


# Comparison of Incisional Hernias with Other Type of Abdominal Hernias in Terms of Predisposant Factors

Yaşar Subutay Peker , Nazif Zeybek 

Department of General Surgery, Health Sciences University, Gülhane School of Medicine, Ankara, Turkey

## ABSTRACT

**Objective:** Incisional hernia (IH) is one of the most common late complications of abdominal surgery. Factors such as wound infection, type of incision, wound closure technique, and suture material used as well as patient-related factors such as age, gender, body mass index (BMI), diabetes mellitus (DM), and smoking are also involved in the development of IH and other types of abdominal hernias (OTAH). In this article, we aimed to compare the predisposing factors for IH and OTAH.

**Methods:** We analyzed predisposing factors for IH and OTAH among 130 patients undergoing surgery for abdominal hernia between January 2015 and December 2018 at the Department of General Surgery of Gülhane Training and Research Hospital.

**Results:** The female/male ratio was 28/102, the mean age of the patients was 58.6 years, and the mean BMI was 29.3 kg. The prevalence of DM and smoking was also evaluated. The rate of drain application was 56.2% and 4.1%, and the duration of hospitalization was 8.6 and 5.3 days in the IH and OTAH groups, respectively.

**Conclusion:** We found male gender to be a dominant risk factor for OTAH and high BMI to be dominant for IH. Age, DM, and smoking were equivalent risk factors for both. Drain application for IH was statistically significant high and resulted in prolonged hospitalization. These results provide evidence for an important complication of DM and obesity and also conclude that obesity is a major risk factor for IH.

**Keywords:** Abdominal hernia, diabetes mellitus, herniorrhaphy, incisional hernia, obesity

## INTRODUCTION

Incisional hernia (IH) is a type of abdominal hernia that occurs at a previous surgical incision site. The incidence of IH of midline incisions is higher than for incisions of other regions. Despite advances in abdominal wall closure techniques, the rate of development of IH following laparotomy ranges from 15% to 20% (1). It has been found that more than 50% of IHs that originate from abdominal incisions occurs within the first year after surgery and 80% within 3 years (2, 3). Other types of abdominal hernias (OTAH) are hernias that do not originate from previous abdominal incisions but rather from anatomical weak sites of the abdominal wall. Abdominal hernias that are not classified as IH or OTAH are associated with a risk of strangulation and may cause other life-threatening complications if they are very large in size, irreducible, or consist of abdominal luminal organs. In such cases, surgical treatment of the hernia is strongly recommended.

Factors such as wound infection, location/type of incision, wound closure technique, and suture materials as well as patient-related factors such as age, body mass index (BMI), presence of diabetes mellitus (DM), and smoking are considered as other important risk factors for the development of IH. In addition, poor nutritional status, chronic lung disease, renal failure, malignancies, and steroid therapies are also considered to be facilitating factors for the development of IH (1-4).

In this study, we examined data from 130 abdominal hernia patients operated between January 2015 and December 2018 at the Department of General Surgery of Gülhane Training and Research Hospital, University of Medical Sciences. Among 130 patients, 32 patients had IH and 98 patients had OTAH. The data from the two groups were compared statistically. The aim of the study was to determine the factors for the development of ab-

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**ORCID IDs of the authors:** Y.S.P. 0000-0001-6059-0629; N.Z. 0000-0001-5033-834X

**Corresponding Author:** Yaşar Subutay Peker **E-mail:** subutaypeker@gmail.com

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**Table 1.** Sociodemographic and clinical features of patients with incisional hernia and other types of abdominal hernias

	IH (n=32)		OTAH (n=98)		Total (n=130)		p
	Male	Female	Male	Female	Male	Female	
Gender	19 (41%)	13 (59%)	83 (84%)	15 (16%)	102 (78%)	28 (22%)	0.02
Age distribution (mean)	24–75 (56.8±5.7) years		21–86 (59.2±8.1) years		21–86 (58.6±7.5) years		0.26
BMI distribution (mean)	18.8–39.8 (29.3±3.4)		19.5–40.1 (27.2±3.6)		18.8–40.1 (27.8±4.1)		0.03
	Yes	No	Yes	No	Yes	No	
DM	6 (18.7%)	26 (83.3%)	14 (14.3%)	84 (85.7%)	20	110	0.57
	Yes	No	Yes	No	Yes	No	
Smoking	14 (44.6%)	18 (55.4%)	47 (47.9%)	51 (52.1%)	61	69	0.67
	Yes	No	Yes	No	Yes	No	
Drain application	18 (56.2%)	14 (43.8%)	4 (4.1%)	94 (95.9%)	22	108	<0.00
Duration of hospital stay (mean)	2–19 (8.6±3.2) days		1–18 (5.1±4.1) days		1–19 (7.2±4.0) days		<0.00

BMI: body mass index; DM: diabetes mellitus; IH: incisional hernia; OTAH: other types of abdominal hernias

dominal hernias and investigate whether the factors have the same impact on both IH and OTAH. In addition, we compared herniorrhaphy repair techniques, drain application, and patient hospitalization duration.

**METHODS**

Data of 130 abdominal hernia patients operated in the General Surgery Department of Gülhane Training and Research Hospital of the University of Medical Sciences between January 2015 and December 2018 were analyzed retrospectively. Analyzed patient data included age, gender, BMI, presence of DM, smoking, hernia repair technique, duration of hospitalization, and drain application. Thirty-two patients who underwent surgery had IH and 98 had OTAH. Because this study is a retrospective analysis of patient medical data that did not collect any personal data, no informed consent was obtained from the patients. All study procedures were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and its later amendments.

**Statistical Analysis**

Gender, age, BMI, presence of DM, smoking, postoperative drain application, and duration of hospitalization of the two groups were analyzed using Statistical Package for the Social Sciences version 16.0 (SPSS Inc., Chicago, IL, USA) for statis-

tically significance.  $p < \alpha = 0.05$  was accepted as statistically significant. A nonparametric chi-square test was applied for gender, presence of DM, smoking, and postoperative drain application. Mann-Whitney U test was used to analyze age, BMI, and hospitalization duration, and these parameters were also evaluated for descriptive statistics. Gender, DM, smoking, and postoperative drain application parameters were evaluated for percentage distribution.

The statistical significance of the 3 different operation techniques used in the two groups was evaluated with SPSS version 16.0. The percentage distribution for the 3 different operation techniques was evaluated, and a nonparametric chi-square test was applied for statistical analysis.  $p < \alpha = 0.05$  was accepted as statistically significant.

**RESULTS**

Most patients with abdominal hernia were male. The female/male ratio was 13/19 in the IH group and 15/83 in the OTAH group, with total of 102 male and 28 female patients (Table 1). There was a statistically significantly higher proportion of males in the OTAH group. The ages of the patients ranged from 24 to 86 years (mean±SD, 58.6±7.5 years); the age distributions of the groups are given in Table 1. There was no statistically significant difference in average age between the groups.

Patients were evaluated for BMI, DM, and smoking. The mean BMI was 29.3±3.4 in patients with IH and 27.2±3.6 in patients with OTAH. The BMI of the patients is given in Table 1. Statistically difference was found between two groups. DM presences for the patients in the two groups were compared, 6 (18.3%) of the patients in the IH group and 14 (14.3%) patients in the OTAH group had DM, which no statistically significant difference between the two groups were found (Table 1). One patient in each group was

**Main Points:**

- Age, DM, smoking are the risk factors for OTAH and IH.
- Male gender is the main risk factor for OTAH
- BMI is the dominant risk factor for IH
- Obesity increases the risk of postoperative late complication IH.

**Table 2.** Distribution of hernia repair types

	IH (n=32)	OTAH (n=98)	Total (n=130)	p
Primary repair	4 (12.5%)	13 (13.2%)	17 (13.1%)	
Mesh herniorrhaphy	9 (28.1%)	60 (61.2%)	69 (53.1%)	<0.01
Fence darning	19 (59.4%)	25 (25.5%)	44 (33.8%)	

IH: incisional hernia; OTAH: other types of abdominal hernias

medicated for insulin and others were medicated for oral anti-diabetics. The prevalence of smoking was found to be 44.8% in the IH group and 47% in the OTAH group (Table 1) with no statistical significance between the groups.

Regardless of the type of repair technique, the rate of drain application was 56.2% in the IH group and 4.1% in the OTAH group (Table 1). There was a statistically significant difference in the rate of drain use between the two groups.

The duration of hospital stay ranged from 1 to 19 days, with mean duration of 8.6±3.2 days in the IH group and 5.3±4.1 days in the OTAH group. The duration of hospitalization was significantly longer in IH patients than in OTAH patients (Table 1).

Patients were categorized into three subgroups based on hernia repair technique: classical herniorrhaphy using primary suturing, herniorrhaphy using mesh repair, and fence darning technique (Table 2). Among the IH and OTAH groups, classical herniorrhaphy using primary suturing was applied in 12.5% and 13.1% of the patients, herniorrhaphy using mesh repair was used in 59.4% and 61.2%, and the fence darning technique was used in 25.5% and 25.5%, respectively. The statistically significant difference between the groups is shown in Table 2.

**DISCUSSION**

Both age and gender were found to be risk factors for abdominal hernias. Older age was associated with wound-healing impairment, as was the presence of DM, which will be discussed below. DM was also found to be a cause of IH. In addition, as patients get older, the strength of the connective tissue decreases, which causes a weakening in the abdominal anterior wall and OTAH. Thus, there is no doubt that age is a predisposing factor for abdominal hernia. However, in our study, we found no statistically significant difference in age between the two groups. We conclude that age is an equivalent risk factor for both IH and OTAH.

