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Original Article

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Effect of Coagulation Status and Co-Morbidity on Flap Success and Complications in Patients with Reconstructed Free Flap

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Abstract

Objective: Free flap surgeries constitute the basis of reconstruction surgery in patients with major defects. Prediction of complications that cause flap loss in such patients is important in terms of reducing the length of hospital stay and expenses. We aimed to retrospectively investigate the effect of co-morbidities and the coagulation status on flap loss and complications in patients with reconstructed free flap.

Methods: Demographic data, smoking, alcohol habits, co-morbidities, coagulation tests and thromboelastogram results from preoperative, intraoperative and postoperative anaesthesia and surgical records of patients undergoing free flap surgeries between January 2015 and June 2017 were retrospectively screened.

Results: Flap success rate was found to be 96.1% in total 77 patients with free flap. Coagulation related complication rate, such as thrombosis, haematoma and partial necrosis, were 22.1%. There was a significant relationship between age, chronic obstructive pulmonary disease and hypercholesterolaemia and flap loss (p=0.006, p=0.025 ve p=0.025, respectively). Flap complications were more frequent in patients with chronic obstructive pulmonary disease and hypertension. Laboratory test results revealed no statistical correlation between flap complications and flap loss with preoperative and postoperative TEG.

Conclusion: Advanced age, co-morbidities such as hypertension and chronic obstructive pulmonary disease are associated with complications and flap loss in free flap surgery. However, there were no clinically significant association of complications and flap loss with laboratory tests showing coagulation. We believe that standardised protocols should be established in terms of preparation, intraoperative management and postoperative follow-ups because the time between taking the coagulation tests and postoperative anticoagulant administration should be standardised in such surgeries.

Keywords: Coagulation tests, co-morbidities, complications, free flap, thromboelastography

Introduction

Today, as a result of improvements in microvascular tissue transfer techniques and monitoring, free flap operations have an important role in reconstructive surgery. However, despite all these developments and increased success rates in flap surgery, flap loss continues to be a concern for both patients and surgeons, leading to an increase in hospital stay and cost (1, 2).

Although there are different definitions for complications seen in free flap surgery in the literature, generally, complications are considered major if they require surgical intervention (e.g., total flap loss, thrombosis, and haematoma) and minor flap complications if they can heal with minor intervention (e.g., infection, seroma, wound site problems, and partial

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loss). Flap complications and flap loss in these types of surgical interventions may occur due to patient (comorbidities), surgery (applied techniques), or anaesthesia (e.g., hypoxia, acidosis, and hypotension). The most important complication leading to flap loss is pedicle thrombosis due to local, systemic (coagulopathy), or technical reasons (intima injury and pedicle kinking) (1-4). Recognition of risky patients before operation and knowing the coagulation status of the patients during or after the operation are very important in the prevention of pedicle thrombosis.

The tests used to evaluate coagulation in the perioperative period should be simple, reproducible, specific, and cost-effective. Today, none of the routine coagulation tests alone can provide these criteria, and therefore different tests are combined (1, 5). At the same time, problems in the peroperative period, such as hypothermia, renal failure, acidosis, fibrinolysis, platelet dysfunction, and dilution of coagulation factors by supplied fluids, affect the coagulation status of patients and limit the reliability of the tests used. Standardized tests, such as activated partial thromboplastin time (aPTT), prothrombin time, international normalized ratio (INR), and platelet count, which are commonly used to determine coagulation in surgical patients, cannot evaluate haemostasis as a whole. However, viscoelastic methods, such as thromboelastogram (TEG) and rotational thromboelastogram (ROTEM), are better in evaluating clot generation, development, formation, strength, and dissolution. There are many studies showing that preoperative TEG is the most appropriate option for predicting postoperative thromboembolic events. The predetermination of hypercoagulopathy in such cases allows early initiation of appropriate antithromboembolic therapy and thus prevention of complications (1, 5-8).

The aim of the present study was to evaluate the coagulation status of elective free flap reconstructive surgery patients with conventional (standard) tests and TEG and to investigate the effect of the coagulation status on flap complications and consequently on flap success retrospectively. The second aim of our study was to identify other comorbidities that may lead to flap complications and flap loss.

