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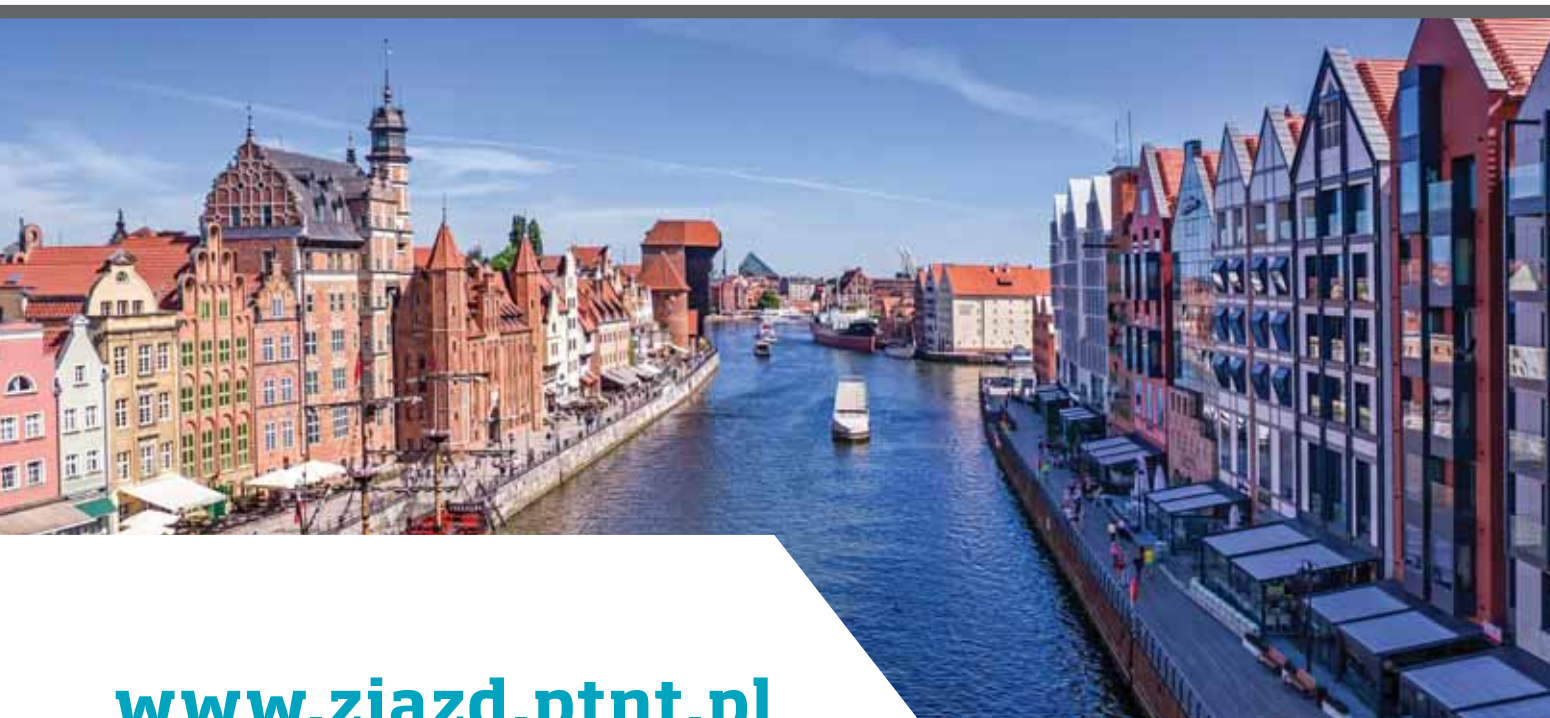
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# Commentary to the guidelines: “Guidelines on the prevention and treatment of venous thromboembolism in cancer patients treated surgically, including patients under 18 years of age”

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Patients with malignant tumors are at high risk of developing venous thromboembolism (VTE), i.e. deep vein thrombosis and/or pulmonary embolism. Thrombotic events are the second most common cause of death of oncological patients after death due to cancer itself [1]. Therefore, appropriate treatment, i.e. appropriate medication administered for an appropriate period is crucial for the survival of patients with VTE and cancer.

We are witnessing a major shift in the VTE treatment regimens disease as compared to the guidelines published in 2012 and 2016 [2] dictating the use of rivaroxaban and other direct oral anticoagulants (DOACs) in the treatment of deep limb thrombosis and pulmonary embolism in patients without cancer while recommending low molecular weight heparin (LMWH) as the medication of choice in patients with cancer-associated thrombosis (CAT). Cancer-associated venous thromboembolism is thromboembolism occurring in a patient with active malignancy or as the result of oncological treatment. The treatment of VTE in cancer patients is one of the most difficult clinical challenges as delivered simultaneously to the cancer treatment. Oncological therapies often require invasive surgeries, increase the risk of infections, and may lead to thrombocytopenia, consequently increasing the risk of bleeding. In many cancer patients, it is impossible to predict the length of the period in which the risk of VTE will be significantly increased in a particular patient.

In patients requiring long-term anticoagulation treatment, periodic assessment of the risk of bleeding

complications as well as the risk of VTE recurrence (treatment benefit vs. risk of bleeding) is required.

The current guidance as discussed in this commentary highlights the fact that the choice of drugs to be used in VTE treatment no longer depends on whether or not the patient’s thrombosis is associated with cancer DOACs, albeit only xabans are now considered to be the first-line drugs in all cancer patients with thrombotic complications. In short, all cancer patients excluding pregnant women and other contraindications specific to the selected direct factor Xa inhibitor may be treated with rivaroxaban, apixaban, or edoxaban just as non-cancer patients. The shift can be seen in the documents published by the American Society of Clinical Oncology (ASCO 2019), National Comprehensive Cancer Network (NCCN 2018), International Society on Thrombosis and Hemostasis (ISTH 2018 and 2019), European Cardiology Society/European Respiratory Society (2019), as well as the most recent, document published in 2021 by the American Society of Hematology [3–8].

Most recommendations regarding anticoagulation therapy assume that the treatment is in line with patient’s preference regarding the objective of care and life expectancy. Venous thromboembolism often develops in the natural history of cancer. Cancer management, particularly interventional treatment, may also increase the risk of this complication. Surgical procedures affect the risk of thrombosis in a multifactorial fashion; factors of importance include intraprocedural damage to the tissues, periprocedural immobilization, blood and plasma replacement, positive pressure ven-

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tilation, presence of potential infectious foci, or central venous catheters. Therefore, when treating VTE in patients with malignant tumors one must take into account the higher rates of thrombotic recurrence as well as the high risk of bleeding complications in this group of patients.

In the light of current knowledge, it is also important to take into account the presence of other risk factors, particularly those related to concomitant diseases and clinical conditions contributing to the increased risk of VTE (obesity, prolonged immobilization, varicose veins, hormonal therapy, history of stroke with paresis, history of VTE episodes etc.). Notably, conditions which have been until recently considered to be within the domain of non-interventional disciplines, such as exacerbations of chronic circulatory failure and inflammatory bowel diseases, are now considered the factors for VTE. Other potential risk factors, such as postoperative infection – intraabdominal abscess or other surgical site infection following a colorectal procedure – as well as any other acute infection, should also be taken into account. All of the above-mentioned conditions are very important in the context of the choice of a particular anticoagulant for VTE therapy, with limitations associated with renal and hepatic function and drug-drug interactions being considered.

Rivaroxaban is one of the most commonly used non-vitamin K agonist oral anticoagulants and the first xaban to feature an indication for use in oncological patients in its summary of product characteristics. Thanks to numerous large-scale clinical trials conducted in diverse patient groups, DOACs have become the first-line treatment, particularly in patients in whom anticoagulant therapy is being initiated for the first time [9–11].

Therefore, our commentary to guidelines on the prevention and treatment of venous thromboembolism in cancer patients undergoing surgical treatment, will be based on EBM-based data not included or included only to a small extent in the above document. The importance of these data consists in that they confirm the role of this medication in CAT treatment.