Gender is also known to be a risk factor for abdominal hernia; however, its effect on OTAH and IH is unknown. We compared the predisposing effect of gender in each group separately. We found that male gender is a stronger risk factor for OTAH than IH. This may be because males deal more with heavy works which cause abdominal muscles to contract and increased intra-abdominal pressure. When males undergo surgery, they tend to

decrease the use of their muscles in line with the advice of the surgeon; therefore, male gender is ultimately not a dominant predisposing factor for IH.

Obesity is one of the most important risk factors for the development of IH after abdominal surgery, and it may cause problems with wound healing in a significant proportion of patients with a BMI greater than 30 kg/m<sup>2</sup> in the early or late postoperative period (2, 5, 6). Wound complications, including wound infections and wound separation, are frequently associated with obesity because of the poor vascularization of increased adipose tissue and the proliferation of proinflammatory tissue factors. Obesity increases the rate of IH by impairing wound healing or causing infections. In addition, the increase in the risk of IH development may be the result of increased intra-abdominal pressure in obesity. In many animal experiments, physical and pathological events that increase intra-abdominal pressure have been shown to cause herniation of the abdominal wall from weak areas or from surgical incision sites. The weak areas of the abdominal wall include not only the incisional scars but also physiological anatomical locations, such as the umbilicus and inguinal region. Thus, obesity is also considered to be a risk factor for OTAH (7). However, our study results showed that obesity is a more dominant risk factor for IH.

It is very difficult to conduct human experimental studies on intra-abdominal pressure and tissue resistance. The results of animal studies are not scientifically fully valid for humans because of their different anatomical structures. Therefore, Kroese et al. created a simulator called AbdoMAN and carried out different studies on this model, which has very similar features to the muscles and fascia of the human abdominal wall. They clearly demonstrated the importance of increased intra-abdominal pressure for the development of IH (8, 9). These studies have shown that factors that increase intra-abdominal pressure, such as coughing, straining, vomiting, obesity, and heavy physical exercise, may increase the risk of IH independent of other factors. Therefore, patients should be evaluated in the postoperative period for constipation, pulmonary infection, or urination difficulty, and if necessary, medical treatment should be initiated for the diseases causing these symptoms.

In our study, we evaluated obesity by measuring the BMI of patients in both the IH and OTAH groups. We found that the BMIs of the two groups were statistically different. This result also supports the data in the literature demonstrating that obesity can cause both IH and OTAH and is a more dominant risk factor for IH. From this result, it can also be stated that incisional scars are weaker than the anatomical weak areas of the abdominal wall. In conclusion, we believe that obesity is a risk factor for both IH and OTAH, and to reduce the risk of IH, patients with a high BMI should be advised to lose weight.

DM is one of the known risk factors for the development of IH and is responsible for many possible local and systemic complications (10, 11). It is known that the adverse effects of DM

occur through the disruption in vascular structures, resulting in ischemia in the tissues, or by further compromising the general condition of patients as a result of previously developed systemic complications related to the cardiac or nephrologic systems. DM, which causes a delay in wound healing and increases wound complications, also demonstrates these effects by impairing collagen synthesis. Similar to DM, smoking also has a negative impact on wound healing through the mechanism of collagen synthesis and is therefore considered to be a risk factor for the development of IH. Studies have shown that approximately 8% of patients with abdominal hernias have DM and 43% are smokers. Our results showed that the frequency of DM was slightly higher, but the remaining results were consistent with the data in the literature (9, 12–15). However, we did not observe a statistically significant difference in the presence of DM or smoking between the IH and OTAH groups. Because DM and smoking are associated with wound-healing impairment and weakening of normal tissue, we found that these factors have an equal effect on both IH and OTAH. This may be the result of both the effects on wound healing and also the weakening of the abdominal wall by the pathophysiology described above.

Studies on the role of obesity, DM, smoking, and related collagen synthesis disorders in the etiology of IH have yielded conflicting results. The connective tissue consists of three groups of extracellular proteins: proteoglycans, glycoproteins, and collagens. Proteoglycans regulate the structure and permeability of tissues, whereas glycoproteins are proteins that are effective in cell-to-cell interactions. Because collagen is responsible for matrix structure and connective tissue support, dysfunction of the connective tissue is associated with collagen synthesis disorders (16). In fact, some experimental studies have found that the most intense changes in cellular metabolism occur directly in the anterior sheath of the abdominal rectus muscle. However, despite these proven functional properties of collagen structures, many clinical observational studies showed no significant difference in age, presence of DM, or smoking between patients with different hernia types (9, 17). A published systematic analysis analyzed 55 original articles evaluating connective tissue changes in patients with abdominal hernias and showed no significant difference in collagen changes between IH and OTAHs (18). The findings of this previous research support the results of our study, namely, that there is no statistically significant difference in the presence of DM or smoking between patients with IH and OTAH.

Apart from DM and smoking, wound infection, location, type of incision, wound closure material, and wound closure technique are other important factors involved in the etiology of IH. The development of wound infection leads to the release of many mediators in the surgical area, disrupts the general resilience of the patient, delays the formation of granulation tissue in the wound area, and prevents wound healing by disrupting collagen synthesis. It has been shown that collagen synthesis is especially reduced after contaminated surgical procedures and in patients

with infected wounds, and this result is defined as a risk factor for the development of IH. One study reported that IH developed in the first postoperative year in 21% of patients who underwent colorectal surgery (6). The published series reported that half of patients with IH had a history of wound infection in the postoperative period and that the risk of development of IH in the first postoperative year was fivefold higher in patients with wound infection than in those without wound infection (4, 8). In our study, none of the patients had postoperative wound infections, and thus, we cannot declare a result for the effect of wound infection in the IH and OTAH groups. In addition, we did not evaluate the location of the incision, type of incision, or wound closure material in our patients. However, we found a statistically significant difference between the wound closure techniques applied for the repair of IH and OTAH.

The closure techniques and materials used for abdominal incisions are thought to have an effect on the development of IH (19, 20). Although there are ongoing discussions about the proper wound closure technique and materials used in surgery, it is considered sufficient to use any nonallergic material that does not increase the risk of infection and can provide adequate tissue resistance. Abdominal closure is underestimated by most surgeons and is generally considered an educational activity for inexperienced residents. Closure of laparotomy should be taken as seriously as all prior operative procedures and handled with appropriate techniques and materials (9). One of the key techniques in preventing the development of IH is the use of fascia sutures, which can last for a long time and resist tissue resistance. In patients undergoing laparotomy, only 70% of the fascia's tensile strength can be recovered 1 year after fascia repair. Therefore, suture materials that are absorbed and lose their strength in a short time are not suitable for fascia repair. Although there are studies indicating that the wound-stretching force is higher with the use of the single-suture technique as compared with the continuous-suture technique for laparotomy closure, single or continuous monofilament/polypropylene sutures were not shown to have a significant effect on wound healing or the development of IH. Some authors have argued that the use of the continuous-suture technique increases the risk of IH based on studies indicating that this suture technique causes insufficient wound tensile strength (21, 22).

The data in the literature given above obviously state that the closure technique is a factor in abdominal hernias, and we compared the wound-closure technique used in both groups. Although we did not evaluate relapse rates after the individual wound closure techniques, we found that the primary saturation technique was applied in the same ratio for both IH and OTAH. However, the fence darning technique was applied more often in IH, and mesh herniorrhaphy was applied more frequently in OTAH. This may be the result of surgeon habits for inguinal herniorrhaphy, which is the Lichtenstein technique. Because the Lichtenstein technique is the gold standard for inguinal hernia repair, which is evaluated in the OTAH group, the rate of mesh herniorrhaphies was higher in the OTAH group than in the IH group. However,



fence darning is safer because there is no application of prosthetic material, resulting in a lower risk of wound infection. Thus, surgeons often choose the fence darning technique in reoperated wounds, such as IH.

In patients undergoing mesh repair, some precautions should be taken, such as the use of drains and antibiotics to avoid the risk of seroma, hematoma, and mesh reactions. For this reason, we compared the drain application in both groups. We found that the application of drains was statistically significantly higher in the IH group as compared with the OTAH group. However, the use of mesh herniorrhaphy was greater in the OTAH group, which is in contrast to the indication of drain application in the presence of mesh. This may be because the main indication for drain application is not the presence of mesh. Drains are also applied in cases with a risk of hemorrhage. Because reoperated IHs have a greater risk for bleeding, surgeons may choose to apply a drain to the incisional IH.

The duration of hospitalization is related to the expected postoperative complications and also the patient's postoperative recovery. In our study, we found that the hospitalization of IH patients was longer than that of OTAH patients. This may be because IH is more complicated than OTAH. We also found that the rate of drain application was higher in the IH group than in the OTAH group. This may also be the cause for the longer hospitalization of the patients, as the drain needs to be monitored. However, because no bleeding or wound infection was found in either group, it appears that the application of the drain was unnecessary and merely a result of the surgeons' habit. (23)

## CONCLUSION

Many of the factors described above are known to be predisposing for abdominal hernias, but the significance of these factors for IH and OTAH has not undergone much discussion. In this study, we aimed to specify the significance of the predisposing factors according to the type of abdominal hernia (i.e., IH or OTAH). We found that male gender is the dominant risk factor for OTAH and obesity is the dominant factor for IH, whereas age, presence of DM, and smoking are equivalent risk factors for both IH and OTAH. We also found a statistically significantly high frequency of drain application in IH patients, resulting in delayed hospitalization. All of these results indicate that age, DM, and smoking are not the only risk factors for IH but are also risk factors for OTAH. In addition, we found that abdominal hernias are a complication of both DM and obesity. Thus, physicians have an additional reason to treat obesity and DM aggressively. Finally, obesity was found to have a greater effect on the occurrence of IH, so we suggest that surgeons recommend that patients with a high BMI lose weight postoperatively in order to prevent IH.

