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Review article

Treatment of patients with spontaneous coronary artery dissection - is there a difference?

Vladimir Mitov[1], Aleksandar Jolic[1], Dragana Adamovic[1], Milan M. Nikolic[1], Svetlana Apostolovic[2], Vladimir Zdravkovic[3], Milenko Cankovic[4], Zlatko Mehmedbegovic[5], Bojan Maricic[2], Aleksandra Djokovic[6], Gordana Krljanac[5], Ivan Ilic[7]

[1] Invasive Cardiology Department , Zajecar Health Center, [2]Cardiology Clinic, University Clinical Center Nis, [3]Cardiology Clinic, Clinical Center Kragujevac, [4]Cardiology Clinic, Institute for cardiovascular diseases Vojvodina, [5]Clinic of Cardiology, Univeristy Clinical Centre of Serbia, Belgrade, [6]Department of cardiology Clinical-Hospital Center, Bežanijska Kosa, Belgrade, [7]Department of cardiology, Institute for cardiovascular diseases Dedinje, Belgrade

Abstract Patients with spontaneous coronary artery dissection (SCAD) do not differ from any other acute coronary syndrome (ACS) patients from the first medical contact to coronary angiography; the diagnostic approach and therapy are the same. SCAD patients are identified only based on coronary angiography findings. Perhaps the "SCAD Patient Model" can help. By analyzing registries of SCAD patients, we can see that 90% are women, with 87-95% aged 44-53 years, who may have a personal or family history of fibromuscular dysplasia, and may be correlated with the use of hormone therapy or with changes in hormonal status during pregnancy. Based on this data, we can identify a model of SCAD patient, which is presented by a young woman suggesting a SCAD patient with clinical presentation of ACS. This is almost certain if we have a young pregnant woman or a woman in the postpartum period with ACS. Considering that the use of fibrinolytic therapy in SCAD patients is absolutely contraindicated, and that the diagnosis of SCAD is made only by coronary angiography, it should be considered whether patients with a possible SCAD pattern should not receive fibrinolytic therapy but should be transported to an available PCI center. PCI is indicated in patients with SCAD in cases of TIMI 0 flow on coronary angiography, significant reduction in blood flow in the vessel and persistent chest pain, or hemodynamically unstable patients. The pathophysiological mechanism in SCAD patients is not atherosclerotic disease but an intramural hematoma in the coronary artery wall. Medical treatment of SCAD patients is different from that of patients with an atherosclerotic form of acute coronary syndrome. Dual antiplatelet therapy is administered for a duration of 12 months only in the group of patients undergoing PCI, while others are taking it for a duration of 1 month. Statins, ACE inhibitors are given only to selected patients. It is recommended that beta-blocker therapy be applied to all patients who can tolerate the medication.

Key words spontaneous coronary artery dissection, acute coronary syndrome, therapy

Introduction

According to guidelines for the diagnosis and treatment of patients with acute coronary syndrome (ACS), 4% of patients with clinically manifested ACS on coronary angiography are diagnosed with spontaneous coronary artery dissection (SCAD). Out of this number, 22-35% are women under the age of 60 (1). Patients with SCAD do not differ from any other ACS patients from the first medical contact to coronary angiography; the diagnostic approach and therapy are the same. SCAD patients are identified only based on coronary angiography findings. According to current guidelines, ACS patients receive dual antiplatelet therapy (DAPT) after the first medical contact, consisting of acetylsalicylic acid (ASA) with the addition of Clopidogrel, Ticagrelor, or Prasugrel in loading doses. It should be noted that according to guidelines, Ticagrelor and Prasugrel, as more potent drugs, are preferred over Clopidogrel. The same patients also receive low molecular weight heparin (LMWH) in therapeutic doses[2]. If the first medical contact is in a PCI center, LMWH is often not given, and unfractionated heparin (UFH) is used during the procedure itself. This therapeutic approach has been used for almost 20 years and has shown a significant difference in survival, with fewer recurrent infarctions during hospitalization and within the first year in patients with ACS and primarily due to atherosclerotic disease[3].
Unlike atherosclerotic lesions, SCAD is pathophysiological characterized by the occurrence of an intramural hematoma within the tunica media of the coronary artery, which, by its propagation and enlargement, partially or completely, in shorter or longer artery segments reduces blood flow in the infarcted coronary artery (Figure 1.).

