

Outcomes of Open Surgery for Retroperitoneal Hematoma in Covid-19 Patients: Experience from a Single Centre

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Rezumat

Rezultatele intervenției chirurgicale deschise pentru hematomul retroperitoneal la pacienții cu Covid-19: experiență dintr-un singur centru

Context: Hematomul retroperitoneal spontan este o complicație severă și potențial fatală care apare în timpul terapiei anti-coagulante. Dozele terapeutice de heparină cu greutate moleculară mică (LMWH) sunt utilizate pentru a preveni tromboza la pacienții grav bolnavi de Covid-19.

Metode: Descriem 27 (0,14%) pacienți cu hematoame retroperitoneale care au necesitat intervenții chirurgicale de urgență, dintr-un total de 19108 pacienți cu Covid-19 care au fost internați în Spitalul Batajnica Covid în perioada martie 2021 - martie 2022. Toți pacienții au primit doze terapeutice LMWH. Prezența hematomului retroperitoneal a fost confirmată prin ecografia abdomenului și tomografie computerizată.

Rezultate: intervenția chirurgicală deschisă a fost efectuată la 27 de pacienți cu hematoame retroperitoneale spontane (12 femei și 15 bărbați). Vârsta medie a populației studiate a fost de 71,6±11,9 ani. D-dimerul a fost semnificativ crescut cu două zile înainte de operație comparativ cu valorile din ziua intervenției chirurgicale ($p=0,011$). Șase dintre pacienți (22,23%) au supraviețuit, în timp ce 21 (77,77%) pacienți au decedat.

Concluzie: Hemoragia la pacienții cu Covid-19 tratați cu LMWH este asociată cu un risc crescut de dezvoltare a hematomului retroperitoneal. Operația deschisă a hematomului retroperitoneal a pacienților cu Covid-19 sub tratament anticoagulant este o procedură asociată cu o rată ridicată de mortalitate.

Received: 29.07.2022
Accepted: 04.09.2022

Cuvinte cheie: hematom retroperitoneal spontan, abordarea operațiunii deschise, pacienții cu Covid-19, D-dimer, terapia anticoagulantă

Abstract

Background: Spontaneous retroperitoneal hematoma is a severe and potentially fatal complication that appears in the course of anticoagulation therapy. Therapeutic doses of low molecular weight heparin (LMWH) are used for the prevention of thrombosis in patients seriously ill with Covid-19.

Methods: We describe 27 (0.14%) patients with retroperitoneal hematomas who required emergency surgery out of 19108 patients with Covid-19 who were hospitalized in Batajnica COVID Hospital between March 2021 and March 2022. All the patients were on therapeutic doses of LMWH. The existence of retroperitoneal hematoma was confirmed by abdominal ultrasound and computed tomography scans.

Results: Open surgery was performed on 27 patients with spontaneous retroperitoneal hematomas (12 female and 15 male). The mean age of the study population was 71.6 ± 11.9 years. D-dimer was significantly elevated two days before the surgery in comparison with the values on the day of surgery ($p=0.011$). Six patients (22.23%) survived, while 21 (77.77%) patients died.

Conclusion: Bleeding in Covid-19 patients treated by LMWH is associated with an increased risk of developing retroperitoneal hematoma. Open surgery for retroperitoneal hematoma in Covid-19 patients on anticoagulation therapy is a procedure associated with a high rate of mortality.

Key words: spontaneous retroperitoneal hematoma, open surgery approach, Covid-19 patients, D-dimer, anticoagulant therapy

Introduction

Spontaneous retroperitoneal hematomas (SRH) may occur in hospitalized patients with Covid-19 pneumonia in the course of anticoagulation therapy (1). SRH is defined as bleeding into retroperitoneal space without an associated trauma or iatrogenic manipulation, and a common site for this bleeding is the iliopsoas muscle (1,2). Bleeding diathesis is likely multifactorial, related to the Covid-19 illness severity itself or the use of anticoagulation. It was reported that therapeutic anticoagulation treatment may be beneficial for critically ill patients with Covid-19 infection (3). The incidence of SRH is 3-4 times higher in Covid-19 patients on anticoagulation therapy than that in patients on anticoagulant therapy without Covid-19 (1). Bleeding was detected in 5.6% of the critically ill patients receiving anticoagulant thromboprophylaxis, while baseline

