of blood product utilization during surgery of those using prophylactic LMWH was statistically significantly higher in comparison to those not on prophylactic LMWH ($P = 0.034$). There has not been determined any statistically significant difference in the means of the bleeding amount during the operation and post-operative bleeding. There has not been determined any statistically significant difference in the means of the bleeding amount during the operation and the post-operative period use and do not use any AA. **Conclusion:** In the geriatric group of age, which shall undergo vertebral surgery, it seems like an appropriate approach to discontinue AA and OAC 7 days before the operations. We have observed that the utilization of LMWH either for prophylactic purposes or for bridging purposes in the group using OAC does not significantly increase the bleeding probability.

Key words: Bleeding; Orthopedic surgery; Elderly; Blood coagulation tests

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v14i5.51532

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

The frequency of vertebral surgery in orthopedics is increasing day by day and more complex operations are made by means of advancing techniques. Vertebral surgery comprises operations with considerable blood loss. Since blood loss may cause major fluid shifts, it changes the cardiac, pulmonary, and renal status. Significant blood

Address for Correspondence:
Bulent Yardimci, Associate Professor, Department of Internal Medicine, Medical Faculty, Yeni Yuzyil University, Istanbul, Turkey.
Mobile: +905325431408. **E-mail:** drbyardimci@gmail.com

loss causes systemic effects and results in coagulopathy, disseminated intravascular coagulation, and neurological complications. Besides, blood transfusion is risky in terms of surgical area infection and urinary infection among these patients. The fact that patients are on antiaggregants (AAs) and oral anticoagulants (OAC) increases the risk of bleeding in these surgical interventions. Therefore, there is the general tendency to discontinue the AA and OAC used before the operation.[1,2]

The two agents, which are frequently used in the AA treatment, are acetylsalicylic acid (ASA) and clopidogrel (CLP). Whereas the medications used as anticoagulant are, along with coumadin, the factor Xa inhibitors, which have come into use in the recent years. In case of patients on AAI, the drugs are generally discontinued before surgery. Since, the risk of thrombose and emboly is high for those on OAC, low-molecular-weight heparin (LMWH) is introduced. This is called bridging treatment. LMWH is also introduced to the cancer patients due to the risk of thromboembolism. There are studies which demonstrate that bleeding risk increases in patients undergoing bridging treatment and using LMWH.[3,4] In clinical practice, taking the profit/loss balance into consideration, decision is made to use LMHW.

Since in patients aged 65 years and over, who are defined as the geriatric group, the frequency of diseases such as the cerebrovascular disease, atrial fibrillation, coronary artery disease increases, the use of AAs, and anticoagulants are seen frequently. In addition, due to the frequency of comorbid diseases, the age group is risky in terms of post-operative thrombose incidents.[5] It is also required to prevent any thrombotic incidents, while minimizing the hemorrhage risk in these patients.

In this study, our aim was to investigate how effective the use of AA and anticoagulants (OAC and LMWH) are on bleeding during and after the surgeries performed on geriatric group patients. We also investigate how helpful the pre-operative bleeding and coagulation tests are in this regard.

Aims and objectives

The aims of this study were to research how effective the use of antiaggregants (AAs) and anticoagulants (oral anticoagulants [OAC] and low-molecular-weight heparin [LMWH]) is on operations and post-operative bleedings in surgery performed at our orthopedics clinic especially in the geriatric age group.

MATERIALS AND METHODS

This study was made retrospectively on 80 patients aged 65 years and over, who have undergone vertebral surgery on hospitalization at the Istanbul Florence Nightingale Hospital's Orthopedics Clinic between the months of January 2017 and December 2019. Before the study, the Local Ethics Committee approval has been obtained (Ethical clearance number and date: 44140529/2015-95-May 05, 2015).

Diseases of the patients other than the pathology that caused the vertebral operation were recorded. Hematological disease, malignancy, use of AAs, use of anticoagulants, and steroid use, which may affect the bleeding coagulation system, were recorded. Infection and antibiotic use were also evaluated.

The patients' blood loss during the operation, blood products given to the patients during surgery, the post-operative bleeding amount, and the post-operative blood products were all recorded.