**Ethics Committee Approval:** No Ethics committee approval was received because the study was done by collecting data retrospectively from the patient files and no personal data of the patients were used.

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

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**Conflict of Interest:** The authors have no conflicts of interest to declare.

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Withdrawn

# Knowledge of Dentistry Students about Local Anesthetic Systemic Toxicity and Intravenous Lipid Rescue Therapy: A Cross-Sectional Questionnaire-Based Study

Berna Kaya Uğur 

Department of Anesthesiology and Reanimation, Gaziantep University School of Medicine, Gaziantep, Turkey

## ABSTRACT

**Objective:** The aim of this study was to evaluate the level of consciousness of local anesthetic systemic toxicity (LAST) among dentistry students, which would provide helpful information for scheduling the educational content of future syllabus before graduation to prepare students for possible challenges in the future.

**Methods:** This study included 234 dentistry students, who were in the 3<sup>rd</sup>, 4<sup>th</sup>, and 5<sup>th</sup> degrees during the period 01 December 2018–01 April 2019, and was conducted using a cross-sectional, questionnaire-based design. The revised questionnaire form includes questions addressing the frequency of encountered LAST cases, signs of LAST they had seen, and treatments for LAST, particularly lipid treatment, they had used.

**Results:** The questionnaire was sent to 234 dentistry students in the 3<sup>rd</sup>, 4<sup>th</sup>, and 5<sup>th</sup> degrees at the Faculty of Dentistry, Gaziantep University, Gaziantep, Turkey, of whom 215 (91.88%) responded. The majority of participants (93%, n=200) declared that they received training about local anesthetics (LAs). Only one LA agent was preferred among 38.60% (n=83) of participants, whereas other participants preferred multiple agents. A significant majority of the participants (79.5%; n=171) declared that they did not observe LAST before this study, whereas only 15 (7%) students mentioned that they had encountered LAST but used an alternative therapy rather than intravenous lipid rescue therapy. None of the students personally applied lipid rescue therapy.

**Conclusion:** The results of this study implicate the evident need for additional educational effort to create awareness about LA use and effective management of LAST among dentistry students.

**Keywords:** Dentistry, lipid emulsion, local anesthetic systemic toxicity, local anesthetics, toxicity

## INTRODUCTION

Local anesthetics (LAs) are frequently used in routine clinical practice and sometimes may be associated with systemic toxicity. However, there is a lack of studies in the literature concerning the awareness of local anesthetic systemic toxicity (LAST) among different medical specialties due to misdiagnosis or underreporting of similar events (1-3).

Therefore, we conducted a cross-sectional questionnaire-based study to determine the level of knowledge about LA use and the effective management of LAST among dentistry students at the Faculty of Dentistry, Gaziantep University. Our aim was to evaluate the level of consciousness of LAST among dentistry students, which would provide helpful information for scheduling the educational content of future syllabus before graduation to prepare students for possible challenges in the future.

## METHODS

After obtaining approval from Gaziantep University Clinical Researches Ethical Committee (2019/318), a total of 234 dentistry students, who were in the 3<sup>rd</sup>, 4<sup>th</sup>, and 5<sup>th</sup> degrees during the period 2018–2019, were included in this study. Verbal informed consent was obtained from these participants before they filled in their questionnaire form. This study was conducted in a cross-sectional, questionnaire-based manner, which was adapted from a previous study conducted by Oksuz et al. (4). Students are supposed to have one semester of a lesson entitled “Local anesthesia in dentistry” in the 3<sup>rd</sup> year and one semester in “General anesthesia in dentistry,” including LA lessons in the 4<sup>th</sup> degree at the Faculty of Dentistry, Gaziantep University. All the 4<sup>th</sup> and 5<sup>th</sup> degree students use local anesthesia during their clinical practice on behalf of their preceptors in various divisions.

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**ORCID ID of the author:** B.K.U. 0000-0003-0044-363X

**Corresponding Author:** Berna Kaya Uğur **E-mail:** bernakayaugur@hotmail.com

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The revised questionnaire form includes questions addressing the frequency of encountered LAST cases, signs of LAST they had seen, and treatments for LAST, particularly lipid treatment, they had used. The questionnaire contains multiple-choice questions that are shown at Appendix 1.

**Statistical Analysis**

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS Inc.; Chicago, IL, USA) for Windows version 11.5<sup>o</sup>, and the results are shown in tables presented as descriptive statistics.

**RESULTS**

The questionnaire was sent to 234 dentistry students, who were in the 3<sup>rd</sup>, 4<sup>th</sup>, and 5<sup>th</sup> degrees at the Faculty of Dentistry, Gaziantep University, of whom 215 (91.88%) responded. Mean age of the participants was 22.52±1.41 years (range 20–27 years). The majority of them (93%, n=200) declared that they received training about LAs. Most of them preferred LAs as shown in Table 1.

Only one LA agent was preferred among 38.60% (n=83) of the participants, whereas others preferred multiple agents. The degrees of knowledge of the participants about the LAs they used are presented in Table 2.

**Table 1.** Most commonly preferred LA agents among participants

Agent preferred	Number of participants	(%)
Lidocaine	160	74.41
Lidocaine+vasoconstrictor	4	1.86
Articaine+vasoconstrictor	2	0.93
Articaine	88	40.93
Bupivacaine	18	8.37
Prilocaine	9	4.18
Mepivacaine	7	3.25

LA: local anesthetic

A significant majority of the participants (79.5%; n=171) stated that they did not observe LAST before this study, whereas only 15 (7%) students mentioned that they had encountered LAST but used an alternative therapy rather than intravenous lipid rescue therapy. None of the students personally applied lipid rescue therapy.

We also observed that 42.8% (n=92) of the participants had heard about lipid rescue therapy for LAST, but they did not remember how to manage this clinical situation. Among the study participants, 12 (5.6%) mentioned that they knew how to use lipid rescue therapy with intravenous lipids. A total of 23 (10.7%) participants had read articles about the therapy, whereas 88 (40.9%) participants stated that they did not hear anything about this therapy. Table 3 shows the most common LA-related adverse effects observed in clinical practice.

**DISCUSSION**

The side effects frequently observed in the use of LAs are often minor and/or transient. The symptoms of side effects fall on a broad spectrum, ranging from mild to life-threatening severe ones, including cardiac arrest, to the involvement of the central nervous system.

Individual patient risk factors, concurrent medications, location and technique of block, specific LA compound, total LA dose, timing of detection, and adequacy of treatment are the risk factors that entail the severity of LAST. The history of articles on LAST published in the literature goes back to 1884, with the introduction of cocaine to clinical practice in 1884, bupivacaine in 1970s, and ropivacaine and levobupivacaine in late 1980s (5, 6). Research studies are aimed at lightening up the pathophysiology of LAST and on novel treatment modalities such as lipid emulsion. The first guideline regarding the role of lipid emulsion in the management of LAST was published by the Association of Anaesthetists of Great Britain and Ireland in 2007 (7). The American Society of Regional Anesthesia and Pain Medicine (ASRA) reported practice guidelines regarding the prevention and treatment of LAST in 2010 (8). These guidelines state that the treatment for refractory LAST can be performed using conventional therapies (airway management with 100% O<sub>2</sub>, convulsion therapy, and cardiopulmonary resuscitation if cardiac arrest occurs) and lipid emulsions using 20% intravenous

**Table 2.** The degree of knowledge of the participants regarding LAs they use

	Know very well % (n)	Know well % (n)	Not sure % (n)	No idea % (n)
LA doses	10.7 (23)	33.5 (72)	46 (99)	9.8 (21)
LA contraindications	8.4 (18)	23.3 (50)	56.3 (121)	12.1 (26)
LA complications	8.4 (18)	25.1 (54)	52.6 (113)	14 (30)
LA maximum doses	4.2 (9)	34.9 (75)	45.6 (98)	15.3 (33)
Adverse effects of LA	8.4 (18)	21.4 (46)	56.7 (122)	13.5 (29)
Management of adverse events	11.2 (24)	40 (86)	37.7 (81)	11.2 (24)

LA: local anesthetic



**Table 3.** Most common LA-related adverse effects observed in clinical practice

Signs and symptoms	(%)	Number
Tachycardia-palpitation	52.09	112
Syncope	27.44	59
Irritability	24.18	52
Tinnitus	5.58	12
Metallic taste in the mouth	6.04	13
Allergic reactions	25.11	54
Hypotension	21.86	47
Hypertension	9.30	20
Stupor	4.18	9
Convulsion	0.93	2
None	0.93	2

LA: local anesthetic

lipid solutions with a dose of 1.5 mg/kg intravenously followed by 15 mL/kg/h infusion for maintenance. In case of persistent symptoms, a bolus dose can be applied twice more without exceeding a limit of 10 mL/kg.

The occurrence of LAST cases in dentistry is rare. However, they can become a serious issue if the clinical symptoms and signs are underestimated and appropriate steps are not taken. Unfortunately, to the best of our knowledge, there are no epidemiologic studies regarding the frequency of LAST in dentistry (9).

Inferior alveolar nerve blockade is relatively commonly performed in dentistry (15.3%); therefore, the expected risk of LAST may be higher while performing this nerve blockade procedure. The frequency of the use of ester-type LA agents is not high. Among amide-type LAs, lidocaine is the most commonly used LA agent, which has low potency (10).