Methods

Approval for the study was obtained from Ege University Medical Faculty Hospital Clinical Research Ethics Committee (decision no.: 17-7/12, 2017). Preoperative, intraoperative, and postoperative anaesthesia and surgical records of elective microvascular tissue transfer with free flap cases between January 2015 and June 2017 were retrospectively reviewed. Data obtained from anaesthesia records included gender, age, height, weight, previous operations, alcohol and smoking habits, obesity (body mass index >30 kg m^{-2}), concomitant diseases, complications, such as hypotension during operation (systolic blood pressure < 90 mmHg), bradycardia (50 beats min^{-1}), hypoxaemia (SpO_2 <90%), hypothermia (esophagus temperature <35°C), and thrombocytopenia (<50,000 µL), amount of supplied fluid, and duration of operation. Data were recorded in the case report forms.

According to the standard anaesthesia protocol applied in our clinic, 10 µg kg^{-1} atropine, 1-2 µg kg^{-1} fentanyl, 2-3 mg kg^{-1} propofol, and 0.6 mg kg^{-1} rocuronium were required for free flap surgery anaesthesia induction; 1%-2% sevoflurane, 50% O_2/air and taking into consideration the basal values of the patient and maintaining the systolic blood pressure 80-100 mmHg, and 0.25-1 µg kg^{-1} min^{-1} remifentanil infusion administered were required for the maintenance. In the postoperative period, the patient is monitored in the postoperative care unit for 24 h, and for pain relief, morphine is administered via patient-controlled analgesia technique (loading dose: 0.05 mg kg^{-1}, bolus dose: 0.02 mg kg^{-1}, 30-minute lockout interval).

Postoperative complications were evaluated in surgical records. Preoperative presence of concomitant diseases, such as diabetes mellitus, hypertension, hypercholesterolaemia, peripheral vascular diseases, cerebrovascular diseases, and respiratory diseases (e.g., chronic obstructive pulmonary disease (COPD) and asthma), renal dysfunction (creatinine >1.4 mg dL^{-1} or diagnosed renal failure), preoperative and postoperative blood tests (haemogram and standard coagulation tests), and TEG results were recorded. The reference values of the standard coagulation tests that are studied pre- and postoperatively are 0.9-1.2 for INR and 22.5-31.3 s for aPTT in our hospital. Accordingly, the coagulation status of the patients was evaluated and recorded as normal, hypocoagulation, or hypercoagulation. Flap-related complications were recorded as major and minor flap complications. Major complications include vein/artery thrombosis, haematoma, and partial flap necrosis, whereas minor complications include wound site infection, wound healing, fat necrosis, and seroma, among others (2). However, for the purpose of our study, complications, such as thrombosis, partial necrosis, and haematoma, associated with the coagulation status of the patient, which is effective on flap success, were evaluated statistically.

Statistical analysis

Data were analyzed by the Department of Biostatistics and Medical Informatics using the IBM SPSS version 21.0 program (IBM Statistical Package for the Social Sciences Corp., Armonk, NY, USA) for statistical analysis. Data were expressed as mean±standard deviation, percentage (%), and median (minimum-maximum). Chi-square test was used for categorical variables, and Kruskal-Wallis test was used for quantitative variables. Correlation, chi-square, and Fisher's exact tests were used to analyze the relationships of complications of the free flaps with the coagulation status and concom-

itant diseases of the patients. A p value < 0.05 was accepted as statistically significant.

Results

A total of 77 patients who underwent free flap operation between January 2015 and June 2017 were included in the study (Table 1). There were 40 (51.9%) male and 37 (48.1%) female patients. The mean age of the patients was 49.3±13.6 (8-80) years. Of the patients, 18 were >60 years, 3 were <20 years, and the remaining 56 were between 20 and 60 years. While there was no statistical relationship between age and flap complications (p=0.2), all patients with flap loss were >65 years old, and there was a significant relationship between flap loss and age (correlation coefficient: 0.3, p=0.006). Other demographic data and surgical characteristics of the patients are shown in Table 2. Standard coagulation tests and hemogram values before and after the operation are shown in Table 3.