Pre-operative complete blood count, prothrombin time (PT), and activated partial thrombin time (aPTT), as thrombocyte function test the Epinphrine-stimulated *in vitro* aggregation response (EPN) tests were made, the bleeding risk was evaluated. Pre-operative examinations were accepted as the 1st day, and blood values were followed for a total of 10 days.

For the statistical analysis, the SPSS 15.0 for Windows program was used. Descriptive statistics were given for categorical variables as number and percentage, for the numerical variable as mean value, standard deviation, and median. Since the comparisons of two independent groups did not fulfill the numerical variables normal distribution condition, the Mann–Whitney U-test was made. The alterations monitored in the independent groups were reviewed by the repetitive measurement variance analysis. The statistical alpha significance level was assumed as $P<0.05$.

RESULTS

A total of 80 patients, which consist of 32 male and 48 female patients, were admitted to the study. Their average of age was 68.5±14.1. The patients' demographic features, chronic diseases, drugs used, and perioperative blood losses and blood products utilization rates are shown in Table 1.

Considering the blood counts, there has not been determined any statistically significant difference in the hemoglobin and hematocrit mean values observed in patients, who do or do not use any AAs.

There was no statistically significant difference in the bleeding amount during the operation, the erythrocyte suspension (ES) given during the operation, the amount of ES given after the operation, and the rate of blood product

Table 1: Demographic particulars of patients participating in the study

Age Mean±SD (min-max)	68.5±14.1 (65–88)
Gender n (%)	
Male	32 (40.0)
Female	48 (60.0)
Additional diseases n (%)	
HT	42 (52.5)
DM	22 (27.5)
COPD	8 (10.0)
IHD**	5 (6.3)
Malignity n (%)	17 (21.3)
Utilization of antiaggregants n (%)	30 (37.5)
LMWH* prophylaxis n (%)	47 (58.8)
Blood loss during operation mean±SD (min-max)	1025.6±842.2 (400–5000)
Blood product utilization during operation n (%)	52 (65.0)
Post-operative bleeding n (%)	5 (6.3)
Blood product utilization after operation n (%)	37 (46.3)

*LMWH: Low-molecular-weight heparin, **IHD: Ischemic heart disease, DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease, HT: Hypertension

transfusion use between those who stopped using AA and those who did not use AAs (Table 2).

The rate of blood product utilization during surgery of those using prophylactic LMWH was statistically significantly higher in comparison to those not on prophylactic LMWH (P=0.034) (Table 2).

In the comparison made between patients with an EPN test of 100 and above, and those patients with an EPN test below 100, there has not been determined any statistically significant difference in the means of the bleeding amount, the ES, the fresh frozen plasma (FFP) number given during the surgery, the means of the ES, the FFP number given after the operation, and the blood products transfusion utilization rates (P>0.005).

There was no statistical correlation apart from the weak correlation between EPN, entry APTT, PT levels and the blood amount given during the operation and the ES, the FFP number given during the surgery, the ES, FFP number given after the operation, hemoglobin, thrombocyte levels, as well as the EPN thrombocyte 3 level (Table 3).

There was no statistically significant difference in the amount of bleeding during the operation, the ES given in the operation, the number of FFPs, the ES given after the operation, the amount of FFP in the patients with or without malignancy, and the rate of blood product transfusion use (P>0.005).

There was no statistically significant difference in the amount of bleeding during the operation, the ES given in the operation, the number of FFPs, the ES given after the operation, the amount of FFP in patients with malignancy and using AA, and the rates of blood product transfusion use (P>0.005).

There was no statistically significant difference in the amount of bleeding during the operation, the number of ES given in the operation, the number of FFP, the ES given after the operation, the amount of FFP in the patients with malignancy who did not use prophylactic LMWH, and the rates of blood product transfusion use (P>0.005).

DISCUSSION

As a result of the study, we have observed that there was not any increase of bleeding in the perioperative period in patients aged 65 years and over, who have undergone vertebral surgery, after the discontinuation of ASA and CLP. We have just observed a slight increase in the rate of post-operative blood products utilization in those patients having undergone LMWH prophylaxis.