platelet count below $150 \times 10^9/L$ and D-dimer levels above 2500 ng/ml were identified as independent predictors of the risk of major bleeding (4,5). However, intensified anticoagulation regimens may reduce the risk of a thrombotic event, increasing at the same time major bleeding rates to unacceptable levels in critically ill patients (5). Recently, with Covid-19 pandemic spreading all over the world, it has been demonstrated that patients with severe Covid-19 pneumonia on anticoagulant/antithrombotic therapies have an increased risk of spontaneous bleeding (6). Mechanism by which heparin or LMWH provide protection is still not clear, and it is questionable whether an individual patient's bleeding risk outweighs the benefit of their use (7).

Management and treatment of SRH is still controversial due to a lack of specific guidelines to suggest the best treatment option (1). There are three possible ways for managing

SRH: conservative; open surgery approach; and interventional radiology with intra-arterial embolization or stent-grafting (8). Open surgery is considered in very selective cases, because surgical removal may impair retroperitoneal tamponade effects, resulting in increased bleeding. Endovascular treatment with percutaneous trans-arterial embolization is an effective treatment for SRH and represents a life-saving procedure (1).

During Covid-19 pandemic, a rising number of sporadic cases of SRH, which were treated differently and with different outcomes, relative to the experience of the staff and the equipment of the hospital in question, have been reported in literature. The knowledge related to the disease progression, treatment strategies, and indications for surgical interventions is still quite limited, though (9). Having worked in a large specialized Covid-19 hospital, we had an opportunity to treat a group of critically ill Covid-19 patients with SRH using the open surgery approach. The aim of our study was to analyze the outcomes of open surgery for retroperitoneal hematoma in patients seriously ill with Covid-19 pneumonia on anticoagulants, as well as to investigate their clinical and laboratory data.

Materials and Methods

We retrospectively analyzed all consecutive patients with a confirmed Covid-19 infection who developed SRH and who underwent emergency surgery between March 2021 and March 2022 in Batajnica COVID Hospital, University Clinical Centre of Serbia. The study was approved by the local Institutional Review Board of University Clinical Centre of Serbia; Number 878/5. In the observed period, the total number of Covid-19 patients was 19108 and of them, on 27 (0.14%) open surgery was performed because of uncontrolled bleeding into the retroperitoneal space. Patients on whom open surgery was performed belonged to an older age group (71.6 ± 11.9 years), were slightly overweight (BMI: 28.0 ± 2.4 kg/m²), and predominantly male (55.6%). Five (18.5%) patients were vaccinated against Covid-19,

while 22 (81.5%) were not. Baseline demographic and clinical data of the patients studied are presented in *Table 1*. The average length of hospitalization was: 13.07 ± 7.54 days.

Statistical Analysis

Descriptive statistics were calculated for the baseline demographic and clinical features, as well as for the treatment outcomes. Continuous variables were presented as means with standard deviations or medians with 25-75 percentiles according to the data distribution. Categorical variables were presented with numbers and percentages. Continuous data before, during, and after the surgery were compared with the Repeated measures ANOVA or Friedman test, according to the data distribution. Tuckey post or Wilcoxon sum rank test was used for the post-hoc comparison. A p value of less than 0.05 was considered statistically significant. Statistical analysis was performed by IBM SPSS Statistics 26 (IBM SPSS Inc., Chicago, IL).

Results

All patients were on standard therapeutic anticoagulation regimen with low molecular weight heparin (Fraxiparine®) (1.0-1.8 ml per day, divided into two doses), in accordance with local protocol recommendations based on suggestions made by the ATTACC, ACTIV-4A, and REMAP-CAP Investigators (10), and they were in intensive care unit on continuous monitoring. Some of the patients used anti-thrombin inhibitors or Aspirin before hospitali-