Table 1. Distribution of free flap operations

Flap operation applied	n, %
Unilateral DIEP	32 (41.6)
Bilateral DIEP	5 (6.5)
Fibula	20 (26)
ALT	8 (10.4)
Radial forearm	10 (13)
Latissimus dorsi	2 (2.6)

n: number of patients; %: rate of patients; DIEP: deep inferior epigastric perforator; ALT: anterolateral thigh

Table 2. Demographic and surgical characteristics

	Mean±SD
Age (year)	49.3±13.63
Weight (kg)	69.06±13.8
Height (cm)	164.19±9.71
BMI (kg m^{-2})	25.38±3.72
Duration of operation (h)	7.81±1.83
Peroperative fluid used (mL)	3774.68±1005.72
Duration of hospitalization (day)	14.58±17.86

SD: standard deviation; BMI: body mass index

In 53 (68.8%) of 77 free flap patients, there was no complication related to the flap, and 24 (31.2%) had major and minor complications. Distribution of flap complications was as follows: 4 (5.2%) patients had partial necrosis, 5 (6.5%) had thrombosis, 8 (10.4%) had hematoma, 6 (7.8%) had wound dehiscence, and 1 (1.3%) had seroma. Of the total 24 flap complications, 17 (22.1%) were associated with coagulation, and 3 (3.9%) were flap loss. Of the 3 patients who developed flap loss, 2 were caused by thrombosis, and 1 by haematoma.

When the relationship between standard coagulation tests and complications of 17 patients with coagulation-associated flap complications was investigated, only a significant relationship was found between preoperative INR values and haematoma (p=0.011). Only 1 of 8 patients who developed haematoma had a tendency to bleed in preoperative INR (hypocoagulopathy), and flap loss occurred in this patient (p<0.001). In the same patient, hypocoagulopathy in TEG and hypercoagulopathy in aPTT were detected in the postoperative period. In 1 patient who developed flap loss due to thrombosis, only postoperative aPTT showed hypercoagulopathy and was found to be statistically significant (p=0.001) (Tables 4 and 5).

When the comorbidities of patients are examined, 14 of 68 patients with a history of malignancy developed coagulation-related flap complications, but there was no statistically significant difference between them. Of the 9 patients with a history of hypertension, 5 had flap complications, and there was a statistical relationship between hypertension and partial necrosis (p=0.014). Among 4 patients with a history of COPD, 1 patient had partial necrosis (p=0.067), 2 had haematoma, and there was a statistically significant correlation between COPD and haematoma (p=0.008). Flap loss was associated with COPD and hypercholesterolaemia (p=0.025) (Table 6).

Table 3. Preoperative and postoperative laboratory tests of patients

	Preoperative period		Postoperative period	
	Mean±SD	Median (min-max)	Mean±SD	Median (min-max)
Hb (g dL^{-1})	12.99±1.54	13 (9.3-16.8)	10.12±1.46	9.9 (7.5-15)
Htc (%)	39.38±4	39.5 (27.6-49.3)	30.53±4.17	30.1 (22.4-43.3)
Platelet (10^3/µL)	269.99±81.81	250 (124-546)	217.53±78.06	215 (42-552)
aPTT (s)	24.8±2.42	24.9 (19.4-32.8)	26.85±2.84	27 (19.4-33.2)
INR	0.97±0.083	1 (0.8-1.3)	1.01±0.07	1 (0.9-1.3)

SD: standard deviation; Hb: haemoglobine; Htc: haematocrit; aPTT: activated partial thromboplastin time; INR: international normalized ratio

Table 4. Coagulation-associated flap complications with standard coagulation tests and TEG

	Normal (n)	Hypocoagulation (n)	Hypercoagulation (n)
Preoperative standard tests			
Partial necrosis (n=4)	4	0	0
Thrombosis (n=5)	4	0	0
Haematoma (n=8)	7	1[#]	0
Postoperative standard tests			
Partial necrosis (n=4)	4	0	0
Thrombosis (n=5)	3	1*	1*
Haematoma (n=8)	6	0	2*
Postoperative TEG			
Partial necrosis (n=4)	4	0	0
Thrombosis (n=5)	4	0	1
Haematoma (n=8)	7	1	0

[#]INR. *Related to aPTT. aPTT: activated partial thromboplastin time; INR: international normalized ratio; TEG: thromboelastogram