In our opinion, the first of the documents of importance is the meta-analysis by Yang et al. [12]. The objective of this meta-analysis was to compare direct Xa inhibitors with LMWH in the treatment of VTE in patients with cancer based on data from all available randomized and retrospective cohort studies encompassing a population of > 4000 patients. Direct Xa inhibitors were shown to be associated with a 33% reduction of VTE recurrence in cancer patients as compared to LMWH. No significant difference was observed between the two treatments as regards the occurrence of major bleeding. Subgroup analyses revealed that only

rivaroxaban was associated with a reduction in the rate of VTE recurrence. The previous guidelines recommended direct Xa inhibitors being used to prevent VTE recurrence on the basis of evidence obtained from patients without malignant tumors, and that is what has changed since that time. Bleeding is the main adverse effect of direct Xa inhibitors. In their meta-analysis, Yang et al. [12] demonstrated no significant difference in the incidence of major bleeding between the use of direct Xa inhibitors and LMWH. The meta-analysis suggests that direct Xa inhibitors outperform LMWH in terms of reducing VET recurrence rates in cancer patients without putting these patients at high risk of major bleeding. Another valuable paper regarding the use of rivaroxaban in a group of CAT patients was published by Streiff et al. [13].

In 2013–2015, the team analyzed the cases of newly diagnosed cancer patients in whom the treatment with rivaroxaban, LMWH, or warfarin was initiated. A total of 2428 patients (rivaroxaban: 707; LMWH: 660; warfarin: 1061) were included in the analysis. A trend toward lower VTE recurrence rates was observed in rivaroxaban users compared to LMWH users after 6 months (13.2% vs. 17.1%;  $p = 0.060$ ); the difference was even greater after 12 months (16.5% vs. 22.2%;  $p = 0.030$ ) (HR [hazard ratio]: 0.72; 95% CI [confidence interval]: 0.52–0.95;  $p = 0.024$ ). The VTE recurrence rates in rivaroxaban users were also lower when compared to those in warfarin users after 6 months (13.2% vs. 17.5%;  $p = 0.014$ ) and 12 months (15.7% vs. 19.9%;  $p = 0.017$ ; HR: 0.74; 95% CI: 0.56–0.96;  $p = 0.028$ ). The incidence of severe bleeding was similar in all groups. The results of the analysis by Streiff et al. [13] suggest that cancer patients with VTE receiving rivaroxaban are at a significantly lower risk of recurrence and a similar risk of bleeding than patients treated with LMWH or warfarin.

Real-world data are very important as they may sometimes contradict the results from randomized design studies; such data were published by an expert in CAT and author of numerous guidelines — Khorana et al. [14]. In this publication, Medicare patients' data were compared in terms of the efficacy and risk of severe bleeding associated with the use of anticoagulation (rivaroxaban, warfarin, LMWH) in the group of patients with primary CAT. VTE relapses were defined as hospitalizations due to the primary diagnosis of VTE  $\geq 7$  days after the first incident of VTE. A total of 12,457 patients (LMWH = 4313; warfarin = 4774; rivaroxaban = 3,370) were included in the study. The baseline demographic and clinical characteristics of the enrolled patients were well balanced. The average age of patients ranged from 61.3 to 63.6 years. The median follow-up time for the LMWH treatment group was

shorter than that for rivaroxaban (6.8 vs. 8.3 months;  $p < 0.001$ ) and warfarin (7.4 vs. 9.8 months;  $p < 0.001$ ). Notably, the treatment time was significantly shorter for heparins which may also speak in favor of DOACs. The VTE recurrence rates in rivaroxaban users was significantly lower than in warfarin users after 6 months (8.7% vs. 11.7%;  $p = 0.003$ ) and 12 months (11.9% vs. 14.7%;  $p = 0.006$ ); HR: 0.83;  $p = 0.010$ . The incidence of severe bleeding was similar in rivaroxaban and LMWH users after 3 months (3.2% vs. 3.5%;  $p = 0.592$ ) and 6 months (4.4% vs. 4.9%;  $p = 0.438$ ); HR: 0.91;  $p = 0.455$ ). The VTE recurrence rates in patients receiving rivaroxaban and warfarin was similar after 6 months (8.2% vs. 8.8%;  $p = 0.530$ ) and 12 months (11.3% vs. 11.6%;  $p = 0.675$ ; HR: 0.95;  $p = 0.456$ ). The incidence of severe bleeding among patients using rivaroxaban and warfarin was similar after 3 months (3.2% vs. 2.8%;  $p = 0.199$ ) and 6 months (4.2% vs. 3.8%;  $p = 0.362$ ); (HR: 1.08;  $p = 0.500$ ). A surprising fact consisted is the significantly lower VTE recurrence rates in patients receiving warfarin as compared to patients on LMWH after 6 months (10.2% vs. 12.4%;  $p = 0.006$ ) and 12 months (13.3% vs. 15.3%;  $p = 0.011$ ), although the overall recurrence rates did not differ significantly between the two groups in the entire follow-up period (HR: 0.91;  $p = 0.103$ ). The conclusions from the aforementioned study are very practical; importantly, they were derived from regular clinical practice. In this large group of cancer patients treated for VTE, the treatment times were shorter in patients treated with LMWH than in those receiving oral medications. Rivaroxaban was associated with significantly lower VTE recurrence rates and major bleeding rates were similar for all study groups. Although in previous clinical trials carried out in CAT patients LMWH was shown to be associated with lower VTE recurrence rates as compared to warfarin, the much shorter duration of LMWH treatment (and thus its much lower efficacy in recurrence prevention) in real world settings may explain the lack of comparable efficacies shown in the analysis.

Concluding our commentary to the 2021 Polish guidelines on CAT treatment, we dare say that the era of warfarin and LMWH use has been superseded by the DOAC era. For oncological patients, only xabans can be taken into consideration; among these, rivaroxaban stands out in terms of large study populations and recommendations from recognized bodies.

### Conflict of interest

Zbigniew Krasinski: Yes. Educational lectures: Bayer, Boehringer Ingelheim, Sanofi, Aspen, Pfizer, Alpha Sigma, COOK, GORE, Pierre Fabre, ADAMED.  
Beata Begier-Krasinska: No.

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# The phenomenon of stent-graft “shortening” during implantation of endovascular stent-graft in an abdominal aortic aneurysm in cases involving significant tortuosity of the aorta and iliac arteries

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## Abstract

**Introduction:** One of the main problems with the implantation of stent-graft (STG) in the abdominal aortic aneurysm (AAA) remains its proper fit. Minor differences in distances from the relevant structures can result in life-threatening complications. This article aims to show the problem of aortic stent-graft shortening during implantation. This occurs in the case of significant tortuosity of the abdominal aorta vessels and iliac arteries. Our study has found a significant correlation between vessel tortuosity and erroneous results of preoperative sizing (using the centerline). The new measurement system developed (along long curves) seems to correlate better with intraoperative images.

**Material and methods:** The study involved the evaluation of 70 patients sized classically and with the use of the described technique, and then operated on with the EVAR technique. In all patients, stent-grafts were sized classically (using the central lumen line) and along the curvature line of the sized vessels. The dimensions of the stent-graft were selected according to the standard method (classical sizing), and the fit of the STG in relation to the calibrated catheter (“pigtail”), and the final postoperative result was considered to be the final result. There were 44 men (62,8%) and 26 women (37,2 %) in the study group. The mean age of patients was 74 years. Eighty-nine percent of patients were classified as NYHA (Class I-II) and 11 % of patients as NYHA Class III.

**Results:** Average measurement of the aorta and iliac arteries using the centerline was 201.8 mm, and average measurement based on the curvature of vessels was 222.2 mm. Average measurement using calibrated catheter was 218.1 mm. The results of the analysis showed significant differences between the measurements (centerline and long curvature of vessel):  $Z = 7.17$ ;  $p < 0.001$ ;  $r = 0.87$ .

**Conclusions:** The measurement made along the long curves is more accurate than the measurement made with the centerline. The measurement made with the centerline is underestimated (it indicates a smaller value than the actual measurement).