In our study, a major part of our patients was on AA. The first of these drugs, that is, ASA, is the AA most frequently used for the purpose of the primary and secondary protection in cardiovascular diseases. AA causes the irreversible acetylation of the serine residues of the cyclooxygenase 1 enzyme in the position 529. Thereby, it prevents the formation of thromboxane A2, which is a potent activator and vasoconstrictor for thrombocyte aggregation. In patients on ASA treatment, a decrease of 34% was seen in non-fatal myocardial infarct, of 25% in non-fatal stroke, and 18% in vascular incidents.[6-9] Since ASA is an irreversible COX inhibitor, it is considered as increasing the bleeding risk in operations. However, studies made related to the effect of AAs in operations do not provide a homogeneous implementation in clinic practice. Multicenter and placebo-controlled double-blind STRATAGEM study resulted with the conclusion that there was not any difference in ASA utilization or stopping in non-cardiac surgery in major thrombotic terms and in terms of bleeding.[10] It has been published that despite the fact that ASA utilization was discontinued 1 week before in patients who have undergone spinal fusion surgery, post-operative drainage increased.[11] Whereas in another study, it has been stated that along with the fact that the ASA and CLP utilization in patients with hip fracture increases blood loss, it does not cause any severe blood loss to an extent which prevents this operation.[12] However, in two major randomized studies, it was stated that the probability of bleeding during the operation increases when ASA is not discontinued[6,7] Therefore, in clinical practice, it is a common practice to discontinue ASA before the operation in elective cases. Studies related to the correlation between

Table 2: Perioperative bleeding and blood products amount used in patients who are/are not on antiaggregants and LMWH

Blood loss and Erytrocyte suspension transfusion in operation and after operation	Antiaggregant utilization				P	Prophylactic LMWH* utilization				P
	No. (n=52)		Yes (n=30)			No. (n=33)		Yes (n=47)		
	Mean±SD	Median	Mean±SD	Median		Mean±SD	Median	Mean±SD	Median	
Blood loss during operation	1049.0±742.1	800	986.7±999.5	550	0.166	863.6±554.1	550	1139.4±986.1	750	0.127
ES* given during operation (cc)	864.4±984.1	800	1040.0±1434.9	800	0.874	612.7±726.4	400	1153.2±1360.9	800	0.083
ES* given after operation (cc)	192.0±389.6	0	240.0±453.0	0	0.622	206.1±459.6	0	212.8±380.9	0	0.327
	n	%	n	%		n	%	n	%	
Blood products during operation	34	68	18	60	0.468	17	51.5	35	74.5	0.034
Post-operative bleeding	3	6	2	6.7	1	3	9.1	2	4.3	0.644
Blood product given after operation	22	44	15	50	0.602	11	33.3	26	55.3	0.052

ASA and vertebral surgery are limited, and there is not any standard approach as to the number of days when ASA shall be discontinued before the operation. In the studies, ASA was discontinued 3, 4, 7, and 10 days before the operation, whereby all of them have been efficient in reducing bleeding. There has not been determined any distinct difference between them in clinical terms.[1]

One of the AAs most frequently used in the geriatric group is CLP, a potent AA of the thienopyridine group. CLP causes an irreversible platelet adenosine diphosphate receptor blockage. It is assumed to be better in secondary cardiac protection in comparison to ASA. It is frequently used following coronary stent placements and bypass surgery. It is recommended that CLP is discontinued 7 days before elective operations. It is reported that the bleeding risk decreased at the end of this period.[13] By the utilization of ASA and CLP jointly, efficiency increases in the prevention of cardiovascular incidents. However, the bleeding risk increases at the same time.[7,8]

About 30% of our patients used ASA or CLP, or both. In all cases, the AA treatment was discontinued 7 days before the operation. In these patients, there has not been determined any difference in terms of bleeding and the utilization of blood products during and after the operation in comparison to the group not using any AAs. These findings suggest that discontinuing the AA treatment 7 days before the operation is significant in terms of minimizing the bleeding risk.

In pre-operative evaluations, apart from the hemogram, PT, aPTT and as thrombocyte aggregation test the EPN in PFA 100 have been applied to the patients.