Table 5. Complications and relationship of flap loss with coagulation tests

	Conventional tests			TEG		
	PR- INR	PST-INR	PR-aPTZ	PST aPTZ	PR- TEG	PST-TEG
Complications						
Thrombosis (n:5)	0.86	-	0.61	0.23	0.79	0.66
Partial necrosis (n:4)	0.89	-	0.67	0.7	0.81	0.65
Haematoma (n:8)	0.011*	-	0.43	0.1	0.73	0.48
Flap outcome	p<0.000*	-	0.75	0.001*	0.83	0.14

*p<0.05. PR: preoperative; PST: postoperative; INR: international normalized ratio; aPTT: activated partial thromboplastin time; TEG: thromboelastogram

Table 6. The relationship between perioperative features and complications and flap loss

	Flap complications			
	Thrombosis (n=5)	Partial necrosis (n=4)	Hematoma (n=8)	Flap loss
Smoking (n=28)	0.43	0.56	0.1	0.91
Alcohol (n=4)	0.58	0.63	0.32	0.67
Malignancy (n=68)	0.4	0.45	0.27	0.52
Hypertension (n=9)	0.5	0.014*	0.21	0.23
Diabetes (n=5)	0.2	0.58	0.43	0.054
Hypercholesterolaemia (n=4)	0.12	0.63	0.48	0.025*
Obesity (n=4)	0.54	0.12	0.46	0.642
COPD (n=4)	0.58	0.06	0.08*	0.025*
Renal dysfunction (n=1)	0.79	0.81	0.73	0.83
Aspirin use (n=4)	0.58	0.63	0.48	0.67
Peroperative complications (n=8)	0.96	0.64	0.9	0.98
Peroperative heparin use (n=26)	0.024*	0.7	0.17	0.98
Postoperative anticoagulants (n=73)	0.76	0.19	0.36	0.85

*p<0.05. COPD: chronic obstructive pulmonary disease

In 26 of 77 patients, intravenous (iv) heparin was applied intraoperatively, and 4 patients had postoperative thrombosis (p=0.024). In terms of intraoperative complications, 5 (6.4%) patients had hypotension, 1 (1.3%) had hypoxaemia, 1 (1.3%) had thrombocytopenia, and 1 (1.3%) had bradycardia. One patient with hypotension had partial necrosis, but the patient was discharged without flap loss. There were no statistically significant differences between complications in the intraoperative period and flap complications.

In the postoperative period, 73 (94.8%) patients underwent anticoagulant therapy, and 15 developed flap complications. Of these patients, 42 (54.5%) had low-molecular weight heparin, 19 (24.6%) had acetylsalicylic acid, and 12 (15.5%) had both treatments. However, among 4 patients not given anticoagulants, 1 (1.3%) had haematoma, and 1 (1.3%) had partial necrosis. There was no statistical difference between the use of anticoagulants and flap complications (Table 6).

Discussion

In 77 patients who had free flap surgery, flap success rate was found to be 96.1%, rate of complications, such as thrombosis, haematoma, and partial necrosis, was 22.1% (n=17), and flap loss was 3.9% (n=3). Flap loss was observed in 2 patients due to thrombosis and in 1 patient due to haematoma, and all of these patients were >65 years old. There was a statistically significant relationship between age and flap loss. When the standard coagulation tests and TEG results to evaluate the coagulation status of the patients were analyzed, there was no significant relationship between preoperative and postoperative TEG and flap complications and loss. Although there was a statistically significant difference between preoperative INR and flap loss, preoperative INR and haematoma, and postoperative aPTT and flap loss, it was observed that hypocoagulation or hypercoagulation cases were not supported by clinical findings; hence, it was not considered as a clinically important finding. Flap complications were associated with hypertension and COPD; flap loss was associated with COPD and hypercholesterolaemia. One of the most striking points in the present study was that although not statistically significant, approximately 59% of patients with flap complications had more than one comorbidity.

Flap success has been reported to be between 87% and 99.5% although it is affected by many factors, such as flap type, surgical techniques, age of the patient, smoking, alcohol use, malignancy and radiotherapy history, comorbidities, and complications in the intraoperative period (2, 6, 8-13). Zhang et al. (14) reported the flap failure in 4640 free flap cases to be 2.4%, and Zhou et al. (15) to be 2.9%. In our study, flap success rate was found to be 96.1%, and flap loss was seen in 3 (3.9%) patients.