**Key words:** abdominal aortic aneurysm AAA, EVAR management, measurement of EVAR device, kinking (tortuosity) of iliac arteries in AAA

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## Introduction

Techniques of surgery for abdominal aortic aneurysms have changed dramatically over the past 15 years. The traditional technique of aortic prosthesis implantation has gradually become limited due to the development and expansion of indications for endovascular surgery to stent-graft implantation.

Graft implantation into the abdominal aorta is a relatively simple and minimally invasive operation. However, the prevailing problem remains proper stent-graft fitting, with particular consideration of anatomical problems related to the course of the abdominal aorta and the location of its important branches (e.g. renal arteries, visceral trunk, superior mesenteric artery). The proper selection (sizing) of the graft is crucial in the process of endovascular treatment of AAA. Small differences in the distances to relevant structures may result in life-threatening complications (e.g. insufficiently long “aortic neck”, excessively long iliac branches which may cut off the internal iliac branch, and others).

The preoperative evaluation to match the stent-graft to the anatomy of the aneurysm is based on imaging studies, mainly computed tomography or, less frequently, vascular magnetic resonance imaging. Detailed anatomical sizing and selection of equipment are carried out with the help of specialized computer programs that allow for graphic processing and spatial reconstruction of abdominal organs. The most useful feature is the ability to draw a centerline for the vessels under evaluation and determine the precise dimensions of the aneurysm [1–3].

Such measurements are taken preoperatively to select the equipment used for the operation. It is necessary to take into account not only the width of the vessels at particular locations but also their length. The correct sizing and the subsequent selection of equipment based on the obtained measurements is the prerequisite to avoiding some postoperative complications, e.g. leakage into the aneurysm sac, undesirable covering of arterial branches from the aorta or iliac arteries, displacement of stent-graft elements, or thrombosis of the prosthesis [4–6].

One of the anatomical phenomena occurring in a significant proportion of patients during the process of formation and enlargement of aneurysms of the abdominal aorta and iliac arteries is the tortuosity of these vessels.

When the examined vessels are kinked or coiled, the measurement using the centerline may not reflect the actual length of the vessel that needs to be covered with the stent-graft because the stent-graft material

must fit tightly to the curvature of a given vessel. This may cause the intraoperative “shortening” of the stent-graft, which, in turn, may result in the distal end of the stent-graft after implantation being closer than planned preoperatively.

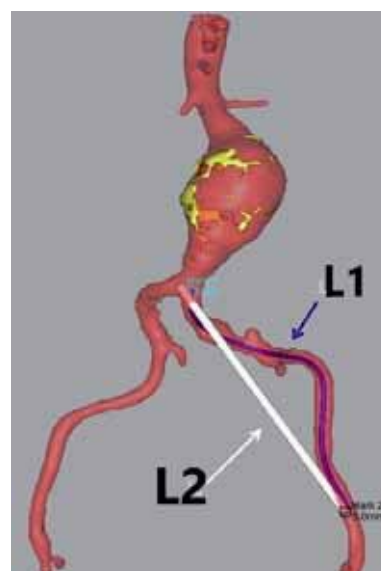
The shortening of stent-graft length in tortuous vessels has been described in reports of earlier studies. Lee et al. [3] described stent-graft shortening by more than 15 mm in patients with severe aortic and iliac vessel tortuosity. Based on this report, the phenomenon of stent-graft shortening and the mechanism of complications, such as internal iliac artery coverage or leakage resulting from insufficient distal landing zone coverage, can be better understood.

The aim of the study included:

1. To compare the accuracy of the two methods used to size STGs in patients with AAA: the traditional, commonly used, central axis-based sizing and the measurement based on vessel curvature.
2. To evaluate the usefulness of the method of sizing based on the curvature of vessels, especially in patients with tortuosity of the aorta and iliac arteries, as a method complementary to the one previously used.

## Material and methods

Seventy patients with abdominal aortic and possibly iliac artery aneurysms who underwent stent-graft surgery were enrolled in the prospective study. In all patients, the aortic tortuosity index (ATI) and iliac artery index (IAI) were calculated, and the obtained results were used to analyze the results of vessel tortuosity measurements with the use of both methods (Fig. 1).



**Figure 1.** Calculating the aortic tortuosity index: L1 — length of the central line, L2 — the distance between the end and the beginning of the measured artery. Curvature index = L1/L2

To achieve the objectives, two sizings of the aorta were used for STG selection in all patients:

1. The standard central axis-based method.
2. The assessment method based on the curvature of the vessel edge.

The findings were compared against intraoperative evaluation with a calibrated “pig-tail” catheter.

A comparative scheme of the classic technique of measuring aortic aneurysm length (Fig. 2A) versus the technique including the ATI (Fig. 2B).

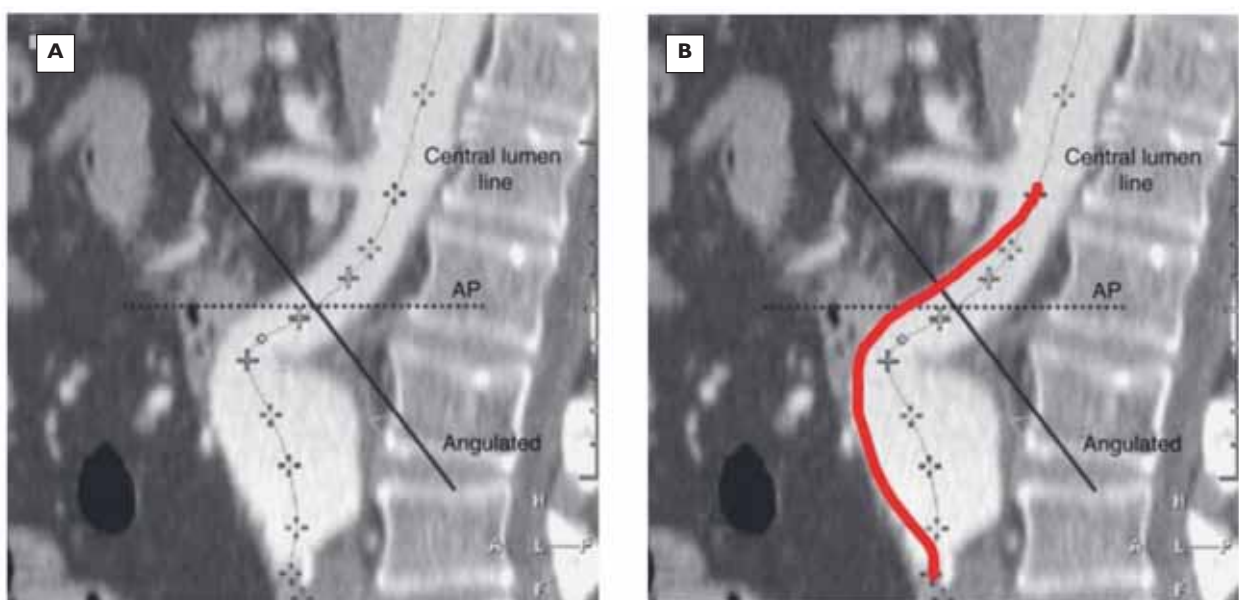
Both groups of patients underwent surgical implantation of a nitinol, polyester-coated, multiple overlapping stent-graft. Preoperative angio-CT examinations of the aorta and iliac arteries were conducted with the use of Endosize computer software and after carrying out anatomical measurements of the aneurysms, appropriate stent-graft components were selected according to the manufacturer’s recommendations. In each patient, the actual vessel length was additionally assessed intraoperatively with the use of calibrated catheters and on this basis, irrespective of earlier calculations, in case of discrepancies, the length of iliac stent-graft extensions was finally adjusted.

Correct stent-graft sizing confirmed by arteriography after stent-graft implantation was considered the primary endpoint. To enhance the accuracy of the evaluation of stent-graft sizing (arteriography), it is advisable to carry out an additional intraoperative verification with the use of a calibrated catheter to have a comparison with the measurements obtained preoperatively.