Table 1. Baseline demographic and clinical data of the studied patients

	n (%)
Gender (m), n (%)	15 (55.6)
Vaccination, n (%)	5 (18.5)
Without vaccination, n (%)	22 (81.5)
Age, $\bar{x} \pm \text{sd}$	71.6 ± 11.9
BMI (kg/m ²), $\bar{x} \pm \text{sd}$	28.0 ± 2.4
Hematoma size (mm), Med (25 th -75 th percentile)	140 (90-180)
Hematoma volume (mm ³), Med (25 th -75 th percentile)	702.2 (392-1733.7)
Survived, n (%)	6 (22.2)



Figure 1. Contrast enhanced abdominopelvic CT, axial image, arterial phase: huge retroperitoneal hematoma located in the right posterior pararenal and lateroconal fascia without contrast "blush". No sign of active bleeding



Figure 2. Contrast enhanced abdominopelvic CT, coronal reconstruction, arterial phase: Huge bilobar retroperitoneal hematoma located in the posterior pararenal and right iliac region, without signs of active bleeding

zation and initialization of LMWH, while there was not an association between LMWH and Aspirin or any other thrombin inhibitors in the treatment protocol. A sudden decrease in the patients' hemoglobin levels and their clinical picture raised a suspicion of bleeding. After the first LMWH administration bleeding occurred in patients as follows: first week (day 1: 1 patient; day 2: 1; day 5: 2; day 6: 1 and day 7: 1); second week (day 8: 2 patients; day 9: 1; day 10: 1; day 11: 2; day 12: 1; day 13: 1 and day 14: 1); third week (day 15: 1 patient; day 16: 1; day 18: 2; day 19: 1; day 21: 2); fourth week (day 22: 1 patient; day 23: 1; day 25: 1;

day 26: 1 and day 28: 1). After the initial surgical examination and a clinical suspicion of the existence of retroperitoneal hematoma, further diagnostics was done by ultrasound and multi-slice computed tomography (MSCT) examination (SIEMENS SOMATOM go. All). MSCT findings for four patients are given in *Figs. 1, 2, 3, 4*. The median size of the retro-peritoneal

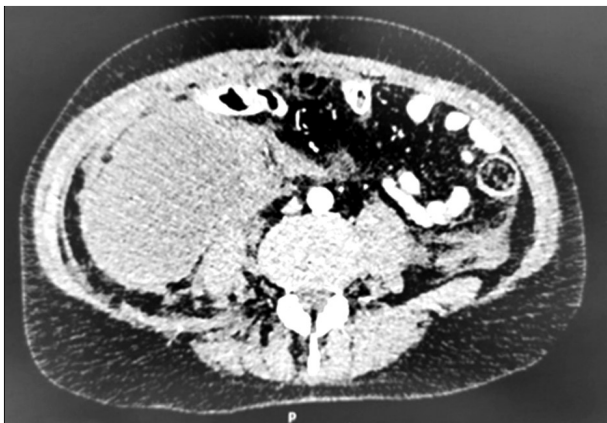


Figure 3. Contrast enhanced abdominopelvic CT, axial image, arterial phase: Huge retroperitoneal hematoma located in the right posterior pararenal and lateroconal fascia with compression to ascending colon without contrast "blush". No CT sign of active bleeding

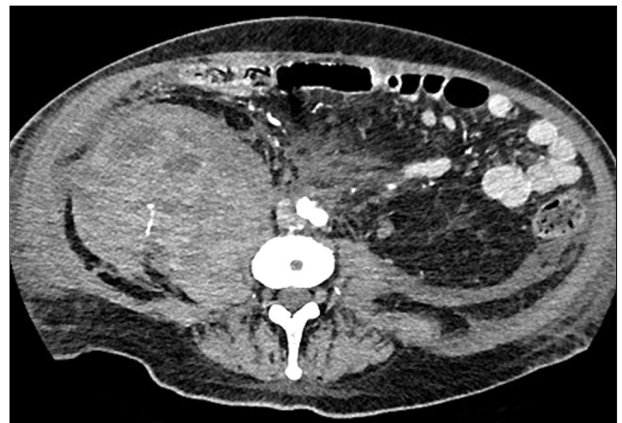


Figure 4. Contrast enhanced abdominopelvic CT, axial image, arterial phase: Huge retroperitoneal hematoma located in the right posterior pararenal and lateroconal fascia with small contrast "blush" in medial region of hematoma- CT sign of active bleeding