According to our results, the most commonly used LA agent was lidocaine (74.41%). Bupivacaine is a long-acting LA agent with a severe cardiotoxic potential. Cardiac arrest cases caused due to bupivacaine-induced LAST are known as resuscitation-resistant cases (11). Among the amide-type LAs, the percentage of choice of bupivacaine was relatively low (8.37%). One has to consider that our study population consisted of dentistry students. The more they become experienced, the more they can treat complicated cases that may require long-acting nerve blockade with bupivacaine.

Even when the practitioner's choice is amide-type LAs, the risk of LAST is still present. Furthermore, if a patient is allergic to this drug, one has to choose the ester-type LAs that have high potency (9).

Unfortunately, most of the clinics that apply LAs do not readily have anesthesiologists in charge at their clinic. All nonanes-

thesiologist practitioners, including dentists, have to be alert of LAST symptoms and signs and hence the therapy modalities. In a study conducted by Oksuz et al. (4) among 600 dentists, 404 (67.3%) respondents mentioned that they had no idea about lipid treatment, 128 (21.3%) had heard about lipid treatment but said that they did not have sufficient knowledge about it, and 59 (9.8%) had read an article about lipid treatment, but only 9 (1.5%) knew how to use lipid treatment. Another study conducted among 124 dentists demonstrated that the subjects were aware of some side effects about LAs with vasoconstrictors; however, they had inadequate knowledge about the signs and symptoms of overdose of LAs (12).

Published case reports regarding LAST (13-15) in the literature most commonly depend on the experience of nonanesthesiologists. Interestingly, a Danish survey study conducted among anesthesiologists in 2011 concluded that the study subjects had limited knowledge about lipid rescue therapy for LAST (3). It can be speculated that the guidelines about lipid emulsion therapy were relatively new at the study time period. A study performed at a similar time period among dermatologists reported similar results, wherein the awareness of intravenous lipid rescue therapy was lower than expected (22%) (2).

Nurses who work in preoperative and postoperative care units, outpatient services, and labor and delivery units and even operation room circulating nurses generally do not receive formal education or training about the recognition and treatment of LAST events (16).

Ophthalmologists are another group of specialists who frequently use LAs. A questionnaire-based study performed among 104 ophthalmologists reported that 76% of the participants declared that they used LAs every day or more than twice a week, whereas 56.7% of them had no specific training about this clinical situation (17).

Dentistry practitioners who perform various nerve block procedures multiple times a day also have to be aware of LAST. A dentist who confronts a LAST case should accurately understand about rapid recognition and also consider about treatment with lipid emulsion therapy. Therefore, we have to incorporate education on LA safety as a treatment for LAST in mandatory training sessions. In addition, introduction of national guidelines on lipid rescue therapy would probably accelerate this process.

## CONCLUSION

In this context, academic trainers have a very important mission to prepare their students to encounter possible challenges in the future. The content of local anesthesia lessons has to be reviewed and arranged in view of these concerns. The results of this study implicate the evident need for additional educational effort to create awareness about LA use and effective management of LAST among dentistry students.

You can reach the questionnaire of this article at <https://doi.org/10.5152/EurJTher.2020.19094>.

**Ethics Committee Approval:** Ethics committee approval was received for this study from Gaziantep University Clinical Researches Ethical Committee with approval number: (2019/318).

**Informed Consent:** Verbal informed consent was obtained from patients who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept, Design, Supervision, Resources, Materials, Data Collection and/or Processing, Analysis and/or Interpretation, Literature Search, Writing Manuscript, Critical Review – BKU.

**Conflict of Interest:** The authors have no conflicts of interest to declare.

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**Appendix 1. Study Questionnaire (revised from Oksuz et al.)**

**Thank you for participating in our questionnaire about local anesthetic systemic toxicity (LAST) and treatment.**

1. **Age:**
2. **Degree of class:**
3. **Did you have training about local anesthesia (LA)?**  
Yes ( ) No ( ) Don't remember ( )
4. **Choose the local anesthetics that you most frequently use.**  
Articaine ( ) Bupivacaine ( ) Lidocaine ( ) Prilocaine ( ) Mepivacaine ( )  
Articaine with vasoconstrictor ( ) Lidocaine with vasoconstrictor ( ) Prilocaine with vasoconstrictor ( )  
Mepivacaine with vasoconstrictor ( )

**Evaluation of degree of knowledge about local anesthetics.**

5. **LA dose:** No idea ( ) Not sure ( ) Know well ( ) Know Very Well ( )
6. **LA contraindications:** No idea ( ) Not sure ( ) Know well ( ) Know Very Well ( )
7. **LA complications:** No idea ( ) Not sure ( ) Know well ( ) Know Very Well ( )
8. **LA maximum dose:** No idea ( ) Not sure ( ) Know well ( ) Know Very Well ( )
9. **LA side effects:** No idea ( ) Not sure ( ) Know well ( ) Know Very Well ( )
10. **Treatment of LA side effects:** No idea ( ) Not sure ( ) Know well ( ) Know Very Well ( )
11. **Recognize signs and symptoms:**  
  
Tachycardia ( ) Syncope ( ) Irritability ( ) Tinnitus ( ) Metallic taste in the mouth ( ) Allergic reactions ( ) Hypotension ( )  
Hypertension ( ) Stupor ( ) Convulsion ( )
12. **Have you ever seen LAST?**  
Yes ( ) No ( ) Unaware ( ) Don't remember ( )
13. **Do you know intravenous lipid treatment in LAST?**  
Had no idea about intravenous lipid rescue therapy ( )  
Had heard but did not have enough knowledge about it ( )  
Had read an article about lipid rescue therapy ( )  
Know how to use lipid rescue therapy ( )
14. **Have you ever used intravenous lipid treatment in LAST?**  
Had never seen local anesthetic toxicity ( )  
Had seen it but used treatments other than lipid rescue therapy ( )  
Had seen it and used intravenous lipid therapy ( )

# Effects of Dapagliflozin on Serum Low-Density Lipoprotein Cholesterol and Triglyceride Levels

Eren Gürkan 

Department of Endocrinology and Metabolism, Mustafa Kemal University School of Medicine, Hatay, Turkey

## ABSTRACT

**Objective:** The aim of this study is to assess the effects of dapagliflozin, a sodium/glucose cotransporter 2 (SGLT2) inhibitor, on serum triglyceride and low-density lipoprotein (LDL) cholesterol levels in patients with type 2 diabetes mellitus (DM).

**Methods:** A total of 40 patients with type 2 DM, who were followed up regularly in the Endocrinology and Metabolism Outpatient Clinic of State Hospital, were evaluated retrospectively. In these patients, dapagliflozin was added to their regular treatment for glycemic control. The patients' anthropometric measurements, glycemic regulation status, and serum LDL cholesterol and triglyceride levels were retrieved from the system records. A statistical analysis of drug effects was performed using the repeated measures analysis of covariance test, keeping the effects of HbA1c and body mass index (BMI) covariates constant.

**Results:** In addition to the improvement in fasting blood glucose levels, HbA1c, and body weight of the patients, a reduction by 10 mg/dL and 43.04 mg/dL was observed in serum LDL cholesterol and triglyceride levels, respectively. The evaluation of BMI and HbA1c covariates together revealed a statistically significant reduction in triglyceride levels ( $p=0.032$  and  $p=0.008$ , respectively).

**Conclusion:** Besides glycemic control and weight loss, addition of dapagliflozin to the type 2 DM therapy is associated with an improvement in serum triglyceride levels, suggesting that together with other benefits, SGLT2 inhibitors appear to provide an additional benefit of reducing the risk of cardiovascular diseases.

**Keywords:** Cardiovascular diseases, dapagliflozin, hyperlipidemia, SGLT2 inhibitor

## INTRODUCTION

Diabetes mellitus (DM) is associated with an increased risk of cardiovascular diseases (CVD), which is the major cause of morbidity and mortality in patients suffering from type 2 DM (1, 2). Other risk factors for CVD include hypertension, hyperlipidemia, obesity, and smoking. Hyperlipidemia is a common metabolic disorder among patients with type 2 DM (3). Particularly, an increase in triglyceride and low-density lipoprotein (LDL) cholesterol levels is pronounced (4).

Although the risk of CVD is reduced by decreasing LDL cholesterol to target levels, a substantial proportion of patients with type 2 DM fail to achieve target LDL cholesterol levels. Hence, a significant number of patients suffering from type 2 DM remain at risk of CVD (5).

With this in view, new therapeutic options for type 2 DM provide us with new opportunities. Sodium/glucose cotransporter 2 (SGLT2) inhibitors help to provide glycemic control by inhibiting glucose reabsorption through proximal renal tubules

(6). In addition, SGLT-2 inhibitors show favorable effects on blood pressure, body weight, arterial stiffness, visceral adiposity, albuminuria, and plasma uric acid concentration (7). Considering the effects of SGLT-2 inhibitors on lipid parameters, in addition to studies showing an increase in both high-density lipoprotein (HDL) and LDL cholesterol levels, there are studies reporting an increase in HDL cholesterol but not in LDL cholesterol (7, 8).

In the present study, we evaluated the effects of dapagliflozin that was added for 24 weeks to current treatment plans of patients with type 2 DM, who were receiving oral antidiabetics (OAD) and/or insulin on lipid parameters.