Address for correspondence: Vladimir Mitov, MD, PhD, Invasive Cardiology Department , Zajecar Health Center, Zajecar, Serbia.
E-mail: drvladimirmitov@gmail.com

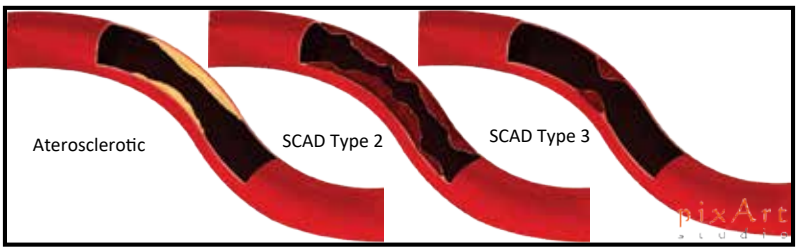

Figure 1. Aterosclerotic vs SCAD Type 2 and Type 3 lesion oronarne aerterije

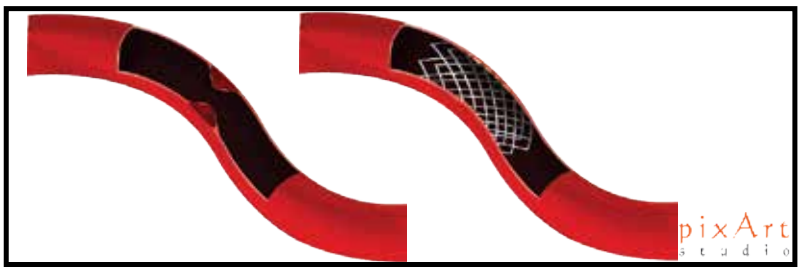

Figure 2. PCI with single stent implantation

Knowing that SCAD is fundamentally characterized by hemorrhage and the occurrence of a hematoma within the wall of the coronary artery, rather than atherosclerosis, it is clear that the application of standard ACS therapy from the first medical contact to coronary angiography and definitive diagnosis of SCAD can be problematic. How can we differentiate SCAD patients at this stage of clinical presentation? Perhaps the "SCAD Patient Model" can help. By analyzing registries of SCAD patients, we can see that 90% are women, with 87-95% aged 44-53 years[1], who may have a personal or family history of fibromuscular dysplasia[4], and may be correlated with the use of hormone therapy or with changes in hormonal status during pregnancy[5]. Based on this data, we can identify a model of SCAD patient, which is presented by a young woman without traditional risk factors for atherosclerosis (except smoking and hypertension), suggesting a SCAD patient with clinical presentation of ACS. This is almost certain if we have a young pregnant woman or a woman in the postpartum period with ACS.

The aim of this study is to point out the difference in therapeutic approach between patients with an atherosclerotic disease and patient with spontaneous coronary artery dissection that both present themselves clinically with acute coronary syndrome.

If we go back to the fact that only 4% of patients with ACS have SCAD as the underlying cause, it is not expected that the therapeutic strategy for patients with ACS will change from the first medical contact to coronary angiography. However, the therapy for patients with SCAD has its specificities.

Fibrinolytic therapy

A portion of patients with SCAD who clinically present as ACS are treated in centers where PCI is not available as a therapeutic option. According to the protocol for patients with STEMI ECG presentation, these patients receive fibrinolytic therapy. According to data from the Can SCAD registry, 29.7% of patients present as STEMI patients at the first medical contact, and 11% received fibrinolytic therapy[6]. Considering that the use of fibrinolytic therapy in SCAD patients is absolutely contraindicated[7,8], and that the diagnosis of SCAD is made only by coronary angiography, it should be considered whether patients with a possible SCAD pattern should not receive fibrinolytic therapy but should be transported to an available PCI center.

Percutaneous coronary intervention (PCI)

After coronary angiography and definitive diagnosis of SCAD based on lesion characteristics and TIMI flow, a decision is made regarding further conservative medical treatment or PCI[1]. According to the CanSCAD registry of 750 patients, 86.4% were treated conservatively. Their conclusion is that in the most experienced centers, the majority of patients are treated conservatively, and in 95% of patients, complete recovery of the coronary artery was found on follow-up coronary angiography after 30 days[6,9]. Coronary artery recovery is high, with low mortality, 1% during a 3-year follow-up period, but a large number of patients continue to experience frequent symptoms and poor quality of life even after the acute phase of the disease[10].

PCI is indicated in patients with SCAD in cases of TIMI 0 flow on coronary angiography, significant reduction in blood flow in the vessel and persistent chest pain, or hemodynamically unstable patients[1]. PCI techniques in SCAD patients include:

1. PCI with a single stent - suitable for patients with SCAD Type 3, when the affected part of the coronary artery is short. Primo-implantation of a stent placed in the middle of the lesion is used, and the upper and lower edges of the stent need to be 5-10mm longer than the lesion. (Figure 2.).