Table 2. Laboratory data of the studied patients

	Before	Surgery	Post-surgery	p
HGB (g/l)*	113.4 ± 22.7	76.7 ± 26.4	96.3 ± 20	<0.001
HCT (L/L)*	0.3 ± 0.1	0.3 ± 0.2	0.3 ± 0.1	0.164
Platelets x10 ⁹ /L	168(121-251)	175(99-232)	88(57-149.5)	<0.001
Urea (mmol/l)	14.7(10-20.7)	20(13.1-29.9)	20.9(11.8-24.2)	<0.001
Creatinine (μmol/l)	118(74-226)	179(76-363)	127.5(69-339)	0.038
Ferritin (μg/L)	861.2(461.4-1383)	1004(654-1438)	1516(608.3-5068.6)	0.028
CRP (mg/L)	41.6(20.8-68.1)	13.6(9-47.5)	103.4(13-156.6)	0.047
Fibrinogen (g/L)	4.3(3.1-6.2)	2.9(2.1-4.3)	3.6(2.8-5)	0.048
D-dimer (mg/L)	1.1(0.7-3.1)	0.7(0.4-1.7)	1.2(0.7-3.2)	0.028
Albumin (g/l)	31(27-35)	27(25-30)	28(26-29)	<0.001

Data are expressed as Med (25th-75th percentile) and analyses with Friedman test;

*data are expressed as $\bar{x} \pm sd$ and analyzed with repeated measures ANOVA

hematoma on MSCT was 140 mm (*Table 1*).

Conservative treatment was administered to each patient when the first symptoms of SRH developed. In cases when the clinical picture worsened significantly, which was accompanied by a progressive decrease in hemoglobin levels – indications that conservative treatment had failed – a decision to perform explorative laparotomy with tamponade was made. Indications for immediate surgical intervention was hemoglobin level below 50 g/l and/or active bleeding described on MSCT. Since at that time interventional radiology was not available in our hospital, the only surgical option at our disposal following laparotomy was to use a large amount of abdominal gauze packing. LMWH was reinstated in the postoperative drug treatment protocol.

The following comorbidities (expressed in percentage) were found in these 27 patients: hypertension (47.00%); chronic renal insuffi-

ciency (25.00%); acute renal insufficiency (3.12%); atrial fibrillation (37.50%); diabetes mellitus (28.00%); chronic hemodialysis (16.00%); and chronic obstructive pulmonary disease (6.25%).

The patients' laboratory test results two days before operation, on the day of the operation, and two days after the operation are given in *Table 2* and *Table 3*, as well as the significance of differences between the values.

D-Dimer was significantly elevated two days before surgery in comparison with the values on the day of the surgery ($p=0.011$). Platelet counts were significantly lowered two days after the surgery in comparison with the values two days before the surgery ($p<0.001$). Creatinine values were significantly elevated on the day of the surgery in comparison with those of two days previously ($p=0.09$).

Six (22.23%) patients survived open surgery, while 21 (77.77%) died. There was no early or late complications (e.g. rebleeding or sepsis) in

Table 3. Significance of differences between the values

	Post hoc test		
	Before vs. surgery	Before vs post-surgery	Surgery vs post-surgery
HGB*	<0.001	0.002	0.002
Urea	<0.001	0.001	0.240
Platelets	0.089	<0.001	0.005
Creatinine	0.009	0.833	0.034
Ferritin	0.685	0.010	0.031
CRP	0.072	0.015	0.011
Fibrinogen	0.001	0.211	0.167
D-dimer	0.011	0.987	0.145
Albumin	0.002	0.003	0.332

wilcoxon test*Tuckey post hoc test;

survived patients after the surgery. Post-mortem examinations were not performed.