To answer the research questions and test the hypotheses, statistical analyses were performed using the IBM SPSS Statistics package version 25. The software was used to analyze basic descriptive statistics. Then, the Wilcoxon signed-rank test was used to compare the differences between centerline measurements and outer curvature measurements with the actual artery length. Correlation analysis was used to determine the relationship between the tortuosity index and the difference between the actual length of the artery and its measurement with the centerline. The prediction model for the difference based on the tortuosity index was then checked using linear regression. The value of  $\alpha = 0.05$  was used as the significance level for the interpretation of the analyses.

## Results

The outer curvature measurement was found to be more accurate than the measurement along the central axis. The results of the analysis showed significant differences between the measurements:  $Z = 7.17$ ;  $p < 0.001$ ;  $r = 0.87$ . The mean difference for the centerline measurement compared with arteriography was  $M = -16.31$  ( $SD = 15.08$ ), whereas the difference for the outer curvature measurement was  $M = 4.10$  ( $SD = 2.79$ ). The outer curvature measurement is, therefore, more accurate than the centerline measurement. The centerline measurement is underestimated (it indicates a lower value than the actual measurement), while the outer curvature measurement is overestimated (it



**Figure 2 A** — the classical technique for measuring aortic aneurysm length; **B** — the technique for measuring aortic aneurysm length with the ATI

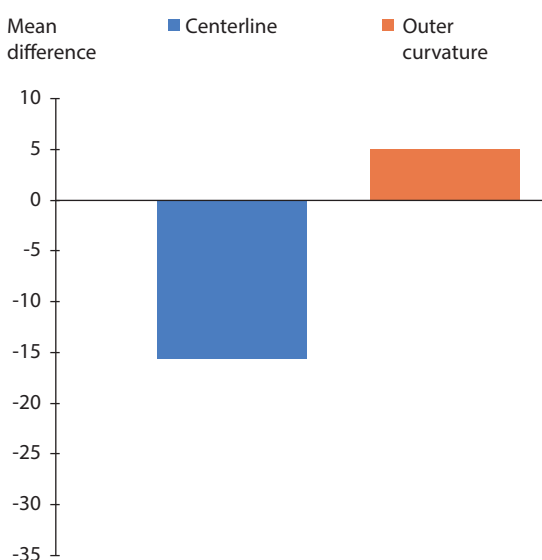
indicates a higher value than the actual measurement). The differences between the measurements are illustrated in Figure 3.

## Discussion

The mechanism of stent-graft “shortening” is related not only to the anatomy of the aneurysm but also to its structure. The metal skeleton is covered with material in such a way that it forms rings with gaps between them, in which there is only the stent-graft material. On the one hand, it enables the stent-graft element to adapt to the curvature of the vessel during implantation; on the other hand, it allows the metal elements of the prosthesis to come closer together or even overlap, which is responsible for its physical “shortening” in relation to the long axis of the vessel (Fig. 4).

Our study shows that the greater the angle of vessel kinking and the greater the number of kinks in the vessel, the more pronounced is the phenomenon of shortening of the prosthetic component. This observation coincides with the results obtained by other researchers [1–3].

This study shows a statistically significant difference between preoperative length assessment and intraoperative actual stent-graft length needed to cover the planned vessels to achieve the desired seal. The higher the value of the tortuosity index, the higher the difference between the centerline measurement and the actual length. Thus, in patients with an index value below 1.3, the differences in length measurements do



**Figure 3.** Mean and standard deviation for the differences in centerline and outer curvature measurements versus actual measurement



**Figure 4.** Stent-graft in a straight and tortuous vessel

not exceed 10%; with the index above that value, they may quickly reach 20%.

In practice, intra-implantation shortening of the stent-graft by approximately 2–3 cm was observed in patients with the highest tortuosity index. Taking into account the structure of the stent-graft, the 2–3 cm length is equivalent to two nitinol rings, which, according to the manufacturer’s recommendations, are the minimum length needed to properly seal the stent-graft termination site [1, 2]. At the same time, the study shows that in patients with a low tortuosity index, there is no shortening of the stent-graft and the preoperative length assessment coincides with the intraoperative assessment.

Moreover, like other authors, we have observed a decrease in vessel tortuosity after stent-graft implantation. The reason for this phenomenon is the stiffness of the metal components of the implanted stent-graft, which causes the vessels to “straighten” in most patients. This may explain why there is a need to implant unplanned iliac extensions of the stent-graft only in some patients.

In practice, shortening of the stent-graft during implantation in patients with significant vascular tortuosity means the necessity to prepare preoperatively different lengths of iliac extensions. In addition to preparing for unplanned implantation of another extension, it may also entail adding another element if coverage of



the planned vessel segment fails the first time. This increases the cost of surgery and the number of steps, which results in its prolongation. Nowadays stent-graft manufacturers offer ready-made elements of various lengths, and elements ordered individually cannot be used for another patient. Therefore, in patients with a large tortuosity of vessels, if we have a selection of various extension lengths, we often opt for extensions of a longer length than suggested by our measurements. Most often, however, while preparing for the operation, we order different lengths of extensions, and during the implantation, depending on the vessel's susceptibility to straightening under the influence of the stent-graft's rigid elements, we decide on the length of the implanted extension.







### Conflict of interest

None.

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# Prevalence and impact of metabolic syndrome on outcomes of acute coronary syndrome patients in two different countries

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## Abstract

**Introduction:** This study aimed to ascertain the prevalence of metabolic syndrome (MetS) in patients from Hungary and Iraq, suffering from acute coronary syndrome (ACS) and investigate the effects of MetS on hospital outcomes, in particular mortality and its relation to differences in patients' baseline characteristics.

**Material and methods:** A prospective cohort study was conducted in two cardiac centers between May 2018 and May 2019. It included 164 consecutive ACS patients: 64 patients from the Cardiac Clinic in Pécs, Hungary and 100 patients from Al Nassiryah Heart Center, Iraq. Baseline characteristics, clinical management, and in-hospital and 30-day post-discharge outcomes were recorded.

**Results:** Prevalence of metabolic syndrome among ACS patients in Iraq<sup>?</sup> was not significantly higher than in Hungary (25.0% vs 34.1%;  $P = 0.306$ ). There were no significant differences in age between those with and without MetS (64.2 vs 63.3 years;  $P = 0.394$ ). MetS was associated with a higher median BMI (28.0 vs 23.7 kg/m<sup>2</sup>;  $P < 0.001$ ), hyperlipidemia (37.8% vs 12.8%;  $P < 0.001$ ), hypertension (48.8% vs 27.4%;  $P = 0.024$ ), high cholesterol (5.4 vs 4.1 mmol/L;  $P < 0.001$ ), high LDL-C (3.5 vs 2.6 mmol/L;  $P < 0.001$ ), and high triglycerides (1.4 vs 1.1 mmol/L;  $P < 0.001$ ). MetS was associated with a higher risk of out hospital re-infarction (12.8% vs 3.7%;  $P = 0.031$ ) and MACE (17.7% and 6.1%;  $P = 0.027$ ).

**Conclusions:** Current study did not show any significant difference in the incidence of MetS between ACS patients in the two countries. But patients with MetS were significantly more likely to be associated with MACE ( $P = 0.027$ ).

**Key words:** metabolic syndrome, outcomes, acute coronary syndrome, prevalence, major adverse cardiovascular events

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## Introduction

Metabolic Syndrome (MetS) is a cluster of risk factors that includes abdominal obesity, high triglyceride, low high-density lipoprotein cholesterol (HDL-C), raised blood pressure (BP), and raised fasting blood glucose [1–3]. The incidence of metabolic syndrome often parallels obesity and Type 2 diabetes [4]. Metabolic syndrome is a complex pathophysiological state associated with an imbalance of calorie intake and energy expenditure but is also affected by individual genetic/epigenetic makeup, predominance of a sedentary lifestyle, and other factors like quality and composition of food and composition of gut microbes [4]. The incidence can not be reduced by taking any drugs [5], but dietary intervention and regular exercise are essential as the first-line treatment for obese patients with MetS, and the principal rule of every dietary modification is caloric restriction and consequent weight loss. Adherence to the Mediterranean diet has also been shown to decrease the risk of MetS [6, 7].