Since AAs dissolve the thrombocyte adhesion, we have applied EPN as their effects' control test. By means of this test, we have evaluated the correlation with perioperative bleeding amount. A weak statistical correlation was just determined between the EPN value and the thrombocyte number on the postoperative 3rd day. On total evaluation, it is observed that there is not any significant increase of bleeding in the perioperative period even if the EPN values are above 100.

In our study, there was just a single case on oral anticoagulant and was using Rivaroksaban, which is a factor Xa inhibitor. The treatment of this patient was also discontinued 7 days before and LMWH was introduced. There was not any perioperative increase of bleeding in this patient neither. About 47% of the patients, including this one, have used prophylactic LMWH.

Heparin is a polysaccharide consisting of D-glucosamine and iduronic acid, which include sulfate roots at various

Table 3: Correlation between bleeding coagulation tests and perioperative bleeding and blood products used

Blood Loss, Transfusion in operation and after operation; Hematocrit and Trombocytes counts 1-10 days after operation	EPN*		APTT** ENTRY		Prothrombin time ENTRY_sn		Prothrombin time ENTRY act_yzd		Prothrombin time ENTRY_INR	
	rho	P	rho	P	rho	P	rho	P	rho	P
Blood loss in operation	−0.068	0.567	−0.130	0.252	−0.150	0.188	0.143	0.208	−0.140	0.218
ES*** given in operation (cc)	−0.083	0.481	−0.107	0.349	−0.210	0.063	0.173	0.127	−0.189	0.095
FFP**** number given in operation	−0.089	0.453	−0.013	0.909	−0.190	0.093	0.162	0.154	−0.176	0.122
ES after operation (cc)	−0.061	0.603	−0.040	0.723	−0.037	0.746	0.057	0.615	−0.029	0.803
FFP number after operation	0.030	0.801	0.118	0.300	0.023	0.841	−0.018	0.875	0.030	0.790
Hct1*****	−0.039	0.738	−0.111	0.329	−0.165	0.147	0.148	0.193	−0.162	0.153
Hct2	0.084	0.475	0.127	0.264	0.090	0.433	−0.134	0.239	0.101	0.376
Hct3	−0.034	0.781	0.061	0.601	−0.060	0.608	0.086	0.459	−0.062	0.594
Hct4	−0.137	0.256	0.071	0.541	0.000	0.999	0.032	0.783	−0.007	0.951
Hct5	−0.196	0.101	0.105	0.367	−0.040	0.731	0.043	0.710	−0.036	0.758
Hct6	−0.188	0.116	−0.110	0.343	0.009	0.938	0.006	0.961	0.006	0.960
Hct7	−0.079	0.510	−0.045	0.703	0.046	0.691	−0.111	0.340	0.080	0.494
Hct8	−0.185	0.123	−0.095	0.416	−0.064	0.583	0.028	0.814	−0.048	0.682
Hct9	−0.141	0.242	−0.069	0.551	−0.136	0.240	0.073	0.528	−0.104	0.371
Hct10	−0.228	0.056	0.022	0.853	−0.064	0.585	0.049	0.674	−0.048	0.678
Tr1******	0.055	0.641	0.095	0.404	−0.118	0.301	0.089	0.437	−0.113	0.321
Tr2	0.106	0.373	0.131	0.253	−0.086	0.455	0.100	0.382	−0.103	0.370
Tr3	0.244	0.040	0.213	0.064	−0.037	0.749	0.077	0.507	−0.051	0.662
Tr4	0.036	0.765	0.102	0.381	−0.081	0.486	0.110	0.345	−0.093	0.423
Tr5	−0.066	0.586	0.038	0.747	−0.171	0.139	0.186	0.108	−0.180	0.120
Tr6	−0.104	0.387	−0.003	0.979	−0.136	0.243	0.130	0.262	−0.137	0.239
Tr7	−0.093	0.442	0.018	0.875	−0.145	0.210	0.107	0.356	−0.126	0.280
Tr8	−0.061	0.611	0.085	0.463	−0.062	0.597	0.024	0.834	−0.045	0.698
Tr9	−0.047	0.694	0.037	0.748	−0.064	0.582	0.027	0.816	−0.046	0.690
Tr10	−0.053	0.658	0.050	0.669	−0.024	0.837	−0.002	0.985	−0.003	0.979