Discussion

Literature data related to SRH occurrence in Covid-19 patients are rare and isolated in most cases (11). Hematomas are relatively rare clinical conditions, but their mortality may be high in Covid-19 patients. Mortality rates in association with retroperitoneal hematoma are highly variable, ranging from 0.6% to 70% (12). Mortality may be reduced by early diagnosis of hematoma and the use of interventional methods (13). All critical patients with Covid-19 infection have a higher risk of hypercoagulable conditions (14). Changes in coagulation may be generated by a direct effect of SARS-CoV-2 on hemostatic changes or may result from a severe pro-inflammatory state (15). Anticoagulation therapy is used in Covid-19 patients in order to prevent or treat thromboembolic events (16). The choice of the optimal anticoagulant drug and dosage for the prevention of venous thromboembolism in acutely ill adults in hospital is still undetermined (17). Both Covid-19 itself and the anticoagulant treatment may induce bleeding, including the development of retroperitoneal hematomas (13). Higher-dose anticoagulants slightly increase major bleeding in people hospitalized with Covid-19 (18).

Open surgery for retroperitoneal hemorrhage is indicated in cases when a patient remains unstable despite adequate fluid and blood product replacement, or if interventional radiology is not successful or available (8). Surgical evacuation is rarely performed because it may release the tamponade effect that might be associated with significant morbidity. It should be considered in cases when conservative management has failed and hemorrhage is ongoing, or in the presence of compartment syndrome (19,20). The primary aim of surgery is to put under control all actively bleeding points, and the secondary aim is to remove the large hematoma. In our study, we analyzed the occurrences of life-

threatening hematomas managed by open surgery approach in some among a large number of hospitalized patients with Covid-19 pneumonia in a specialized Covid-19 hospital. The detection of retroperitoneal hematoma and active extravasation was established with contrast-enhanced computed tomography. In this group of Covid-19 patients on anticoagulants, we detected a relatively rare occurrence of spontaneous development of retroperitoneal hematoma that had to be managed with open surgery. Of 19108 patients who were hospitalized for Covid-19 in Batajnica Covid Hospital between March 2021 and March 2022, 27 (0.14%) developed spontaneous retroperitoneal hematoma. In open surgery procedures, the retroperitoneum may need to be packed and re-explored within 24-48 hours (6,21), as we did with most of our patients. All the blood is to be removed, and the abdomen must be packed with large swabs. According to the suggested procedure, in the next step, swabs can be removed in order to find the source of the bleeding (8). Another indication for open surgery is the development of abdominal compartment syndrome resulting from a large retroperitoneal hematoma (8).

With regard to laboratory data, elevated D-dimer levels at initial presentation may be used to predict bleeding complications, thrombotic complications, critical illness, and death (4,22). Our patients had elevated D-dimer before the intervention (*Table 2*). Intensified anticoagulation use may result in reducing the risk of thrombotic events, increasing meanwhile major bleeding rates in critically ill patients (5). All studied patients were in a critical condition, receiving maximal doses of Fraxiparine®. These findings may indicate the presence of an increased risk of bleeding in the studied group, as it was previously reported for hospitalized patients with Covid-19 (18). It was suggested that anticoagulation dose escalation based on the D-dimer level may not be appropriate for certain patients (22).

Over the last three years of Covid-19 pandemic, sporadic cases of retroperitoneal hematomas have been reported in literature, with different therapeutic approaches and

different outcomes. The first case of retroperitoneal hematoma in a Covid-19 patient was reported in 2020, and it was detected with a CT scan of the abdomen and pelvis with IV contrast (23). Occlusion of the bleeding artery after embolization was successfully achieved (23). The first case of a Covid-19 patient who was on therapeutic anticoagulation and who had lumbar artery bleeding with the development of psoas hematoma was also successfully treated with arterial embolization (24). Singh et al. (25) reported four cases of Covid-19 associated pneumonia that were complicated by bleeding. Among them, two patients were addressed by surgical evacuation of the hematoma, one underwent computed tomography-guided drainage, and one was treated conservatively. A relationship between SARS-CoV-2 and bleeding was also suggested after the evaluation of six cases of abdominal bleeding associated with Covid-19 (26). Three of them were managed conservatively, while in the other three embolization was performed. A catastrophic retroperitoneal hemorrhage under anticoagulant prophylaxis was described in a 65-year-old Covid-19 positive male with diabetes mellitus and hypertension. Massive retroperitoneal hemorrhage involving the psoas muscle was found on the CT scan, and the patient was successfully managed conservatively (27). In another study, five patients with Covid-19 and spontaneous retroperitoneal hemorrhage were presented (28). Four of them were managed conservatively, while on one a surgical intervention was performed. Death from complications of retroperitoneal bleeding of a 51-year-old Covid-19 positive female who was on intermediate-intensity heparin therapy for venous thromboembolism prophylaxis was also reported in literature (29). Surgical exploration of large right-sided retroperitoneal and psoas muscle hematoma was reported in a 57-year-old male with Covid-19 pneumonia who was on prophylactic anticoagulation (30). After the intervention, his condition improved and he was discharged well. In another case report, large right-sided retroperitoneal hematoma extending along with the psoas musculature and the lateral abdominal wall