Studies based on populations at high risk for cardiovascular diseases have shown a very high prevalence of metabolic syndrome. Obesity can be called comorbidity of MetS, but obesity alone is also a risk factor for the incidence of cardiovascular diseases. Obesity induces several cytokines and inflammatory markers which might contribute to adverse cardiovascular outcomes in overweight and obese people [6–11]. The prevalence of MetS among patients with acute coronary syndrome (ACS) varies between 29% and 46%, with a poor in-hospital prognosis. Symptomatic vascular diseases (e.g. coronary artery disease, stroke, or peripheral arterial disease) show that the prevalence of metabolic syndrome is correlated with the extent of vascular damage [12–13]. However, previous research has shown that the presence of metabolic syndrome as a risk factor plays a role in the progression and outcomes, for example, of deep sternal wound infections (DSWI) after CABG operations [14, 15].

Besides MetS the relationship between smoking and cardiovascular risk factors has long been investigated, and a wealth of data was published. Smoking is considered to cause an acutely and chronically accelerated heart rate due to sympathetic stimulation confirmed by numerous research data [16–19]. It is important that other forms of tobacco exposure (chewing, inhalation through water, and secondhand smoke) have also been documented to be important causes of coronary disease worldwide [20].

This study aimed to compare the prevalence of metabolic syndrome in patients from Hungary and Iraq,

suffering from acute coronary syndrome diseases and to examine the effects of metabolic syndrome on hospital outcomes, in particular, death.

## Material and methods

### Study design and population

A prospective cohort study was conducted at two cardiac centers from May 2018 to May 2019. The study included 164 ACS patients: 64 patients from Cardiac Clinic in Pécs, Hungary, and 100 patients from Al-Nasiriyah Heart Center in Iraq. From known conditions of ACS, Troponin T-positive patients with ST-segment elevation and non-ST-segment elevation acute myocardial infarction were studied. ACS diagnosis was based on the guidelines of the European Society of Cardiology (ESC) and the American College of Cardiology/American Heart Association (AHA/ACC) [21, 22]. The study complied with the Declaration of Helsinki of 2003 and was approved by the local ethics committee of the Doctoral School of Health Sciences of the University of Pécs, Hungary. The study was approved by the Regional and Institutional Research Ethics Committee (4511/2016) of the University of Pécs, and all participants gave their informed consent. The study was approved by the Regional and Institutional Research Ethics Committee (4511/2016) of the University of Pécs, and Dhi-Qar health director /Al-Nasiriyah Heart Center. Written consent was obtained from each patient after they were informed clearly about the details of the study. (in the original text before the Dhi-Qar is a “and” conjunction not “in” preposition).

### Data collection

Demographic and other baseline clinical characteristics of the patients along with in-hospital outcomes were evaluated. Outcome parameters evaluated during the hospital stay included in-hospital mortality, recurrent ischemia/re-infarction, heart failure (HF), cardiogenic shock, and major adverse cardiovascular events (MACEs). MACEs were defined as the composite of total death, re-infarction, and stroke. The patients with ACS were stratified into those with and without metabolic syndrome. Metabolic syndrome was defined according to the NCEP ATP III criteria [21, 23–26]. Patients received a diagnosis of metabolic syndrome if they had any 3 of the following 5 criteria: abdominal obesity (waist circumference > 102 cm [> 40 inches] for men and > 88 cm [> 35 inches] for women), high triglyceride levels  $\geq$  150 mg/dL (1.7 mmol/L), reduced or low HDL cholesterol levels < 40 mg/dL (1.04 mmol/L) in men and

< 50 mg/dL (1.30 mmol/L) in women, hyperglycemia (history of diagnosed diabetes mellitus or fasting blood glucose level  $\geq$  110 mg/dL (6.10 mmol/L), and elevated blood pressure (treated hypertension, systolic blood pressure  $\geq$  130 mm Hg, or diastolic blood pressure  $\geq$  85 mm Hg). If patients had only 2 of the following 5 criteria, they were classified as a group without MetS. Patients with acute coronary syndrome have a life-threatening condition, every minute can count on the patient's survival. Because of this, it was not possible to assess abdominal obesity in all cases, instead, we used BMI data to divide patients into 2 groups — patients with MetS and patients without MetS.

### Statistical analysis

Continuous variables are expressed as the mean  $\pm$  SD or median and interquartile range (IQR). Categorical variables are expressed as percentages and frequencies. Differences between groups (metabolic syndrome status, negative/positive) and between the two countries (Iraq and Hungary) were analyzed using the chi-square for the categorical variables and Student's t-test, Fisher's exact test, or the Mann-Whitney U test of continuous variables, based on the normal distribution. Values of  $P < 0.05$  were considered significant. Statistical analyses were conducted using SPSS, version 22.0 (IBM Corporation, USA).

## Results

### Patient demographic and clinical characteristics

The demographic and clinical characteristics of the patients stratified by metabolic syndrome status are summarized in Table 1. The overall prevalence of metabolic syndrome for this population with ACS in Iraq was 34.1% (56 patients) while in Hungary was 25% (41 patients). The mean age of the cohort was  $63.8 \pm 11.9$  years. There was no difference in age between patients with and without metabolic syndrome ( $64.2 \pm 11.5$  y vs  $63.3 \pm 12.6$  y respectively;  $P = 0.394$ ). Most of the admitted patients were males (111; 67.7%). The metabolic syndrome cohort was more likely to be associated with a higher average BMI ( $28.0$  vs  $23.7$  kg/m<sup>2</sup>;  $P < 0.001$ ) and a previous history of hypertension (48.8% vs 27.4%;  $P = 0.024$ ). Hyperlipidemia (37.8% vs 12.8%;  $P < 0.001$ ), excluding the current smoking condition, was low (12.8% vs 16.5%;  $P < 0.01$ ).

Metabolic syndrome was also associated with higher median total cholesterol (5.4 vs 4.1 mmol/L;  $P < 0.001$ ), low-density lipoprotein cholesterol (LDL-

C; 3.5 vs 2.6 mmol/L;  $P < 0.001$ ), and triglycerides (1.4 vs 1.1 mmol/L;  $P < 0.001$ ), except for HDL-C levels were low (0.9 vs 1.2 mmol/L;  $P < 0.001$ ). Ninety-five percent of the participants had at least one criterion for metabolic syndrome. The table also indicates that even though there were no significant differences in the prevalence of metabolic syndrome between Hungarian and Iraqi patients (25.0% vs 34.1%;  $P = 0.306$ ), patients with metabolic syndrome had a higher risk of developing STEMI (29.3% vs 20.1%) and NSTEMI (22.6% vs 12.8%), prior CABG (6.1% vs 3.0%), prior PCI (32.9% vs 17.1%), and renal failure (4.3% vs 3%) (Table 1).

Table 2 shows the prevalence of different types of metabolic syndrome abnormalities in the study cohort stratified by sex and nationality. High blood pressure (83.5%) was the most prevalent abnormality associated with metabolic syndrome; this was followed by high fasting blood glucose (75.3%). Approximately 62.9% of the cohort had increased abdominal obesity while low HDL cholesterol and hypertriglyceridemia were present in 58.8% and 30.9% of the ACS population, respectively. Table 2 also demonstrates that males were associated with a higher percentage of all the metabolic syndrome abnormalities, except high fasting blood glucose and low HDL cholesterol. Moreover, the table shows that Hungarian patients were more likely to be associated with increased abdominal obesity (35.1% vs 27.8%). In contrast, Iraqi patients were more likely to be associated with hypertriglyceridemia (18.6% vs 12.4%), high blood pressure (44.3% vs 39.2%), and high fasting glucose (45.4% vs 29.9%).