In the literature, among the complications associated with coagulation, flap thrombosis is reported to be 1.8%-10%, haematoma 2.5%-18.8%, and partial necrosis 2.1%-3.9% (3, 14, 16, 17). Nahabedian et al. (17) reported that after 240 microvascular breast reconstruction, the rate of necrosis was 3.8%, the rate of re-operation was 8.3%, and the flaps were recovered in 55% of the re-operated patients. In our study, the rate of coagulation-related complications and that are re-operated was found to be 22.1%. In accordance with the literature, flap thrombosis was found to be 6.5%, haematoma 10.4%, partial necrosis 5.2%, and success rate of re-operated patients 82.3%.

Among the factors that may cause flap complications and flap loss are the coagulation problems seen in patients and the use of anticoagulants (1, 18). Venous obstruction was found to be responsible from 8 of 9 flap losses and from 16 of 20 flap re-operations in 198 breast reconstruction cases (17). The risk of venous thromboembolism is higher in people with a history of thromboembolism and malignancy (6, 9). In addition, flap loss and complications are more common in the flap operations involving bone components and malignancies (1, 19). Wang et al. (9) reported that among 2032 free flap cases, 58 of them had a history of thrombophilia or thromboembolism, and thrombosis occurred in 12 (20.7%) cases. In 4640 flap cases performed after head and neck surgery, the main cause of complication and failure was found to be venous thrombosis in the recipient region, and a large number of cases had a history of malignancy (14). Zhou et al. (15) retrospectively examined 881 cases after head and neck surgery and reported that 22 of 30 patients with arterial/venous thrombosis have flap loss, and vascular thrombosis is responsible for 84.6% of failed flaps. In our study, thrombosis (66.6%) was responsible for 2 of 3 patients, and haematoma was responsible of 1; all of these patients had reconstruction operation for head and neck malignancy (2 cases had radial forearm and 1 case had fibula flap). Fourteen of 17 patients who developed flap complications and 4 of 5 patients who developed thrombosis had a history of malignancy. Although there was a history of malignancy in 82.3% of the flap complications and in 100% of the patients with flap loss, there was no relationship between malignancy and complications or flap loss. The reason why this was not significant can be that all of the 77 (88.3%, n=68) patients had a history of malignancy.

In free flap surgery, it is very important to detect and timely treat patients with risk factors in the preoperative or early postoperative period (1, 18). Prediction of the thrombotic events by conventional coagulation tests or by viscoelastic methods, such as TEG and ROTEM, may improve the flap success. Many studies have shown that TEG has detected hypercoagulation in the clinical setting. However, there is no consensus on the evaluation of the results due to differences in the types