*EPN: Epinephrine, **APTT: Activated partial thrombin time, ***ES: Erythrocyte suspension, ****FFP: Fresh frozen plasma v, ***** Hct: Hematocrit, ******Tr: Thrombocyte

positions. Along with classical heparin, its low-molecular-weight derivatives, which are easy to use and follow-up, are commonly used in the clinic. It requires antithrombin (AT), which is a plasma factor, for the anticoagulant effect of the heparin molecule. By means of the pentasaccharide chain in the heparin, the molecule connects to AT. Thus, both standard heparin as well as LMWH inactivates factor Xa through AT. Since heparin effects through AT, it is considered as an indirect thrombin inhibitor. The heparin-AT complex, along with thrombin, inhibits FXIa, FXa, and FIXa as well.[14,15]

Today, post-operative venous thromboembolism is still a significant reason of mortality and morbidity.[16] Therefore, those patients in the risk group in scorings such as "The surgical-thromboembolism-prevention risk assessment model" made on geriatric patient groups undergoing major operations, for example, vertebral surgery, are generally given LMWH, which is introduced in the intraoperative phase and continued in the post-operative phase.[17] Likewise, in our patient group, patients with a high risk of thromboembolism were applied LMWH pursuant to this approach.

In our study, an increase, which might be considered as significant, was just observed in the post-operative blood product utilization in patients using LMWH. In the parameters apart from this, there was not any significant difference. In addition, among these patients, cancer patients were assessed separately. Due to the increase of the coagulation tendency and due to comorbid diseases in cancer patients, AAs and anticoagulants may be used. Therefore, the bleeding tendency increases in cancer patients during and after the operation.[18] In our study, we have seen that bleeding did not increase in the group of cancer patients using LMWH.

Limitations of study

The most important limitation of our study is the fact that it is retrospective.

CONCLUSION

In the geriatric group of age, which shall undergo vertebral surgery, it seems like an appropriate approach to discontinue AA and OAC 7 days before the operations. We have observed that the utilization of LMWH either for prophylactic purposes or for bridging purposes in the group using OAC does not significantly increase the bleeding probability. Therefore, on indication in the geriatric group of patients, we consider the utilization of LMWH,

along with close follow-up and the necessary support, appropriate. Besides, we suggest that in cancer patients, who are assumed as a vulnerable group in operations, LMWH may be used for the purpose of prophylaxis.

ACKNOWLEDGMENT

We acknowledge all the doctors who participated in the study and special thanks to Istanbul Spine Center, Florence Nightingale Hospital, Istanbul, Turkey.