Table 3 shows in-hospital and 30-day post-hospital discharge outcomes for ACS patients stratified by metabolic syndrome. The table shows that there were no statistically significant differences between patients with or without metabolic syndrome regarding in-hospital outcomes. However, patients with metabolic syndrome had a higher rate of in-hospital mortality (3.0% vs 1.2%;  $P = 0.499$ ), re-infarction (4.9% vs 3.0%;  $P = 0.855$ ), cardiogenic shock (4.3% vs 1.8%;  $P = 0.471$ ), stroke (1.2% vs 0.0%;  $P = 0.237$ ) and major adverse cardiovascular events (7.9% vs 3.0%;  $P = 0.232$ ). Moreover, the outcomes of hospital discharge after 30 days showed that patients with metabolic syndrome were significantly more likely to be associated with re-infarction (12.8% vs 3.7%;  $P = 0.031$ ) and MACE (17.7% and 6.1%;  $P = 0.027$ ).

Table 4 demonstrates metabolic syndrome and various in-hospital and 30 days post-discharge outcomes in the cohorts in Hungary and Iraq. There were no statistically significant differences between in-hospital and out-



**Table 1.** Demographic, clinical, and lipid characteristics of the acute coronary syndrome cohort stratified by metabolic syndrome

Variables	All patients (n = 164, 100%)	Metabolic syndrome (n = 97, 59.1%)	Without metabolic syndrome (n = 67, 40.9%)	P value
<b>Nationality, n (%)</b>				
Hungary	64 (39.0%)	41 (25.0%)	23 (14.0)	0.306
Iraq	100 (61.0%)	56 (34.1%)	44 (26.8%)	
Age, mean + SD, years	63.8 + 11.9	64.2 + 11.5	63.3 + 12.6	0.394
Male sex, n (%)	111 (67.7%)	60 (36.6%)	51 (31.1%)	0.055
Family history of CAD, n (%)	30 (18.3%)	22 (13.4%)	8 (4.9%)	0.080
BMI, median (IQR), kg/m <sup>2</sup>	26.8 (23.0–31.9)	28.0 (25.8–32.3)	23.7 (22.0–29.0)	0.000
Current smoking, n (%)	48 (29.3%)	21 (12.8%)	27 (16.5%)	0.010
Hypertension, n (%)	125 (76.2%)	80 (48.8%)	45 (27.4%)	0.024
Diabetes mellitus, n (%)	71 (43.3%)	48 (29.3%)	23 (14.0%)	0.054
Hyperlipidemia, n (%)	83 (50.6%)	62 (37.8%)	21 (12.8%)	0.000
Prior MI, n (%)	87 (53.0%)	56 (34.1%)	31 (18.9%)	0.148
Prior PCI, n (%)	82 (50.0%)	54 (32.9%)	28 (17.1%)	0.081
Prior CABG, n (%)	15 (9.1%)	10 (6.1%)	5 (3.0%)	0.534
Renal failure, n (%)	12 (7.3%)	7 (4.3%)	5 (3.0%)	0.953
Ejection Fraction ≤ 30%, n (%)	7 (4.3%)	5 (3.0%)	2 (1.2%)	0.499
<b>Diagnosis, n (%)</b>				
ST-ACS	81 (49.4%)	48 (29.3%)	33 (20.1%)	0.977
NST-ACS	83 (50.6%)	49 (29.9%)	34 (20.7%)	
Cholesterol, median (IQR), mmol/L	4.7 (3.9–5.8)	5.4 (4.4–6.0)	4.1 (3.4–4.7)	0.000
Triglyceride, median (IQR), mmol/L	1.2 (1.0–1.6)	1.4 (1.1–1.7)	1.1 (0.9–1.5)	0.000
LDL-C, median (IQR), mmol/L	3.0 (2.3–4.0)	3.5 (2.6–4.5)	2.6 (2.1–3.1)	0.000
HDL-C, median (IQR), mmol/L	1.0 (0.9–1.3)	0.9 (0.8–1.0)	1.2 (1.0–1.5)	0.000

BMI: body mass index; CAD: coronary artery disease; MI: myocardial infarction; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; LDL: low-density lipoprotein; HDL: high-density lipoprotein; STE-ACS: ST-segment elevation acute coronary syndrome; NSTE-ACS: non-ST-segment elevation acute coronary syndrome

Data are expressed as mean ± SD or median (IQR) for the continuous variables. Data are expressed as n (%) percentages and frequencies for the categorical variables. Analyses were conducted using Pearson's chi-square test, Fisher exact test, Student's t-test, or Wilcoxon-Mann-Whitney test, whenever appropriate

**Table 2.** Prevalence of different types of metabolic syndrome abnormalities of the study cohort stratified by nationality and sex

<b>Type of metabolic syndrome abnormalities, F (%)</b>					
Parameter	Abdominal obesity	Hypertriglyceridemia	Low HDL-C	High blood pressure	High fasting glucose
Total	61 (62.9%)	30 (30.9%)	57 (58.8%)	81 (83.5%)	73 (75.3%)
<b>Nationality</b>					
Hungary	34 (35.1%)	12 (12.4%)	27 (27.8%)	38 (39.2%)	29 (29.9%)
Iraq	27 (27.8%)	18 (18.6%)	30 (30.0%)	43 (44.3%)	44 (45.4%)
<b>Sex</b>					
Male	38 (39.2%)	23 (23.7%)	25 (25.8%)	50 (51.5%)	28 (28.9%)
Female	23 (23.7%)	7 (7.2%)	32 (33.0%)	31 (32.0%)	45 (46.4%)

Note: The 5 metabolic syndrome abnormalities include increased BMI (higher 25 kg/m<sup>2</sup>), high triglyceride levels (of > 150 mg/dL [1.7 mmol/L] or drug treatment), low HDL-cholesterol levels (of < 40 mg/dL [1.0 mmol/L] for men and < 50 mg/dL [1.3 mmol/L] in women or drug treatment), blood pressure (> 130 mm Hg for systolic and/or > 85 mm Hg for diastolic or drug treatment), and blood sugar (> 100 mg/dL [> 5.6 mmol/L] or drug treatment)

**Table 3.** In-hospital and 30-day post-discharge outcomes of the acute coronary syndrome cohort stratified by metabolic syndrome

In-hospital outcomes	Metabolic syndrome (n = 97)	Without metabolic syndrome (n = 67)	P-value
Death	5 (3.0%)	2 (1.2%)	0.499
Re-infraction	8 (4.9%)	5 (3.0%)	0.855
Cardiogenic shock	7 (4.3%)	3 (1.8%)	0.471
Stroke	2 (1.2%)	0 (0.0%)	0.237
MACE (death, re-infraction, and stroke)	13 (7.9%)	5 (3.0%)	0.232
30-day post-discharge outcomes	Metabolic syndrome	Without metabolic syndrome	P-value
Death	7 (4.3%)	4 (2.4%)	0.754
Re-infraction	21 (12.8%)	6 (3.7%)	0.031
Cardiogenic shock	8 (4.9%)	4 (2.4%)	0.582
Stroke	5 (3.1%)	1 (0.6%)	0.215
MACE (death, re-infraction, and stroke)	29 (17.7%)	10 (6.1%)	0.027

Note: Data are expressed as n (%) percentages and frequencies

MACE: major adverse cardiovascular events

**Table 4.** Metabolic syndrome and various in-hospital and 30-day post-discharge outcomes in Iraq and Hungary

In-hospital outcomes	Metabolic syndrome patients		P-value
	Hungary	Iraq	
Death	2 (2.1%)	3 (3.1%)	0.916
Re-infraction	5 (5.2%)	3 (3.1%)	0.227
Cardiogenic shock	3 (3.1%)	4 (4.1%)	0.974
Stroke	0 (0.0%)	2 (2.1%)	0.221
MACE (death, re-infraction, and stroke)	5 (5.2%)	8 (8.2%)	0.765
30-day post-discharge outcomes	Metabolic syndrome patients		P-value
	Hungary	Iraq	
Death	3 (3.1%)	4 (4.1%)	0.974
Re-infraction	7 (7.2%)	14 (14.4%)	0.349
Cardiogenic shock	3 (3.1%)	5 (5.2%)	0.776
Stroke	3 (3.1%)	2 (2.1%)	0.422
MACE (death, re-infraction and stroke)	10 (10.3%)	19 (19.6%)	0.311

Note: Data are expressed as n (%) percentages and frequencies

MACE: major adverse cardiovascular events

hospital events for metabolic syndrome in Hungary and Iraq. However, Hungarian patients had a higher rate of in-hospital re-infraction (5.2% vs 3.1%  $P = 0.227$ ) than Iraqi patients. In contrast, Iraqi patients had a higher rate of in-hospital mortality (3.1% vs 2.1%), cardiogenic shock (4.1% vs 3.1%), stroke (2.1% vs 0.0%), and MACE (8.2% vs 5.2%). Furthermore, Iraqi patients had a higher rate of out-hospital mortality (4.1% vs 3.1%), cardiogenic shock (5.2% vs 3.1%), re-infraction (5.2% vs 3.1%), and MACE (19.6% vs 10.3%) than Hungarian

patients. In contrast, Hungarian patients had a higher rate of out-hospital stroke (3.1% vs 2.1%).