of operations and the methodologies applied, and the results of the studies are contradictory (6, 7, 20-22). Dai et al. (7) examined 10 studies that aimed at predicting postoperative thromboembolic events with TEG, and, as a result, they stated that although TEG is reported to be beneficial, all studies reported differences in methodologies. In six of the studies, definitive hypercoagulopathy diagnosis was made, but only two studies had information for the evaluation of the patients as normal or hypercoagulopathic. None of the studies had normal or hypercoagulopathy limit values that can be used as a universal definition. While most tests use the MA value for hypercoagulopathy in TEG, there are differences in the type of specimen used (blood collected as whole blood or in citrate tube), the activator used, the time of sampling, the patient characteristics, and the types of surgery. When the diagnostic tests were evaluated, it was found that most studies were of low or medium quality. Therefore, since the results related with estimating the occurrence of postoperative thromboembolic event with TEG are variable and there are not enough suitable data, they concluded that it is not possible to conduct a meta-analysis (7). In addition, it was stated that since predicting thromboembolic complication, hypercoagulation detected in the early postoperative period is more important, and thus early detection of coagulation changes with TEG in the early postoperative period may be effective in preventing thromboembolic events. The early postoperative period was recommended as the most appropriate sampling time for TEG. In 828 liver transplantation patients, Zahr Eldeen et al. (23) reported that preoperative TEG shows confidently the patients with high risk of developing early hepatic thrombosis, but the postoperative TEG results are not significant. They stated that this is due to the dilution of the coagulation factors due to the fluid replacement during the surgery and factors causing short-term coagulopathy, such as peroperative renal failure, acidosis, hypothermia, hypocalcemia, and citrate toxicity. Brill et al. (24) reported that TEG has high sensitivity but low specificity for thromboembolic events. Dunham et al. (25) compared INR, TEG, and r-TEG in the effectiveness of warfarin treatment in their study. They found that while INR is detected in the therapeutic range, TEG results are different. Moreover, they concluded that the intrinsic system activation with kaolin, which is frequently used for TEG measurement, is found to be insufficient to detect changes in the extrinsic pathway. As can be seen in the literature, there are differences in the definition of hypercoagulation, TEG methodology, patient characteristics, type of operations performed, reference values used, and results measured. It has been reported that TEG's success in predicting postoperative thromboembolic events is highly variable, and there is a need for prospective studies to determine whether it is a clinically useful screening test in high-risk surgical populations (7). Wikner et al. (18) reported that they could not predict unintended complications, such as thrombosis, bleeding, or flap loss, with standard test and thromboelastometry in free flap surgery cases. In our study, we defined the TEG results as hypercoagulopathy and hypocoagulopathy, in the kaolin activated blood by using the reference values of the device, and no patient had any hypercoagulopathy in the preoperative period. Only one patient had hypocoagulopathy in the preoperative TEG, but neither flap complication nor flap loss occurred. As a result of the study, we could not find a relationship between preoperative and postoperative TEG and flap complications and flap loss. One of the reasons for this may be the absence of patients with coagulation tendencies, such as thromboembolism or thrombophilia preoperatively. Since preoperative TEG was normal in 76 patients, we could not predict problems, such as postoperative thrombosis and haematoma. Therefore, we think that complications related to coagulation, such as haematoma, thrombosis, and partial necrosis, in the postoperative period are not related to coagulation disorders in the preoperative period. However, we found that intravenous heparin was applied to patients who were thought to have a tendency to thrombosis in the intraoperative period or had venous problems, and this relationship was statistically significant. Iv heparin was administered intraoperatively to 4 of 5 patients who developed thrombosis. It is also emphasized that TEG samples obtained in the early postoperative period are much more important in predicting complications (7). In our study, we found that blood samples were collected at different times for postoperative TEG, and we think that this is why we could not find a statistically significant relationship between postoperative TEG and flap complications. Another reason can be that 94.8% of the patients (73 of 77 patients) had an anticoagulant treatment in the postoperative period. In studies, particularly, it has been reported that TEG may be more effective in predicting thromboembolic events in cases without postoperative thromboprophylaxis (26, 27).

In terms of standard coagulation tests, we found that there was a statistically significant relationship just between preoperative INR and haematoma, preoperative INR and postoperative aPTT, and flap loss, but we think that this is not so important clinically. Since in 1 patient who developed postoperative haematoma, although preoperative INR and postoperative TEG had a tendency to bleed, postoperative aPTT showed a tendency to coagulation, and this patient had flap loss. When these tests were evaluated in their own, only INR and TEG showed the same results, but aPTT did not support this. In this patient, iv heparin was not administered during the operation, and the time to receive TEG and standard coagulation tests and anticoagulant administration were different from each other in the postoperative period. It is stated that the monitoring protocol and anticoagulant use time in the postoperative period may affect the flap results (15). As a result of our study, we have seen that there is no standardization regarding the time of taking the coagulation tests and the

use and time of initiation of anticoagulants. We believe that in this type of surgery where the coagulation status is very important, there should be standard protocols for the preparation and postoperative follow-up of the patients.