was described in a 67-year-old male with bilateral Covid-19 pneumonia. Despite adequate intensive conservative management, the patient died (31). Three cases of abdominal spontaneous retroperitoneal hematoma in Covid-19 patients were confirmed with a contrast-enhanced computed tomography (CEST), and embolization was performed in each of the patients; two patients survived and one died. It was concluded that CEST is the imaging of choice to localize the site of bleeding and plan the endovascular treatment, as well as that embolization in such patients is safe and effective (32). Another three patients with bleeding complications secondary to therapeutic anticoagulation in the setting of Covid-19 infection suffered spontaneous bleeding into either the rectus sheath or retroperitoneum. The hemorrhage was confirmed by CT, and the patients were treated conservatively. Two survived and one died (33). Two cases of spontaneous iliopsoas hematoma caused by anticoagulants during the clinical course of Covid-19 were also reported (34). In both patients hematomas were discovered during CT examination. In one patient successful arterial embolization was performed, while the other patient died because of hemorrhagic hypovolemic shock. In the comparison between prophylactic and therapeutic anticoagulant doses, it was reported that the therapeutic dose was associated with a higher risk of major hemorrhage (1.7% versus 3.0%) (35). In a group of 5 patients with RPH conservatively managed, 3 patients died (22), while in a group of 7 patients with abdominal hematoma no one survived (5 patients were on conservative management, 2 were treated surgically) (16). In a recently published study, eight patients with Covid-19 who required surgery died (36), while in our study group 21 of 27 patients died.

Based on available literature data and clinical evidence, it is recommended that further research concerning acute hemorrhage in Covid-19 patients who are on prophylactic anticoagulant therapy should be done (37). It is expected that the risk of bleeding is even higher for Covid-19 patients who are on

therapeutic anticoagulant therapy. Therefore, it has been suggested that spontaneous hematomas may represent a new surgical challenge in COVID patients (36).

The limitation of our study was the lack of a comparative control group of patients with Covid-19 on conservative treatment for spontaneous retroperitoneal hematomas.

Conclusion

The use of anticoagulants in Covid-19 patients is associated with an increased risk of bleeding and development of retroperitoneal hematomas. This risk is further increased by the age, treatment dose of low molecular heparin, and presence of severe or critical forms of Covid-19 disease. A contributing factor to the adverse outcome of the treatment is the presence of severe comorbidities. Open surgery approach for retroperitoneal hematomas among COVID-patients represents a procedure with a high risk and excessive mortality, which should be used only in patients who are seriously ill and when all other previously performed management procedures have not resulted in a satisfactory response. Having in mind that the Covid-19 pandemic is still ongoing, we suggest, based on the data available from literature and our own experience, that a multidisciplinary team of international experts should develop the management plan that would include recommended procedures and their indications for retroperitoneal hematomas in Covid-19 patients.

Conflicts of Interest and Source of Funding

The authors declared no potential conflicts of interest. No specific grant was received for the publication of this article.

Ethical Statement

The study was approved by the local Institutional Review Board of University Clinical Centre of Serbia: Number 878/5.