## METHODS

The present study included patients with type 2 DM aged 40–70 years, followed up in the endocrinology and metabolism outpatient clinic of Hatay State Hospital from August 2016 through March 2017. Dapagliflozin was added to the OAD and/or insulin therapy. We were able to reach a total of 58 patients. Among these patients,

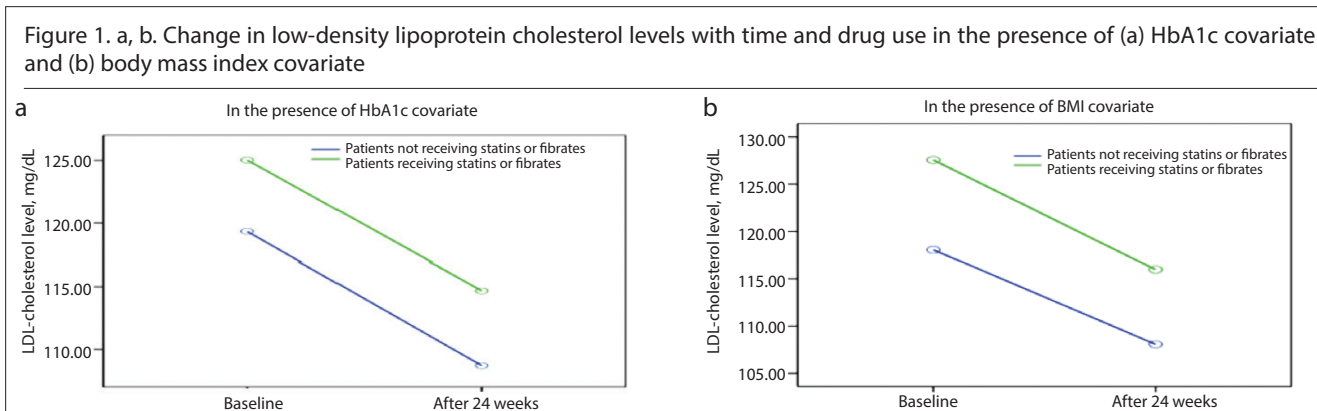
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**ORCID ID of the author:** E.G. 0000-0002-3118-4549

**Corresponding Author:** Eren Gürkan **E-mail:** erengurkan@ttmail.com

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those without the 3<sup>rd</sup> and 6<sup>th</sup> month follow-ups were excluded from the study. The data of the remaining 40 patients were retrospectively reviewed. Ethics committee approval was not obtained because of the retrospective study design. However, the present study was carried out in accordance with the World Health Organization Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants (2011) and the principles of the Declaration of Helsinki of the World Medical Association (2013). All patients were followed up by the same specialist using the same follow-up and treatment protocol.

Weight measurements were performed in the morning on an empty stomach at baseline and follow-up visits. Body mass index (BMI) was computed as a ratio of weight to square of height (kg/m<sup>2</sup>). Ambulatory blood pressure was recorded using automatic blood pressure monitors (Omron M2, HEM-7121-E) in sitting position after at least 5-minute rest.

For biochemical analyses, all blood samples were obtained from venous samples between 08:00 and 10:00 am after overnight fasting. Fasting blood glucose (FBG) and lipid profile were assessed using an automated enzymatic method, and HbA1c was assessed using the turbidimetric inhibition immunoassay (Roche Diagnostics, Mannheim, Germany). Estimated glomerular filtration rate was assessed using the Chronic Kidney Disease-Epidemiology (CKD-EPI) collaboration equation formula. Insulin ad-

ministration and dosage regimens were unchanged at baseline and follow-up visits.

**Statistical Analysis**

Continuous variables were expressed as mean±standard deviation, whereas categorical variables were expressed as frequency (%). The level of significance was predetermined to be 0.05 within the 95% confidence interval for all tests. The Shapiro–Wilk test was used for the Gaussian distribution. As for the univariate analysis, the chi-squared test and paired t-test were used, while the Wilcoxon signed-rank test was used when the condition for normality was not met. Keeping the effects of covariates HbA1c (difference as percentage) and BMI (numeric difference) constant, the change in LDL cholesterol and triglyceride levels between before and after treatment according to the medication was analyzed by repeated measures analysis of covariance (ANCOVA). After providing normality and homogeneity of variances for ANCOVA (using the Box-M test), the assumption of regression curves of the independent variable (drug) and covariates (HbA1c and BMI) being homogeneous (interactions >0.05) was provided. In addition, the linearity of LDL cholesterol and triglycerides with the covariates (HbA1c and BMI) was reviewed. All analyses were performed using the IBM Statistical Package for the Social Sciences Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY, USA).

**RESULTS**

The mean age of 40 patients, of whom 17 (42.5%) were female and 23 (57.5%) were male, was 52.85±9.08 years. The mean duration of DM was 8.07±4.12 years. Laboratory results and anthropometric measurements are summarized in Table 1. The mean weight loss was 1.63±0.32 kg. The pre- and posttreatment changes in FBG, HbA1c, LDL cholesterol, and triglyceride levels were significantly lower in our study group (Table 1).

Of the patients, 26 (65%) were not receiving statins or fibrates, and 14 (35%) were receiving either of the drugs (Table 2).

By keeping the HbA1c and BMI covariates constant over the 6-month treatment period from baseline, a decrease was observed in the LDL cholesterol levels during that time. However, this decrement was not caused by the drug (p=0.663 for the drug with HbA1c as covariate and p=0.525 for the drug with BMI as covariate) (Table 3, Figure 1).

**Main Points:**

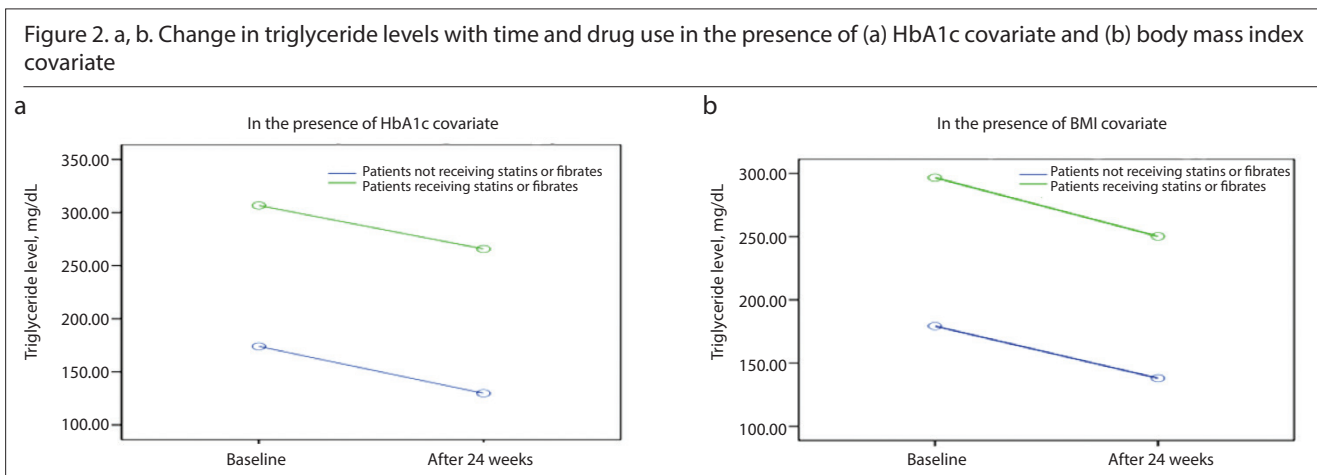
- SGLT-2 inhibitors show favorable effects on blood pressure, body weight, arterial stiffness, visceral adiposity, albuminuria, and plasma uric acid concentration.
- Substantial proportion of patients with type 2 DM fail to achieve target lipid levels.
- Results of studies on the effects of SGLT2 inhibitors on LDL-cholesterol and triglyceride have varied.
- Dapagliflozin, a SGLT-2 inhibitor, included in the treatment plan of patients with type 2 DM and high triglyceride levels not only provides glycemic regulation, but it also shows a beneficial effect on hypertriglyceridemia.
- The positive effect of Dapagliflozin on lipid parameters is an important result in reducing the risk of CVD in patients with type 2 diabetes.



**Table 1.** Univariate analyses and descriptive values for the parameters

Parameter	Baseline	After 24 weeks	p
Age (year), mean±SD	52.85±9.08		
Duration of DM (year), mean±SD	8.07±4.12		
Gender, n (%)			
Female	17 (42.5)		0.352*
Male	23 (57.5)		
Cigarette smoking, n (%)			
Nonsmoker	27 (67.5)		0.001*
Quitted	8 (20)		
Current smoker	5 (12.5)		
Body weight (kg), mean±SD	88.85±15.04	87.22±14.72	0.012**
BMI (kg/m <sup>2</sup> ), mean±SD	32.26±4.50	31.70±4.44	0.014**
SBP (mmHg), mean±SD	126.50±14.59	125.75±10.09	0.520**
DBP (mmHg), mean±SD	80.12±5.60	79.62±5.11	0.562**
FBG (mg/dL), mean±SD	219.62±70.38	172.48±53.08	0.001***
HbA1c (%), mean±SD	10.07±1.70	7.97±1.24	0.001**
LDL (mg/dL), mean±SD	121.23 ±35.81	110.70±35.95	0.041**
TG (mg/dL), mean±SD	219.72±150.63	176.68±125.84	0.002***
Creatinine (mg/dL), mean±SD	0.72±0.19	0.72±0.20	0.513**
eGFR (mL/min per 1.73 m <sup>2</sup> ), mean±SD	101.64±14.13	101.71±14.60	0.938**

\*chi-squared test; \*\*Student's t-test; \*\*\*Wilcoxon signed-rank test. DM: diabetes mellitus; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; FBG: fasting blood glucose; LDL: low-density lipoprotein; TG: triglyceride; eGFR: estimated glomerular filtration rate; SD: standard deviation



By keeping the HbA1c and BMI covariates constant over the 6-month treatment period from baseline, a decrease was also observed in triglyceride levels during that time. Drug use as well as time had an effect on this decrement (p=0.008 for the drug with HbA1c as covariate and p=0.032 for the drug with BMI as covariate) (Table 3, Figure 2).