It is not possible to mention a single cause of flap complications or loss. Several possible risk factors have been reported, such as timing of operation, age of the patient, preoperative radiotherapy, chemotherapy history, hypertension, diabetes, smoking and alcohol use, obesity, and surgery previously applied to that region. However, there is no consensus on this issue, and the results of the studies are contradictory. When all studies are examined, it is seen that different results are obtained for concomitant diseases that may cause flap complications (2, 11, 15, 17, 19). Most of the studies investigating these factors have their own limitations, such as low number of cases, differences in surgeon preferences and experience, different types of complications, and inclusion of breast or extremity reconstruction cases in studies. In 881 free flap cases after head and neck surgery, Zhou et al. (15) stated that only the history of radiotherapy affects the success of the flap; age, diabetes, old operation history, and postoperative anticoagulants are not related to it. In addition, Nahabedian et al. (17) showed that age, smoking, recipient vessel selection, and diabetes are not associated with anastomotic insufficiency. However, Bozikov et al. (10) found that flap complications are 5 times higher in patients with diabetes. Rosado et al. (28) found postoperative complications in patients with diabetes to be 1.76 times, and flap failure was 2.3 times more. le Nobel et al. (19) showed that there is a significant relationship between perioperative complication and tumor stage and reconstruction area in 304 free flap cases, and that smoking, alcohol use, age, and diabetes are not associated with complications. There are also publications mentioning that as long as the normal glycemia is preserved in patients with diabetes, they are not in the high-risk group for flap insufficiency (29). In our study, flap loss occurred in 1 of 5 patients with diabetes, and a statistically borderline value was obtained ($p=0.054$). However, there was no significant difference between flap complications and diabetes. On the other hand, Fischer et al. (2) reported that COPD, obesity, and hypertension are related to flap complications in 1303 flap cases. In their other study, they stated that COPD and intraoperative technical difficulties are associated with complications in lower extremity free flap cases. Flap loss was higher in patients with rectus abdominis flap and venous thrombotic events. Comorbidities and location of the defect were said to be associated with complications, and flap selection and delayed venous thrombotic events may be associated with flap loss (4). In our study, we found a significant relationship between flap complications and patients with a history of COPD and hypertension and between flap loss and COPD and hypercholesterolemia. Ferrari et al. (30) investigated the effect of patient age on flap complications in 360 patients who had free flap for head and neck surgery. There was no significant difference between the young and old patients in terms of major or minor complications, whereas complications were more frequent in younger American Society of Anesthesiologists (ASA) III-IV patients than in ASA I-II patients. There was no statistically significant result for ASA classification, but the investigator attributed this to the insufficient number of patients (55 patients) in the elderly patient group. In our study, there were no patients with ASA grades III and IV. There were 39 patients in ASA I class and 38 patients in ASA II class. However, it was noteworthy that flap complications were seen in people with multiple comorbidities, although not statistically significant. Of the 17 patients with coagulation-related complications, 10 had multiple comorbidities, and only 1 patient had ASA I class. Therefore, it may be thought that more than one comorbidities may be more effective on complications and flap loss, even in ASA II class.

Our study has a few limitations. Since there are studies in which lower case series have been published in the literature (6, 9, 13, 18), we did not make power analysis in the present study that includes a total of 77 patients. Another limitation is that we do not have a standard time to obtain the coagulation tests in the preoperative and postoperative periods.

In this retrospective study on the effects of coagulation status and comorbidities on flap success and complications in patients undergoing reconstruction with free flap, flap loss was found to be associated with advanced age, COPD, and hypercholesterolaemia. There was no clinically significant relationship between standard coagulation tests and coagulation status with viscoelastometric tests and flap complications. In our country, where reconstructive surgery is becoming more common, anaesthesiologists need to know more about the possible complications in free flap surgery and to cooperate more with surgeons to prevent these complications. Predicting the complications that cause flap loss is very important in terms of increasing the success rates by taking the necessary precautions and reducing the length of hospital stay and cost. In the literature, it is stated that viscoelastic methods are more effective than standard coagulation tests in predicting thromboembolic events. However, considering that there are many factors, such as surgical techniques, experience, comorbidities, intraoperative anaesthesia management, and postoperative close follow-up, that affect the success of flap in this type of surgery, it may not be sufficient to evaluate the coagulation status of the patients only with laboratory tests. Flap success is affected by many conditions related to anaesthesiologists, such as identifying the patients with comorbidities and having their operation in clinically optimized conditions, maintaining haemodynamic stability by avoiding sudden hypotension and hypertension in the intraoperative period, ensuring blood

glucose regulation, and protecting the patient from hypothermia and hypoxaemia. The most important factors in terms of success are surgical experience and techniques. We think that in these long-lasting and high-cost surgeries, anaesthesiologists should take an active role with the surgical team in the preparation of the patient for surgery, intraoperative management, postoperative period, standardization of anticoagulant treatment, and timing of the coagulation tests, and common protocols have to be prepared.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Ege University School of Medicine (Decision No: 17-7/12, 2017).

Informed Consent: Due to the retrospective design of the study, informed consent was not taken.

Peer-review: Externally peer-reviewed.

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