References

1. Tiralongo F, Seminatore S, Di Pietro S, Distefano G, Galioto F, Vacirca F et al. Spontaneous Retroperitoneal Hematoma Treated with Percutaneous Transarterial Embolization in Covid-19 Era: Diagnostic Findings and Procedural Outcome. *Tomography*. 2022;8:1228-1240.
2. Sunga KL, Bellolio F, Gilmore RM, Cabrera D: Spontaneous retroperitoneal hematoma: etiology, characteristics, management, and outcome. *J Emerg Med*. 2012;43 (2):e157-e161.
3. Obi AT, Barnes GD, Napolitano LM, Henke PK, Wakefield MD. Venous thrombosis epidemiology, pathophysiology, and anticoagulant therapies and trials in severe acute respiratory syndrome coronavirus 2 infection. *J Vasc Surg Venous and Lymphat Disord*. 2021;9:23-35.
4. Al-Samkari H, Karp Leaf RS, Dziki WH, Carlson JCT, Fogerty AE, Waheed A et al. Covid-19 and coagulation: bleeding and thrombotic manifestations of SARS-CoV-2 infection. *Blood* 2020;136 (4):489-500.
5. Chan CN, Weitz JI: COVID-10 coagulopathy, thrombosis, and bleeding. *Blood* 2020; 136 (4):381-383.
6. Conci S, Ruzzenente A, Donadello K, Cybulski AJ, Pedrazzani C, Campagnaro T et al. Haemodynamic instability in a critically ill patient with Covid-19 pneumonia: searching over the chest – report of a clinical case and mini-review of the literature. *Case Rep Imag Surg* 2020;3:1-3.
7. Ten Cate H: Surviving Covid-19 with Heparin? *N Engl J Med*. 2021; 385(9): 845-846.
8. Chan YC, Morales JP, Reidy JF, Taylor PR. Management of spontaneous and iatrogenic retroperitoneal hemorrhage: conservative management, endovascular intervention or open surgery? *Int J Clin Pract* 2008;62 (10): 1604-1613.
9. Wahren MH, Bhattacharya B, Maung AA, Davis KA. Contemporary management of spontaneous retroperitoneal and rectus sheath hematomas. *Am J Surg*. 2020; 219(4):707-710.
10. The ATTACC, ACTIV-4a, and REMAP-CAP Investigators: Therapeutic Anticoagulation with Heparin in Noncritically Ill Patients with Covid-19. *N Engl J Med* 2021;385(9):790-802.
11. Perfecto A, Villalabeitia I, Sendino P, Sarriugarte A. Spontaneous retroperitoneal hematoma in critical patients with bilateral SARS-CoV-2 pneumonia. *Cir Esp*. 2022;100(6):387-388.
12. Sahu KK, Mishra AK, Lal A, George SV, Siddiqui AD: Clinical spectrum, risk factors, management and outcome of patients with retroperitoneal hematoma: a retrospective analysis of 3-year experience. *Expert Rev Hematol*. 2020;13(5): 545-555.
13. Alakus U, Kara U, Cimen S, Tasci C, Eryilmaz M. Life-threatening hematomas in Covid-19 patients. *Ulus Travma Acil Cerrahi Derg*. 2022; 28: 477-482.
14. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with Covid-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395:1054-1062.
15. Bikdeli B, Madhavan MV, Jimenez D, Chiuch T, Dreyfus I, Driggin E, et al. Covid-19 and Thrombotic or Thromboembolic Disease: Implications for Prevention, Antithrombotic Therapy, and Follow-Up. *JACC* 2020;75(23): 2950-2973.
16. Hajian A. A Case Series of Life-Threatening Hemorrhagic Events in Patients with Covid-19. *Indian J Surg*. 2022;84(2):418-424.
17. Eck RJ, Elling T, Sutton AJ, Wetterslev J, Gluud C, van der Hout ICC et al. Anticoagulants for thrombosis prophylaxis in acutely ill patients admitted to hospital: systematic review and network meta-analysis. *BMJ*. 2022;378: e070022.
18. Flumignan RLG, Civile VT, Tinoco JD, Pascoal PIF, Areias LL, Matar CF et al. Anticoagulants for people hospitalized with Covid-19. *Cochrane Database Syst Rev*. 2022;3(3):CD013739.
19. Donaldson J, Knowles CH, Clark SK, Renefrew I, Lobo MD. Rectus sheath haematoma associated with low molecular weight heparin: a case series. *Ann R Coll Surg Engl*. 2007;89:309-312.
20. Kasotakis G: Retroperitoneal and Rectus Sheath Hematomas. *Surg Clin N Am*. 2014;94:71-76.