**DISCUSSION**

SGLT-2 inhibitors cause a loss of approximately 240–320 calories/day by means of urinary glucose excretion at an average of 60–80 g/day (9). In a study conducted on the patients who were added SGLT-2 inhibitors to their treatment, a weight loss up to

**Table 2.** Drug groups, which might affect lipid levels, used by patients at the beginning of the study

Drug Groups	(%)
Metformin	87
DPP4 inhibitors	75
SU	40
Insulin	20
TZD	5
GLP-1 A	2.5
Statin	20
Fibrate	15
Thiazide	10
Beta blocker	10
LT4	7.5

SU: sulfonylurea; DPP4: dipeptidyl peptidase 4; TZD: thiazolidinedione; GLP-1A: glucagon-like peptit-1 analog; LT4: levothyroxine.

**Table 3.** Effects of dapagliflozin on LDL cholesterol and tri-glyceride levels according to statin and fibrate use in the presence of covariates (BMI and HbA1c)

		Mean±SD	p
Statin and fibrate nonusers	LDL baseline	118.30±37.22	0.145
	LDL final	107.40±36.53	
	TG baseline	180.63±75.00	0.006
	TG final	136.42±45.41	
Statin and fibrate users	LDL baseline	127.10±33.95	0.374
	LDL final	117.30±35.72	
	TG baseline	294.00±223.58	0.214
	TG final	253.20±187.66	

LDL: low-density lipoprotein; TG: triglyceride; SD: standard deviation

1.1–1.8 kg on average was observed in the 6-month follow-up period (10). In the present study, the mean weight loss was 1.63 kg, which is consistent with the literature.

Among the parameters of glycemic regulation, the expected reduction in FBG and HbA1c values with addition of SGLT-2 inhibitors is 20–30 mg/dL and 0.5%–1%, respectively (11). In the present study, the mean decrease in FBG and HbA1c was 47.14 ng/dL and 2.1%, respectively. In patients receiving DPP-4 inhibitors together with SGLT-2 inhibitors, the average reduction in HbA1c has been reported between 1.1% and 1.5% (12). In our study group, the substantial proportion of the patients was receiving DPP-4 inhibitors (75%). The response to antidiabetic medications

is usually far above the expected levels in patients with high baseline HbA1c and FBG values.

Many studies have demonstrated that using statins for either primary or secondary prevention remarkably reduces cardiovascular events and related deaths (13, 14). SGLT-2 inhibitors, which are among the new generation OADs, are OADs with insulin-independent glucose-reducing effect. They lead to calorie loss while reducing glucose absorption through proximal tubules. In case of fasting, calorie deficit is compensated using lipids instead of glucose (15, 16). Various clinical trials performed with SGLT-2 inhibitors have reported increased LDL cholesterol (1.5%–6.3%) and HDL cholesterol (5.5%–9.2%) levels, but decreased triglyceride (1%–9.4%) levels (17). In the present study, we observed that the LDL cholesterol level decreased by 11.53 mg/dL (8.68%), and triglyceride levels decreased by 43.04 mg/dL (19.58%). The evaluation of LDL cholesterol alone revealed that the decrement reached the level of statistical significance; however, considering it together with the changes in BMI and HbA1c, the decrement was not statistically significant. In this sense, the results of the present study are consistent with the literature. The decrement in triglyceride levels was significant both alone and in the presence of other covariates (HbA1c and BMI). The improvement in triglyceride levels might be associated with weight loss and improved insulin sensitivity (18).

The present study has some limitations. First, it is a single-center small-scale study. Second, the study has a retrospective design. Moreover, HDL and total cholesterol measurements were not available as the patients were followed up according to their treatment protocol.

**CONCLUSION**

Addition of SGLT-2 inhibitors in the treatment of type 2 DM improves the lipid profile in addition to glycemic regulation. In this sense, it will be reasonable to mention an additional effect of SGLT-2 inhibitors in reducing the risk of CVD in patients with type 2 DM. Dapagliflozin, a SGLT-2 inhibitor, included in the treatment plan of patients with type 2 DM and high triglyceride levels not only provides glycemic regulation, but it also shows a beneficial effect on hypertriglyceridemia, which is one of the risk factors.

**Ethics Committee Approval:** Authors declared that the research was conducted according to the principles of the World Medical Association Declaration of Helsinki “Ethical Principles for Medical Research Involving Human Subjects”, (amended in October 2013).

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

**Peer-review:** Externally peer-reviewed.

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# Coronary Embolism from Prosthetic Aortic Valve due to Incompliant Warfarin Use: A Rare Cause of Acute Coronary Syndrome

Uğur Canpolat , Yusuf Ziya Şener , Metin Okşul , Mehmet Levent Şahiner ,  
Kudret Aytemir 

Department of Cardiology, Hacettepe University School of Medicine, Ankara, Turkey

## ABSTRACT

Acute ST-segment elevation myocardial infarction (STEMI) is a life-threatening condition for which revascularization should be accessed emergently. Most STEMI cases result from atherosclerotic plaque rupture. However, rare causes such as coronary artery dissection, the vasculitic involvement of the coronary arteries, and coronary artery embolism may result in pathophysiological mechanism. This paper presents the case of a young male patient with subacute anterior STEMI secondary to thrombus embolism from prosthetic aortic valve due to incompliant warfarin use.

**Keywords:** Coronary artery embolism, incompliant warfarin use, prosthetic aortic valve

## INTRODUCTION

Acute ST-segment elevation myocardial infarction (STEMI) develops after coronary artery occlusion due to ruptured coronary artery plaque and results in myocardial necrosis. Coronary artery embolism is a rare cause of STEMI without underlying atherosclerosis. Atrial fibrillation is the most common underlying disease related to coronary artery embolism (1).

This paper presents the case of a young male patient with a prosthetic aortic valve. The patient was admitted to our hospital with subacute anterior STEMI due to coronary artery embolism that potentially originated from prosthetic aortic valve owing to incompliant warfarin use.

## CASE PRESENTATION

A 17-year-old male patient with compression type chest and back pain, which started 3 hours before admission, was admitted to our emergency department. His past medical history revealed Benthal procedure (prosthetic aortic valve and ascending aorta graft replacement) performed two years ago due to severe aortic regurgitation and ascending aorta dilatation related with bicuspid aortic valve. His only daily medication was warfarin, which was not consumed for the last four days. The patient reported that he had not used any other medications and substances during that period. His vital signs were in normal range; physical examination was unremarkable, except the metallic sound

of S2. His electrocardiogram was consistent with subacute anterior STEMI (Figure 1). Hypokinesia at anterior wall mid-basal segments with estimated left ventricular ejection fraction of 50% was established by bedside echocardiographic evaluation. Prosthetic aortic valve functions were normal, and neither thrombus nor vegetation was detected on the valve surface. The international normalized ratio (INR) level was 1.23, which was below the therapeutic range. Cardiac biomarkers were mildly elevated (CK-MB:8.6 (0-6.3 ng/mL) and Tn-I: 0.113 (0-0.04 ng/mL), and coronary angiography was performed emergently. His right coronary artery, circumflex artery, and left main coronary arteries were normal. A huge thrombus obstructing the lumen was detected in the left anterior descending artery (LAD) (Figure 2). Bileaflet prosthetic valve motion was also normal at fluoroscopy. Intracoronary tirofiban was administered, and maintenance infusion of unfractionated heparin and tirofiban was continued for 24 hours. Thereafter, subcutaneous enoxaparin 2x0.6 cc was initiated, in addition to the administration of 100 mg of aspirin and 75 mg of clopidogrel. Transeosophageal echocardiography revealed no thrombus at the heart valves, with prosthetic aortic valve and left atrial appendage and normal prosthetic valve functions. A control coronary angiography was performed 72 hours later, indicating that thrombus in the LAD had disappeared (Figure 3). Rheumatological markers and thrombophilia genetic panel were negative. Homocysteine level was also in the normal range. The patient did not describe dark urine in the morning, and hemo-

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**ORCID IDs of the authors:** U.C. 0000-0002-4250-1706; Y.Z.Ş. 0000-0001-5151-5133; M.O. 0000-0003-0531-3500; M.L.Ş. 0000-0002-0985-3144; K.A. 0000-0001-9279-8424.