2. PCI with multiple stents (Sandwich technique) - suitable for patients with Type 2, when a longer segment of the coronary artery is affected by hematoma. Stents are deployed without prior balloon dilatation, if possible. The first stent is positioned in the proximal part of the

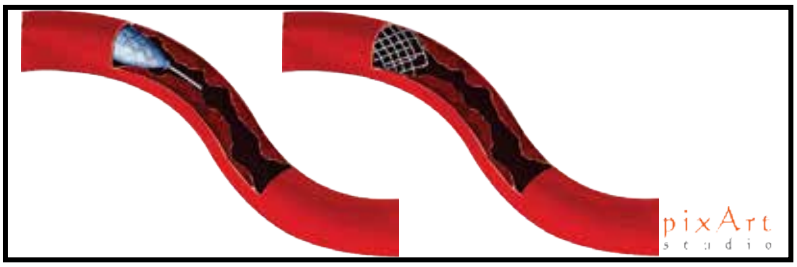

Figure 3a. Sandwich technique - proximal stent implantation

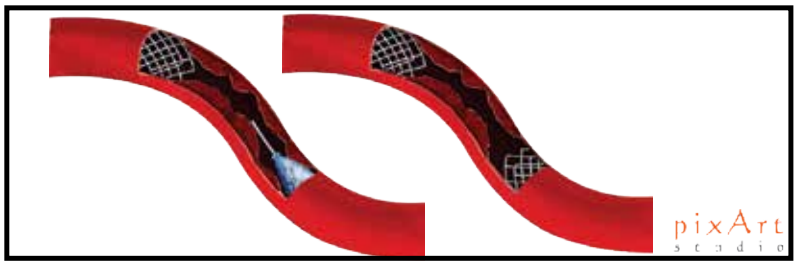

Figure 3b. Sandwich technique - distal stent implantation

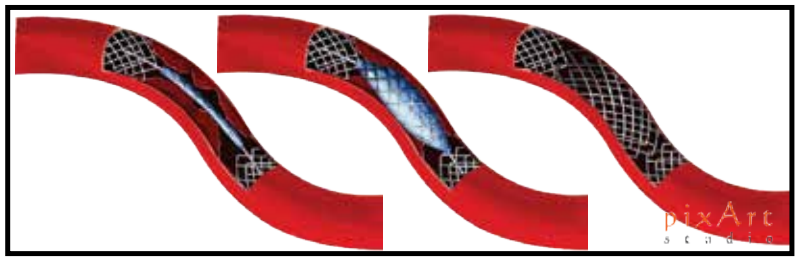

Figure 3c. Sandwich technique - middle stent implantation

Figure 4. PCI with Cutting Balloon

artery, with at least 5-10mm of the stent overlapping the lesion onto the healthy part of the artery (Figure 3a.). This stent localizes the hematoma propagation towards the proximal part of the artery. The second stent is positioned in the distal part of the artery, with 5-10 mm of the stent extending beyond the lesion into the healthy part of the artery (Figure 3b.). This stent isolates the hematoma and prevents its propagation into the distal part of the artery. The third stent is positioned in the central part of the lesion, overlapping with both the proximal and distal stents (Figure 3c.).

3. PCI with Cutting Balloon - in the case of patients with SCAD Type 3, a cutting balloon is positioned at the center of the lesion, while in patients with SCAD Type 2, it is necessary for the cutting balloon to be positioned and expanded at 2 or 3 sites. A cutting balloon with a diameter no greater than 2mm is used and expanded with no more than 2-4 atmospheres. This minimally invasive approach fenestrate the vessel's intima, facilitates drainage of the hematoma into the vessel lumen, and reduces the risk of periprocedural complications on the vessel wall. After the cutting balloon is expanded and an adequate TIMI flow is achieved, the procedure can be terminated or continued with stent implantation (Figure 4.). There is a group of authors who suggest the use of bioresorbable scaffold stents for this purpose (11). This recommendation may be justified given that we know SCAD resolves spontaneously within a few months, and bioresorbable stents completely degrade in about 2 years. After this period, a healthy vessel remains without a metallic stent.

Coronary angiography/PCI in SCAD patients has its specificities:

- Femoral access is recommended for SCAD patients since radial artery dissection is three times more common with radial access[12],
- Manual contrast injection is recommended, avoiding the use of contrast pumps whenever possible.
- If dilation or expansion of the stent is performed near a significant side branch, it is necessary to protect the side branch with an additional coronary wire in case of hematoma propagation towards the side branch.
- "Soft" atraumatic coronary wires should be used.