21. Finlay IG, Edwards TJ, Lambert AW: Damage control laparotomy. *Br J Surg* 2004;91:83-85.
22. Elikowski W, Fertala N, Zawodna-Marszalek M, Karon J, Skrzywanek P, Moser-Lisewska I, et al. Retroperitoneal hematoma in Covid-19 patients – case series. *Pol Med J*. 2022;50(296):118-123.
23. Scialpi M, Russo P, Piane E, Gallo E, Scalera GB: First case of retroperitoneal hematoma in Covid-19. *Turk J Urol*. 2020;46:407-409.
24. Patel I, Akoluk A, Douedi S, Upadhyaya, Mazahir U, Costanzo E, et al. Life-threatening psoas hematoma due to retroperitoneal hemorrhage in a Covid-19 Patient on Enoxaparin Treated With Arterial Embolization: A Case Report. *J Clin Med Res*. 2020;12 (7):458-461.
25. Singh B, Mechineni A, Kaur P, Reid RJ, Maroules M. Covid-19 and bleeding at unusual locations: Report of four cases. *Hematol Transfus Cell Ther*. 2021;43(2):214-218.
26. Sposato B, Croci L, Di Tomassi M, Puttini C, Olivieri C, Alessandri M, et al. Spontaneous abdominal bleeding associated with SARS-CoV-2 infection: causality or coincidence? *Acta Biomed*. 2021;92(2):e2021199.
27. Javid A, Kazemi R, Dehghani M, Samani HB. Catastrophic retroperitoneal hemorrhage in Covid-19 patients under anticoagulant prophylaxis. *Urol Case Rep*. 2021;36:101568.
28. Mahboubi-Fooladi Z, Arabi KP, Khazaei M, Nekooghadam S, Shadbakht B, Moharadz Y, et al. Parenteral Anticoagulation and Retroperitoneal Hemorrhage in Covid-19: Case Report of Five Patients. *SN Compr Clin Med*. 2021;3(10):2005-2010.
29. Ohn MH, Ng JR, Ohn KM, Luen NP. Double-edged sword effect of anticoagulant in Covid-19 infection. *BMJ Case Rep* 2021;14:e241955.
30. Yeoh WC, Lee KT, Yainul NH, Alwi SBS, Low LL. Spontaneous retroperitoneal hematoma: a rare bleeding occurrence in Covid-19. *Oxf Med Case Reports* 2021;9:345-348.
31. Shah M, Colombo JP, Chandna S, Rana H. Life-threatening retroperitoneal hematoma in a patient with Covid-19. *Case Rep Hematol*. 2021;2021: 8774010.
32. Gupta VK, Alkandari BM, Mohammed W, Abdelmohsen MA, Mohammad MGA. Spontaneous retroperitoneal hematoma in Covid-19 severe pneumonia- dual-phase multidetector computed tomography angiogram and role of radiologist. *J Clin Interv Radiol ISVIR*. 2021;6:58-60.
33. Ottewill C, Mulpeter R, Lee J, Shrestha G, O'Sullivan D, Subramaniam A et al. Therapeutic anti-coagulation in Covid-19 and the potential enhanced risk of retroperitoneal hematoma. *QJM*. 2021;114(7): 508-510.
34. Nakamura H, Ouchi G, Miyagi K, Higure Y, Otsuki M, Nishiyama N, et al. Case report: Iliopsoas hematoma during the clinical course of severe Covid-19 in Two Male Patients. *Am. J. Trop. Med. Hyg*. 2021;104(3): 1018-1021.
35. Nadkarni GN, Lala A, Bagiella E, Chang HL, Moreno PR, Pujadas E et al. Anticoagulation, bleeding, mortality, and pathology in hospitalized patients with Covid-19. *JACC*. 2020;76(16):1815-1826.
36. Mirica R, Ungureanu C, Vacarasu A, Ciotirla D, Iosifescu R, Zamfir M, et al. Spontaneous hematomas, the new surgical challenge of COVID patients? Hematomas in COVID patients. *Med. Sci. Discov*. 2022;9(5): 293-299.
37. Kalayci T. Rectus sheath hematoma due to low molecular weight heparin in a Covid-19 patient in Turkey. *Cureus*. 2021;13(5):e14870.