**Corresponding Author:** Uğur Canpolat **E-mail:** dru\_canpolat@yahoo.com

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Figure 1. Electrocardiography on admission indicating pathological Q waves and ST segment elevation in anterior leads consistent with subacute anterior myocardial infarction

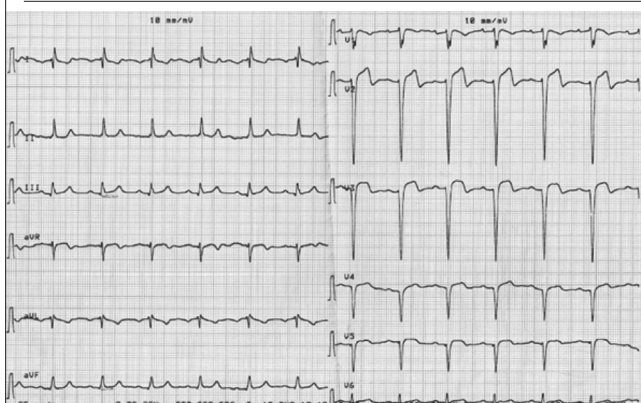
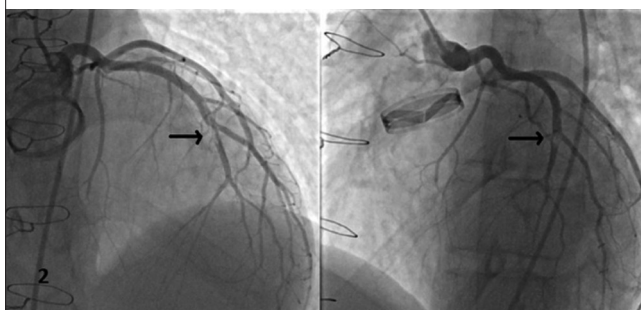


Figure 2. Emergent angiogram at right anterior oblique and left anterior oblique views indicating a huge thrombus at the mid portion of the left anterior descending artery



lytic parameters were normal. Other causes of arterial thrombus were excluded; coronary thromboembolism from the prosthetic aortic valve secondary to incompressible warfarin use and subtherapeutic INR level was proposed as the underlying mechanism. The patient was uneventfully discharged with a triple antithrombotic regimen (including warfarin, 100 mg of aspirin, and 75 mg of clopidogrel) for three months, and warfarin as well as aspirin was continued thereafter. As the past surgical reports were unavailable, the type of prosthetic valve could not be learnt from the patient. The target INR level during follow-up was determined as 3.0 owing to thromboembolic episode in conjunction with mechanical prosthetic aortic valve. Informed consent was obtained from the patient.

**Main Points:**

- An acute coronary syndrome due to coronary thromboembolism should be considered in differential diagnosis among patients with mechanical prosthetic heart valves.
- Effective therapeutic anticoagulation should be maintained in all patients with mechanical prosthetic heart valves.
- Monitoring of effective therapeutic INR levels is very important to prevent inadvertent embolic events in those patients.

Figure 3. Control angiogram at right anterior oblique view indicating the disappearance of thrombus at the left anterior descending artery after heparin and tirofiban infusion therapy



**DISCUSSION**

Plaque rupture is the most common cause of STEMI; of the other rare situations, coronary embolism results in STEMI. STEMI is a life-threatening condition that must be emergently treated with either mechanical or pharmacological revascularization. Primary percutaneous intervention is better than thrombolytic treatment to achieve thrombolysis in myocardial infarction grade 3 flow; accordingly, interventional treatment should always be preferred as the first option if available. Thrombus aspiration can be an option in selected patients with coronary artery embolism. There was a diversity between randomized controlled study results in regard to outcomes of thrombus aspiration during primary PCI. Therefore, routine thrombus aspiration before PCI is not suggested by the American Heart Association (AHA) guidelines, and this option should be only considered in selected cases (1).

The prevalence of coronary artery embolism in patients with STEMI is estimated to be 13% by post-mortem series. Infective endocarditis, atrial thrombus, myxoma, prosthetic valves, calcific aortic stenosis, and biological glue used to repair aortic dissection are common causes of coronary artery embolism (2). Thrombus originating from aortic valve usually goes to left coronary artery presumably associated with aortic valve morphology (3). Anticoagulation with warfarin should be advised to the patients with mechanical prosthetic aortic valve, and the INR level should be maintained between 2.0–3.0 consistent with the recommendations of AHA/ACC guidelines to minimize the risk of thromboembolism. In patients with On-X aortic valve replacement, lower INR levels (1.5–2.0) are acceptable due to lower thromboembolic risk. Aspirin (75–100 mg/day) should be added in anticoagulant therapy (4). No consensus exists regarding the maintenance treatment of coronary embolism. Warfarin and as-



pirin were administered to the patient with STEMI considering mechanical prosthetic aortic valve, and clopidogrel was added for three months.

Similar cases with coronary artery embolism from the mechanical mitral valve, during and just after aortic valve replacement procedure and from blood cyst originated from mitral valve have been reported (5-7). To the best of our knowledge, no case report in the literature showing a coronary artery embolism from mechanical aortic valve as a result of in-compliant use of warfarin and subtherapeutic INR level has been reported.

## CONCLUSION

The most common cause of coronary artery occlusion is a ruptured unstable atherosclerotic plaque; however, coronary artery occlusion due to thromboembolic events should be included in the differential diagnosis of patients with acute coronary syndrome. Patients with prosthetic valves carry a high risk for thrombotic complications; accordingly, these patient groups should be effectively anticoagulated and monitored at regular intervals.

**Informed Consent:** Informed consent was obtained from the patient.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – Y.Z.Ş., M.O., U.C.; Design – Y.Z.Ş., M.O., U.C.; Supervision – U.C., L.Ş., K.A.; Resource – Y.Z.Ş., M.O., U.C.; Materials – Y.Z.Ş., M.O., L.Ş.; Data Collection and/or Processing – Y.Z.Ş., M.O.; Analysis and/or Interpretation – Y.Z.Ş., M.O., U.C.; Literature Search – Y.Z.Ş., M.O., U.C.; Writing – Y.Z. Ş., M.O., U.C.; Critical Reviews – U.C., L.Ş., K.A.

**Conflict of Interest:** The authors have no conflicts of interest to declare.

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# A Rare Involvement of Left Main Coronary Artery Due to Woven Coronary Artery in a Patient with Behçet's Disease

Sefa Tatar , Yakup Alsancak , Ahmet Seyfeddin Gürbüz , Abdullah İçli 

Department of Cardiology, Necmettin Erbakan University Meram School of Medicine, Konya, Turkey

## ABSTRACT

In general, woven coronary artery (WCA) is a benign congenital pathology; occasionally, it may result in adverse cardiovascular events owing to myocardial ischemia. Though all coronary arteries may be affected, the right coronary artery is the most affected. This paper presents an extremely rare WCA affecting the left main coronary artery concurrent with Behçet's disease.

**Keywords:** Behçet's disease, left main coronary artery, woven coronary artery

## INTRODUCTION

Woven coronary artery (WCA) is an extremely rare congenital anomaly with unexplained etiology (1). In this malformation, epicardial coronary arteries divide into long and thin channels. Thereafter, these channels merge to form an artery at the distal vascular bed (2). Normal blood flow after the abnormal coronary segment secures the relevant region, considered to be a good nature of coronary artery anomaly. Although this condition is considered to be benign, it occasionally causes angina pectoris, acute coronary syndromes, or possible sudden cardiac death owing to myocardial ischemia (3-5). Moreover, a few case reports have claimed no adverse cardiovascular events during long-term follow up (6, 7). This paper presents an extremely rare WCA affecting the left main coronary artery (LMCA) concurrent with Behçet's disease (BD).

## CASE PRESENTATION

A 53-year-old male patient with a diagnosis of BD for 20 years was admitted to our department for unstable angina pectoris. The patient had a history of coronary artery bypass surgery 10 years ago. Resting electrocardiogram indicated q waves on D3 and aVF as well as nonspecific ST segment changes in precordial derivations with ventricular extrasystoles. Echocardiography indicated the systolic regional wall motion impairment. Coronary angiography was planned due to recurrent angina pectoris. Coronary angiography revealed a rudimentary right coronary artery (RCA) without a significant stenosis. Left coronary system angiography demonstrated a WCA of LMCA proceeding to the left anterior descending coronary artery (LAD) and circumflex artery (Cx). Furthermore, we observed a functional and well-developed left internal mammary artery (LIMA) to LAD anastomosis that associated dense collaterals with peripheral structures. Moreover, angiography revealed a collateral development between

the left coronary system and RCA (Figure 1, 2). However, no information exists about the patient's coronary anatomy before his coronary artery bypass surgery. We believed that the patient's anginal complaints maybe associated with coronary steal owing to the dense collateral flow of LIMA. Furthermore, WCA of LMCA may have resulted from the decreased blood flow of Cx artery. So, we decided to optimal antianginal medical treatment to control of patient's symptoms. Written informed consent was obtained from the patient.

## DISCUSSION

The etiology of WCA is unclear and is incidentally detected during coronary angiography. The literature indicates a male predominance (10:1) and reveals that RCA is the most affected (1, 4, 6). The recanalized thrombus, antegrade coronary collateral flow, or spontaneous coronary artery dissection should be considered for differential diagnosis (6). In particular, publications have indicated the effectiveness of optical coherence tomography (OCT) in differential diagnosis (8). We believed that the use of intravascular ultrasound or OCT for this patient is inappropriate owing to the diffuse involvement of LMCA. Depending on the affected segment of the coronary system, pharmacological treatment, percutaneous coronary intervention, or coronary artery bypass grafting may be the possible treatment options.