## Discussion

This study is the first to examine the incidence of metabolic syndrome among patients with ACS in Iraq and Hungary by comparing the patient groups in the two countries separately.

### Baseline characters in both countries

Remarkable demographic and clinical differences were found. The patients in Iraq suffered from physical inactivity, a higher prevalence of diabetes, the genetic factor of family history of CAD, and stress. These data are consistent with results proving ACS in Arab/Middle East patients may start when they are about a decade younger than patients in developed countries and Iraq has a higher prevalence of diabetes [27–29].

Ahamad [30] showed that oleuropein is an effective substance molecule in the treatment of metabolic syndrome. It can be found in fruits and oil which are essential components of Mediterranean diets. Oleuropein is reported to have a number of biological activities including antidyslipidemic, antiobesity, antidiabetic, antioxidant, antiatherogenic, antihypertensive, anti-inflammatory, and hepatoprotective properties. The scientific evidence supports the role of oleuropein as a potential agent against metabolic syndrome [30, 31]. Unhealthy lifestyles, like consuming small amounts of extra virgin olive oil instead of more saturated fatty acid, a sedentary lifestyle, too much stress, etc. may cause a higher prevalence of hypertension, dyslipidemia, previous myocardial infarction, and higher BMI in Hungary. Previous research in Hungary has shown that healthy eating and regular exercise are rarely practiced [32, 33]. More than half of overweight and obese patients consider their physical activity and nutrition to be average [34]. According to the 2014 Hungarian Diet and Nutritional Status Survey, the average BMI of men aged 34 to 65 age was 28.9 kg/m<sup>2</sup> (28.1–29.6) and over 65 years of age was 28.9 kg/m<sup>2</sup> (27.9–29.9). The average BMI in women aged 34 to 65 was 28.2 kg/m<sup>2</sup> and in women over 65 years of age was 29.5 kg/m<sup>2</sup> [35]. In contrast with the previous Hungarian survey, the current study shows that the average BMI (26.8 kg/m<sup>2</sup>) of the patients with ACS was lower.

### Comparison of the incidence of MetS

According to a former Iraqi study, the waist circumferences are 99 cm for men, and 97 cm for women [36]. According to the Hungarian Diet and Nutritional Status Survey 2014, the average waist circumference in Hungary was 101 cm for men aged 35–64, 104 cm for over 65 years, 92.1 cm for women aged 35–64, and 97.4 cm for women over 65 years [35]. These average numbers are significantly higher than the metrics identified in the 2007 Iraq study. Despite this, there is no significant difference in the incidence of metabolic syndrome between the two countries in patients with ACS.

Comparing the data of the current study with Farmanfarma (2019) (where the nutritional and lifestyle habits are quite similar to Iraq) it can be found that Iraqi patients with ACS have metabolic syndrome in 56% of cases while in Iran this is 50%, so the results are quite similar also in the general population [37].

### Comparison of outcomes in both countries in patients with or without MetS

Regarding mortality in both countries in hospital and after 30-day follow-up, data show similar results although the complications during hospital admission were higher in Hungary. This difference could have resulted from a higher prevalence of risk factors such as higher age, dyslipidemia, previous MI, hypertension, and a higher average BMI in Hungary than in Iraq. The outcomes 30 days after hospital discharge show that patients with metabolic syndrome were significantly more likely to be associated with re-infarction and MACE. Zeller came in 2005 to similar conclusions to the current research stating that metabolic syndrome worsened the outcome of patients with ACS. Furthermore, the current study indicates that among metabolic syndrome comorbidities, hyperglycemia has the strongest relation to an increased incidence of congestive heart failure in patients with metabolic syndrome and MI [38].

### Conclusions

There was no significant difference in the incidence of metabolic syndrome between ACS patients in the two countries, but there was a higher rate in Iraq. Iraqi patients were more likely to be associated with high fasting glucose (45.4% vs 29.9%). A significant difference was found in the presence of MetS. Patients with metabolic syndrome in our study had a higher BMI rate, a higher LDL cholesterol rate, and a higher rate of fatal outcomes during the hospital stay. A significant majority of the participants met at least one criterion of metabolic syndrome, so it is important to draw further attention to metabolic syndrome not only among ACS patients but also in primary prevention. Studies provided evidence supporting the beneficial role of the traditional Mediterranean diet in preventing diabetes and MetS [6, 7, 31].

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## Conflict of interest

None.

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# Endovascular treatment of false aneurysm of the axillary artery in an obese woman with epilepsy: 5-year follow-up

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## Abstract

False aneurysms of arteries in upper extremities are relatively rare. They occur in 2% of all false aneurysms, and axillary artery aneurysms are very uncommon. Open reconstructive surgery of axillary aneurysms bears a high risk of local and general complications. Progress in endovascular surgery, and especially miniaturization of delivery systems for stents and stent-grafts, has enabled their application in the treatment of small-size, peripheral arteries. Our article presents a case of an extremely obese woman — 170 kg, 57 years old — who presented with a massive, false aneurysm of the left axillary artery that resulted from an epilepsy attack. She was successfully treated with endovascular deployment of covered stent Viabahn™  $\varnothing$  6 mm x 50 mm (W.L. Gore), performed with the rendez-vous technique. After 5-year-long follow-up, the stent-graft is patent, in the correct position, without radiological signs of migration or endoleaks.

**Key words:** axillary artery aneurysm, endovascular treatment, Viabahn stent

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## Introduction

The axillary artery hemorrhage caused by injury, expanding hematoma, or pseudoaneurysm usually requires immediate intervention. In most cases of surgical open repair, a thoracotomy is necessary. The invasiveness of this approach can be escalated due to blood loss, injury to the brachial plexus, infection of vascular prosthesis used for reconstruction, and all other possible complications related to extensive surgery.

Since the 1990s, the development of endovascular procedures in the treatment of abdominal aortic aneurysms has progressively enabled the application of this minimally invasive method for the treatment of peripheral aneurysms.

The first hand-made devices utilized Palmaz™ stents covered with PTFE prosthesis, brachial, or

long saphenous vein [1]. Nowadays, delivery systems, such as Viabahn™ (W.L. Gore), Fluency™ (Bard), and Wallgraft™ (Boston Scientific), are miniaturized, which enables deployment of covered stents in arteries of a smaller diameter [2–4].

In the literature, the application of these systems in the treatment of popliteal artery aneurysms is widely described [5, 6]. There are some data regarding endovascular treatment of carotid artery aneurysms and aneurysms of arteries in upper extremities, mainly due to their less frequent incidence in the population [7, 8].

## Case study

An extremely obese [170 kg (BMI > 60)] 57-year-old woman with diabetes mellitus, hypertension, and chronic obstructive pulmonary disease was admitted to

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the emergency department due to an epilepsy attack occurring on the street.

Because of the rapid progression of neurological symptoms, a head CT scan was performed showing epidural hematoma, requiring immediate neurosurgical decompression. Immediately after surgery, the general status of the patient improved, so respiratory therapy was ceased the next day.

Within the next few hours, the patient presented with increasing pain, subsequent edema, and expanding hematoma of her left arm. Ultrasonographical examination showed an excessive pseudoaneurysm of the axillary artery with a 1-cm long rupture.