• After a successful PCI procedure with stent implantation over the hematoma, repeat coronary angiography is recommended after one month, expecting complete hematoma resorption. Assessment with intravascular imaging (IVUS, OCT) is necessary to determine if there is free space between the coronary artery wall and the stent, with eventual post-dilation of the stent using a balloon to correct any stent malposition that may occur after hematoma resorption.

Coronary artery bypass grafting

According to guidelines for treatment of ACS without ST elevation, coronary artery bypass grafting (CABG) can be performed in specific cases (1). This primarily applies to patients with extensive dissections, dissections of the left main, or after unsuccessful PCI attempts (inability to pass the wire through the true lumen of the coronary artery) (11). The issue with this treatment method lies in the pathophysiological characteristic of SCAD, where in 95% of cases, the dissected artery spontaneously recovers within 1-3 months. After artery recovery, there is competitive flow through the coronary artery, either through venous or arterial grafts. Therefore, there is a risk of graft thrombosis after several months. The experiences of SCAD patients treated with bypass surgery are limited to individual cases.

Medical therapy

1. LMWH and UFH
As noted, patients with clinical and ECG presentations of ACS before coronary angiography routinely receive LMWH. After coronary angiography and the diagnosis of SCAD, further use of any form of heparin is absolutely contraindicated during the course of patient treatment.

2. DAPT (Acetylsalicylic acid and Clopidogrel)
The DAPT therapeutic approach differs for SCAD patients since the underlying pathology is a hematoma within the vessel wall rather than atherosclerotic disease. Based on the TIMI flow on coronary angiography, a decision is made whether the patient will undergo PCI or continue with conservative treatment. The difference lies in the DAPT therapy, which involves the use of ASA in combination only with Clopidogrel. Ticagrelor and Prasugrel, being more potent, are not indicated for this patient population due to a higher risk of new intramural bleeding within the vessel. DAPT with Clopidogrel is recommended for all SCAD patients at discharge, with differences in duration: for patients with SCAD and after PCI, DAPT therapy is recommended for 12 months, while for all others, DAPT therapy lasts for 1 month, followed by ASA alone. In everyday clinical practice, differences are observed compared to the recommended therapy. In the DISCO registry, 66% of patients used DAPT for longer than one month, even without undergoing PCI procedures, leading to twice the frequency of MACE compared to the group of patients using only one drug (13). In the Vancouver registry, 83.1% of patients were treated without PCI procedures. At discharge from the hospital, 62.2% of patients had DAPT, and in 25.4% of cases, this treatment continued after 3 years of follow-up.(14)

3. Statins
The use of statins is not indicated for all SCAD patients since the cause of this disease is not the presence of atherosclerotic plaque. Therefore, statins are only given to selected patients. Statins are indicated for patients with proven hyperlipoproteinemia, type II diabetes mellitus, or previously known atherosclerotic disease. According to the Can SCAD registry, 346 out of 750 patients, or 46.1%, had these indications for the safe long-term use of statins. However, a review of registries reflecting daily clinical practice shows that the majority of patients receive statins after hospital treatment. In the DISCO registry, 70% of patients received statins at discharge, and interestingly, statin use depended on antiplatelet therapy. In the group that received DAPT at discharge, 81.8% also received statins, while in patients who received only one antiplatelet drug, 50.7% received statins (13). In the Vancouver registry, statins were given to only 54.2% of patients at discharge, which is approximately the number of patients with a real indication for their use, but in 36.7% of cases, statins continued to be used after 3 years of therapy (14).

4. Beta-blockers
Beta-blockers are indicated for all SCAD patients with heart failure and reduced ejection fraction. They have been observed to have a favorable effect even in patients with preserved ejection fraction due to reducing shear stress on the vessel wall, thereby reducing the risk of SCAD propagation (a mechanism similar to aortic dissection). Beta-blockers also have a favorable effect due to reducing heart rate, thereby having an anti-arrhythmic effect, and also in lowering blood pressure. There is evidence that beta-blockers significantly reduce the risk of recurrent events in SCAD patients (13). A limitation for the use of beta-blockers may be that SCAD patients are usually young women who often have hypotension and may not tolerate the medication well. In the Vancouver registry, 83% of patients had beta-blockers at discharge, and 80.4% continued their use after 3 years of follow-up (12).