The frequency of vascular involvement among BD patients ranges from 7.7% to 38% and is referred to as vascular BD (9). Males seem to be affected with arterial involvement than females. Vascular involvement more commonly affects the veins than the arteries, and coronary arterial involvement is extremely rare. Cardiovascular involvement in BD patients is estimated to range from 3% to 6%. This may result in pericarditis, myocarditis, coronary artery disease, valvular heart disease or intracardiac thrombus, endocarditis with valvular regurgitation, aneurysms of the coronary arteries or sinus of

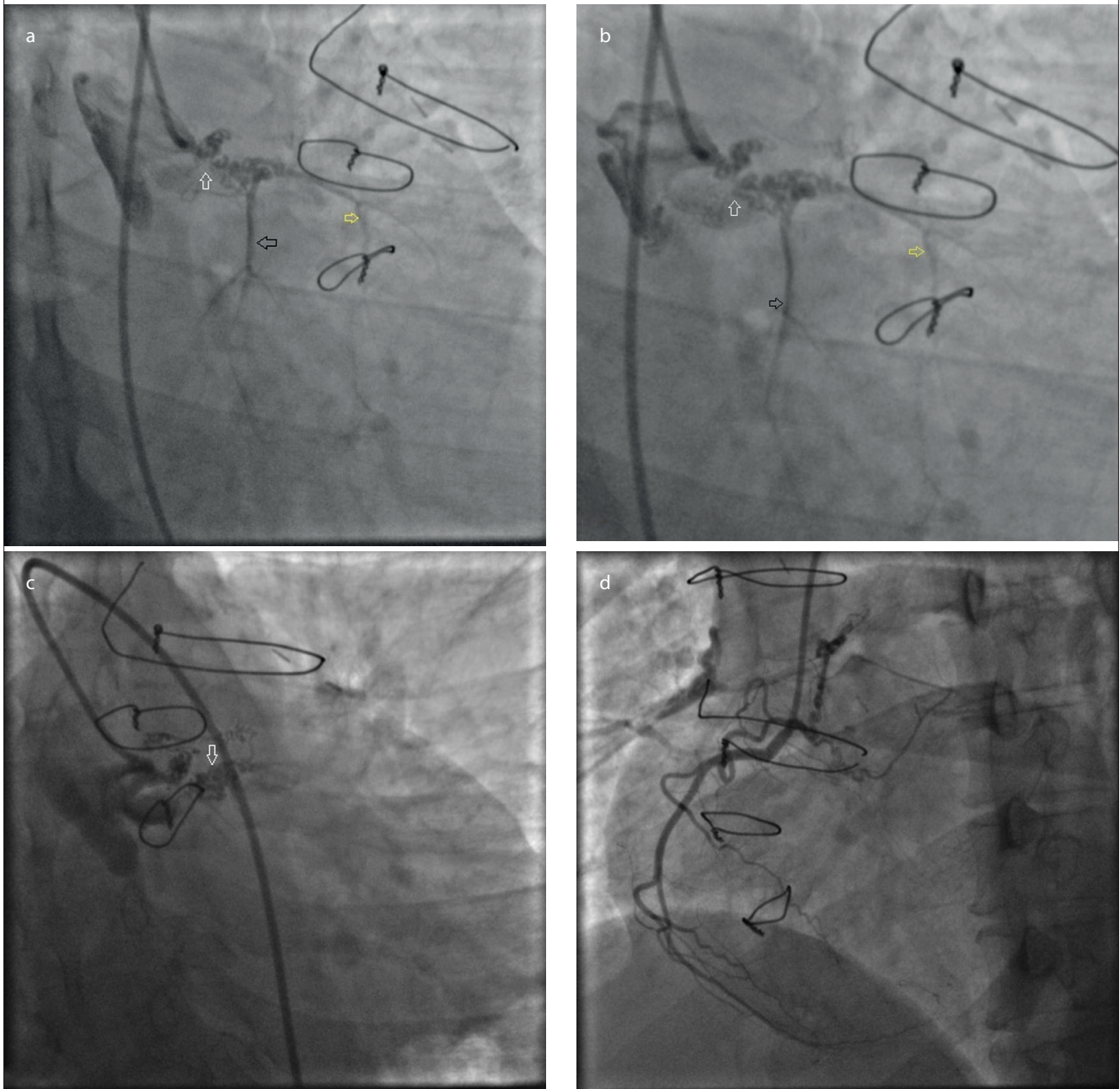
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**ORCID IDs of the authors:** S.T. 0000-0001-8703-5078; Y.A. 0000-0001-5230-2180; A.S.G. 0000-0002-9225-925X; A.İ. 0000-0002-7047-811X.

**Corresponding Author:** Yakup Alsancak **E-mail:** dryakupalsancak@gmail.com

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Figure 1. a-d. Coronary angiography depicts woven coronary artery of the left main coronary artery (white arrow), totally occluded left anterior descending coronary artery, dominant septal artery (yellow arrow), and circumflex coronary artery (black arrow) (a). Anteroposterior and caudal angiographic image of vessels [left main coronary artery (white arrow), septal artery (yellow arrow), and circumflex coronary artery (black arrow)] (b). Left anterior oblique caudal projection (spider view) demonstrating woven coronary artery of the left main coronary artery (white arrow) (c). Nondominant right coronary artery in a left anterior oblique view (d)



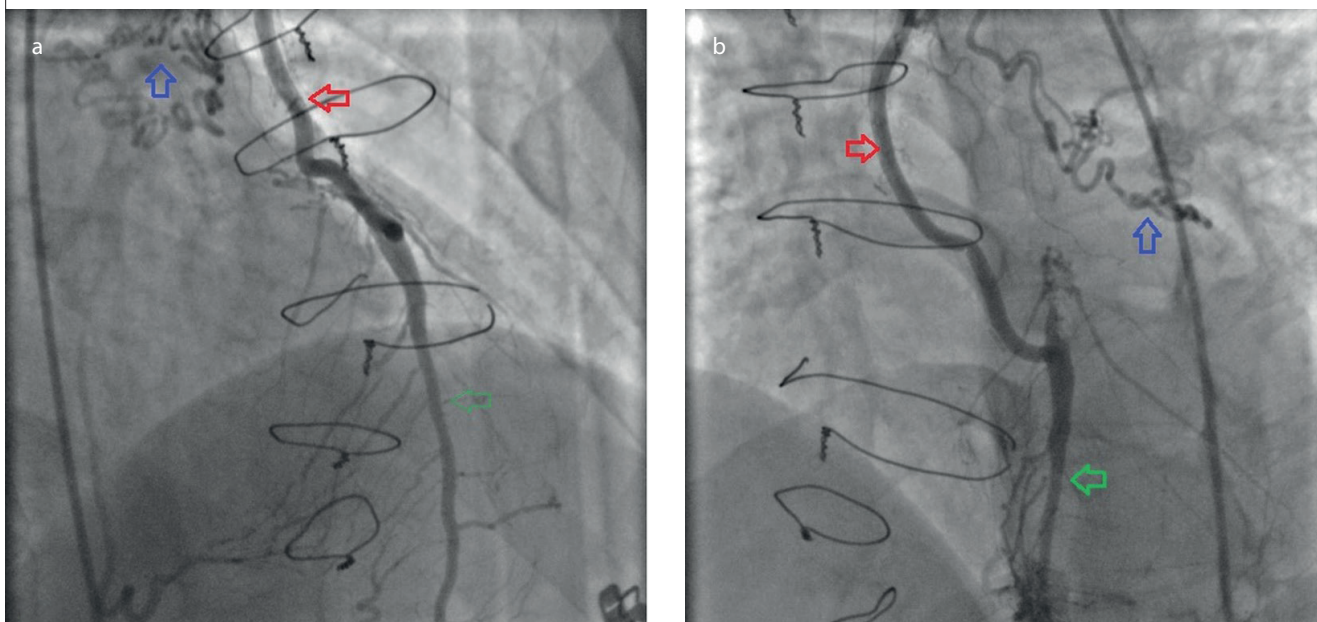
**Main Points:**

- The etiology of the woven coronary artery is still controversial.
- Involvement in the left main coronary artery is rarely reported.
- In this case, the presence of connective tissue disease (Behçet's Disease) with woven coronary artery may provide a different perspective for etiology.

valsalva, and advanced heart failure (10, 11). Lesions of coronary arteries include stenosis, occlusion, aneurysm, and pseudoaneurysm with or without myocardial infarction. A previously published study has demonstrated that silent myocardial ischemia rate was higher among BD patients compared with that of healthy controls at 19.5% and 2.9%, respectively (12). Peripheral arterial involvement in BD patients may range from 1.5% to 7% (9, 13). When a coronary artery pathology is detected in BD patients, the entire arterial or venous



Figure 2. a, b. Left internal mammary artery (red arrows) to left anterior descending coronary artery (green arrows) and anastomosis and well-developed collaterals (blue arrows) to the peripheral structures (a). Another image of left internal mammary artery (red arrows) to left anterior descending coronary artery (green arrows) and anastomosis and well-developed collaterals (blue arrows) (b)



vascular system must be evaluated for involvement. Doppler ultrasound scan of carotid arteries and iliofemoral arterial and venous system was observed to be in the normal range for this patient.

This case may be essential for two reasons. First, WCA can effect the isolated LMCA. To the best of our knowledge, this report is the first case to focus on the condition of WCA in BD patients in the literature. Since the patient's coronary anatomy before his coronary artery bypass surgery was unknown, commenting on congenital or the acquired appearance of LMCA seems impossible. As for the patient in this case, the LMCA lesion may have mortal consequences; thus, it is acceptable to explain this view through a chronic pathology. Furthermore, LMCA thrombosis may have resulted in coronary artery bypass grafting for this patient. Accordingly, this angiographical image may have resulted from chronic thrombosis recanalization. Second, the appearance of BD as a chronic vasculitis syndrome may result from chronic inflammation.

## CONCLUSION

Finally, histopathological examination continues to be the gold standard technique for the diagnosis or differential diagnosis of WCA. This case indicates that the screening of connective tissue diseases may be beneficial in patients with WCA.

**Informed Consent:** Written informed consent was obtained from patient who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author contributions:** Concept - Y.A.; Design - Y.A., S.T.; Supervision - A.I.; Resource - H.G.; Materials - Y.A, S.T.; Data Collection and/or Processing - H.K.; Analysis and/or Interpretation - A.S.G., Y.A.; Literature Search - A.S.G., Y.A.; Writing - Y.A., S.T.; Critical Reviews - A.I.

**Conflict of Interest:** The authors have no conflicts of interest to declare.

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