REFERENCES

1. Bible JE, Mirza M and Knaub MA. Blood-loss management in spine surgery. J Am Acad Orthop Surg. 2018;26(2):35-44.
https://doi.org/10.5435/jaaos-d-16-00184
2. Kato S, Chikuda H, Ohya J, Oichi T, Matsui H, Fushimi K, et al. Risk of infectious complications associated with blood transfusion in elective spinal surgery: A propensity score matched analysis. Spine J. 2016:16(1):55-60.
https://doi.org/10.1016/j.spinee.2015.10.014
3. Douketis JD. Perioperative management of patients who are receiving warfarin therapy: An evidence-based and practical approach. Blood. 2011;117(19):5044-5049.
https://doi.org/10.1182/blood-2011-02-329979
4. Nikolakopoulos I and Spyropoulos AC. Heparin bridging therapy for patients on chronic oral anticoagulants in periprocedural settings. Semin Thromb Hemost. 2020;46(1):26-31.
https://doi.org/10.1055/s-0039-1696945
5. Cloyd JM, Acosta FL Jr. and Ames CP. Complications and outcomes of lumbar spine surgery in elderly people: A review of the literature. J Am Geriatr Soc. 2008;56(7):1318-1327.
https://doi.org/10.1111/j.1532-5415.2008.01771.x
6. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial Infarction: ISIS-2. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Lancet. 1988;2(8607):349-360.
7. Collaborative overview of randomised trials of antiplatelet therapy--II: Maintenance of vascular graft or arterial patency by antiplatelet therapy. Antiplatelet Trialists' Collaboration. BMJ. 1994;308(6922):159-168.
8. Collaborative overview of randomised trials of antiplatelet therapy--III: Reduction in venous thrombosis and pulmonary embolism by antiplatelet prophylaxis among surgical and medical patients. Antiplatelet Trialists' Collaboration. BMJ. 1994;308(6923):235-246.
9. Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. BMJ. 2002;324(7329):71-86.
https://doi.org/10.1136/bmj.324.7329.71
10. Mantz J, Samama CM, Tubach F, Devereaux PJ, Collet JP, Albaladejo P, et al. Impact of preoperative maintenance or interruption of aspirin on thrombotic and bleeding events after elective non-cardiac surgery: The multicentre, randomized, blinded, placebo-controlled, STRATAGEM trial. Br J Anaesth. 2011;107(6):899-910.
https://doi.org/10.1093/bja/aer274
11. Kang SB, Cho KJ, Moon KH, Jung JH and Jung SJ. Does low-dose aspirin increase blood loss after spinal fusion surgery? Spine J. 2011;11(4):303-307.
https://doi.org/10.1016/j.spinee.2011.02.006
12. Chechik O, Thein R, Fichman G, Haim A, Ben Tov T and Steinberg EL. The effect of clopidogrel and aspirin on blood loss in hip fracture surgery. Injury. 2011;42(11):1277-1282.
https://doi.org/10.1016/j.injury.2011.01.011
13. Weber AA, Braun M, Hohlfeld T, Schwippert B, Tschöpe D and Schrör K. Recovery of platelet function after discontinuation of clopidogrel treatment in healthy volunteers. Br J Clin Pharmacol. 2001;52(3):333-336.
https://doi.org/10.1046/j.0306-5251.2001.01453.x
14. Hirsh J and Raschke R. Heparin and low-molecular-weight heparin: The Seventh ACCP Conference on Antithrombotic and Thrombolytic therapy. Chest. 2004;126(3 Suppl):188S-203S.
https://doi.org/10.1378/chest.126.3_suppl.188S
15. Fareed J, Hoppensteadt DA and Bick RL. An update on heparins at the begining of the new millenium. Semin Thromb Hemost. 2000;26(suppl 1):5-21.
https://doi.org/10.1055/s-2000-9498
16. Geerts WH, Bergqvist D, Pineo GF, Heit JA, Samama CM, Lassen MR, et al. Prevention of venous thromboembolism: American college of chest physicians evidence-based clinical practice guidelines (8th edition). Chest. 2008;133(6 Suppl): 381S-453S.
https://doi.org/10.1378/chest.08-0656
17. Chahal R, Alexander M, Yee K, Jun CM, Dagher JG, Ismail H, et al. Impact of a risk-stratified thromboprophylaxis protocol on the incidence of postoperative venous thromboembolism and bleeding. Anaesthesia. 2020;75(8):1028-1038.
https://doi.org/10.1111/anae.15077
18. Johnstone J and Rich SE. Bleeding in cancer patients and its treatment: A review. Ann Palliat Med. 2018;7(2):265-273.
https://doi.org/10.21037/apm.2017.11.01

Authors Contribution:
BY- Definition of intellectual content, literature survey, prepared first draft of manuscript, implementation of study protocol, data analysis, manuscript preparation, and submission of article; **ME**- Manuscript preparation, editing, and manuscript revision; **AH**- Design of study, statistical analysis, and interpretation; **RDK**- Review manuscript concept, design, and clinical protocol; **NB**- Data collection literature survey.

Work attributed to:
Istanbul Spine Center, Florence Nightingale Hospital Istanbul/Turkey.

Orcid ID:
Bulent Yardimci - https://orcid.org/0000-0002-0364-8238
Meric Enercan - https://orcid.org/0000-0003-3263-9290
Azmi Hamzaoglu - https://orcid.org/0000-0003-4785-2617
Reyhan Diz Kucukkaya - https://orcid.org/0000-0001-5814-7118
Nomin Bold - https://orcid.org/0000-0002-6765-8208

Source of Funding: None, **Conflicts of Interest:** None.