5. ACE Inhibitors
ACE inhibitors should be used in all SCAD patients in the presence of heart failure with reduced ejection fraction. In the Vancouver registry, 57.6% of patients had ACEIs in their therapy at discharge, and 49.2% continued their use after 3 years of follow-up. In the same registry, a very small number of patients had heart failure during hospital treatment or during the follow-up period. The justification for the use of ACEIs can only be if they were used in the treatment of arterial hypertension, which was present in 32.1% of SCAD patients (14).

Conclusion

Patients with spontaneous coronary artery dissection are part of the population of patients who clinically present with acute coronary syndrome. The pathophys-

iological mechanism in SCAD patients is not atherosclerotic disease but an intramural hematoma in the coronary artery wall. Medical treatment of SCAD patients is different from that of patients with an atherosclerotic form of acute coronary syndrome. Dual antiplatelet therapy is administered for a duration of 12 months only in the group of patients undergoing PCI, while others are taking it for a duration of 1 month. Statins, ACE inhibitors are given only to selected patients. It is recommended that beta-blocker therapy be applied to all patients who can tolerate the medication.

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Sažetak

Terapija pacijenata sa spontanom disekcijom koronarnih arterija - da li ima razlike?

Vladimir Mitov[1], Aleksandar Jolić[1], Dragana Adamović[1], Milan M. Nikolić[1], Svetlana Apostolović[2], Vladimir Zdravković[3], Milenko Čanković[4], Zlatko Mehmedbegović[5], Bojan Maričić[2], Aleksandra Đoković[6], Gordana Krljanac[5], Ivan Ilić[7]

[1]Odeljenje invazivne kardiologije, Zdravstveni centar Zaječar, [2]Klinika za kardiologiju, KC Niš, [3]Klinika za kardiologiju KC Kragujevac, [4]Klinika za kardiologiju, Institut za kardiovaskularne bolesti Vojvodine, Sremska Kamenica, [5]Klinika za kardiologiju, Univerzitetski Klinički centar Srbije, Beograd, [6]Odsek Kardiologije, Kliničko bolnički centar Bežanijska Kosa, Beograd, [7]Odsek kardiologije, Institut za kardiovaskularne volesti Dedinje, Beograd

Pacijenti sa sponatnom disekcijom koronarne arterije (SCAD) se od prvog medicinkog kontakta do koronarografije ne razlikuju od bilo kojih pacijenata sa akutnim koronarnim sindromom (AKS), isti je dijagnostički pristup, ista je terapija. Tek na osnovu nalaza koronarografje identifikujemo SCAD pacijente. Možda može pomoći „Model SCAD pacijenta". Analizom registara sa SCAD pacijentima uočavamo da su 90% žene, i to 87-95% starosti 44-53 godine života, da mogu imati ličnu ili porodinu anamezu o postojanju fibromuskularne displazije, da može biti u korelaciji sa upotrebom hormonske terapije ili zbog promene hormonskog statusa za vreme trudnoće. Na osnovu ovih podataka možemo uočiti model SCAD pacijenata gde imamo mladu ženu, što nam može sugerisati da se radi o SCAD pacijentu sa kliničkom prezentacijom AKS. Ovo je skoro izvesno ukoliko imamo mladu ženu u trudnoći, ili u postpartalnom periodu sa AKS. S obzirom da je upotreba fibrinolitičke terapije kod SCAD pacijenata apsolutno kontraindikovana, a da se dijagnoza SCAD postavlja upravo na koronarografiji, razmotriti mogućnost da pacijenti sa mogućim SCAD modelom možda ne treba da dobijaju fibrinolitičku terapiju, već da se transportuju u dostupni PCI centar. PCI je indikovana kod pacijenata sa SCAD u slučaju TIMI 0 protoka na koronarografiji, kod značajne redukcije protoka na krvnom sudu, ako perzistira bol u grudima, kod hemodinamski nestabilnih pacijenata. Patofiziološka osnova kod ovih pacijenata nije aterosklerotska bolest već intramuralni hematom u zidu koronarne arterije. Medikamentno lečenje SCAD pacijenata nije isto kao kod pacijenata sa aterosklerozom. Dvojna antitrombocitna terapija se daje u trajanju od 12 meseci samo u grupi pacijenata sa PCI dok ostali imaju u trajanju od 1 meseca. Statini, ACEI daju se samo kod selektovanih pacijenata. Preporučuje se da hronična terapija beta blokatorima bude primenjena kod svih pacijenata koji lek mogu da tolerišu.

***Ključne re**či: sponatna disekciaj koronarne arterije, akutni koronarni sindrom, terapija*