AngioCT confirmed the presence of pseudoaneurysm, with an estimated diameter of 10 cm. Fractures of humeral bone and hemothorax were excluded. The symptoms were masked by the patient's obesity which simultaneously qualified the patient for endovascular treatment. The femoral artery was accessed in local anesthesia. A 7 Fr sheath was inserted, and an aneurysm was visualized on angiography (Fig 1). Multiple attempts to enter the distal segment of the axillary artery were unsuccessful, due to turbulent blood flow in the pseudoaneurysm and the small diameter of the axillary and brachial arteries. Therefore, the brachial artery was accessed distally with a 4 Fr sheath. Rendez-vous technique with application of snare enabled successful pass-through. From femoral access, the Viabahn™ (W.L. Gore) stent-graft 6 mm/50 mm was inserted, accurately positioned, and deployed. Post-deployment ballooning (5 mm/60 mm balloon) was necessary for proper fixation. Control angiography showed complete exclusion of pseudoaneurysm.

Postoperative follow-up was uncomplicated. Control ultrasound examinations showed gradual regression of pseudoaneurysm size, so evacuation of hematoma was not necessary. Postoperative spectrum of blood flow in forearm arteries was normal (Fig. 2). Seven days after the endovascular procedure, prolonged due to a history of previous neurosurgical intervention, the patient was discharged home in good general condition.

Follow-up visits were conducted 1, 3, and 6 months after the procedure and then every half a year, for 5 years. Up to now, the stent-graft is patent, in the correct position, with complete re-absorption of hematoma, and without clinical symptoms of infection (Fig. 3, 4). The patient remains on once-daily 75 mg aspirin antiplatelet therapy.

## Discussion

True aneurysms of axillary artery are relatively rare. Their etiology, similarly to abdominal aortic or peripheral aneurysms, is related to atherosclerosis, collagen

vascular disease, infection, or poststenotic dilatation in patients with thoracic outlet syndrome. The majority of false axillary artery aneurysms are a consequence of penetrating or blunt trauma to the arm region, forced

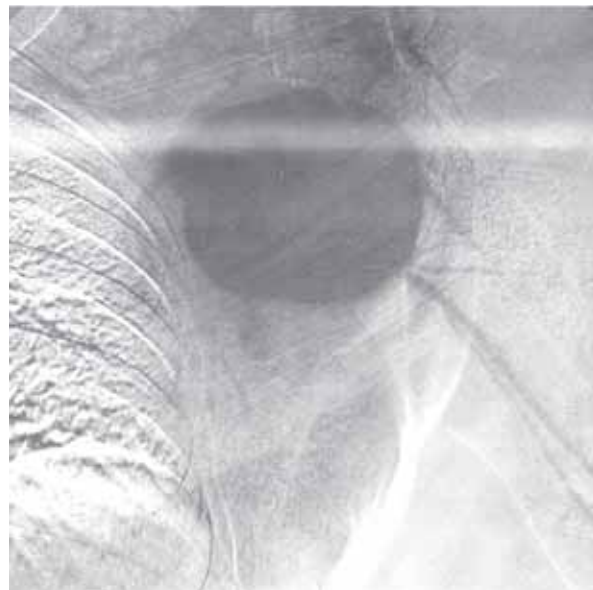


Figure 1. Preoperative angiography

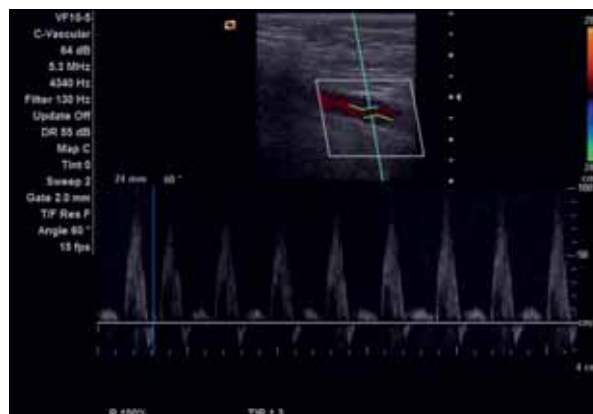


Figure 2. Postoperative ultrasound examination



Figure 3. AngioCT control after 24 months



**Figure 4.** AngioCT control after 60 months

abduction of the upper extremity, and complications after brachial plexus anesthesia or implantation of a pacemaker [9, 10]. The frequency of vascular complications related to trauma of upper extremities that lead to formation of pseudoaneurysm is estimated to be about 2% of all false aneurysms [11]. Mortality associated with penetrating injury of the subclavian or axillary arteries reaches 20% [12] and is mainly caused by technically and anatomically difficult open vascular repair of injury. Minimally invasive treatment of false aneurysms includes, depending on localization and morphology, ablation with thrombin under ultrasound guidance, deployment of uncovered stents with subsequent coiling of the aneurysmal sac. However, this type of treatment is not recommended for the subclavian or axillary arteries. The method of choice in case of false axillary or subclavian artery aneurysms is implantation of stent-graft/covered stent [13].

Small series of cases were described by Toit [14] and Schoder [15]: 57 patients with subclavian artery injury and 12 patients with subclavian artery aneurysm. Patients were treated with endovascular techniques. In the Toit study, after 48-month follow-up, the stenosis of stent-graft was reported in 5 of 25 followed cases, and total occlusion in 3 cases. Schoder reported 100% patency of stent-grafts after 11.6 months of observation.

In our case study, the pathologically obese female patient (BMI > 60), with type I diabetes mellitus, hypertension, and chronic obstructive pulmonary disease underwent the endovascular treatment of pseudoaneurysm of the axillary artery. As a consequence of the epilepsy attack, the patient required neurosurgery to decompress epidural hematoma. Massive, around 10 cm in diameter, false aneurysm of the axillary artery formed most probably due to rapid abduction of the arm during seizures. A similar mechanism of injury of the axillary artery was described in baseball players — pitchers [16].

The pseudoaneurysm was excluded with stent-graft implantation. After 5-year-long follow-up, the

stent-graft is patent, in the correct position, without radiological signs of migration or endoleaks. Color Doppler ultrasound shows a normal spectrum of blood flow within the stent-graft, as well as in the peripheral arteries. The patient remains in good general condition, without any motor dysfunction of the upper extremity.

## Conclusions

Minimally invasive endovascular treatment of vascular trauma and true and false aneurysms of peripheral arteries seem to naturally replace open surgery, similarly to thoracic and abdominal aortic aneurysms repair. Our presented case, with 5 years of follow-up confirms the feasibility of the endovascular approach, but, of course, the analysis of larger series is required to set up standards of treatment.

## Conflict of interest

None.

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# Deep vein thrombosis of the lower limbs in injection drug users

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## Abstract

*Venous thromboembolism is the third most common cardiovascular disease and is associated with a high risk of death or disability. One group of patients at particular risk of developing this disease are injection drug users. A series of five cases of patients addicted to narcotic drugs, hospitalized at the Department of Angiology for venous thromboembolism has been presented. The main risk factor was a venous or subcutaneous tissue injection of drugs. These cases show a complex clinical picture of venous thrombosis, difficulties in selecting and monitoring anticoagulant therapy, coexisting infections, as well as economic and psychosocial aspects.*

*Addiction to drugs administered by injection is a risk factor for venous thromboembolism, the clinical picture is complex, and treatment is a major challenge for vascular medicine and drug addiction therapy. Education and preventive measures within the communities of drug addicts could be the most important actions aimed at reducing the incidence of deep vein thrombosis.*

**Key words:** venous thromboembolism, deep vein thrombosis, injection drug users

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## Introduction

Venous thromboembolism (VTE) is a serious public health problem. It occurs in 1–2 cases per 1000 people; in two-thirds of cases, it manifests as isolated deep vein thrombosis (DVT), and in one-third of cases as a pulmonary embolism (PE). There is a high risk of recurrence of the disease, development of post-thrombotic syndrome, and in the more severe cases chronic complications leading to permanent disability [1]. There are many risk factors for this disease, including old age, cancers, use of contraceptives, injuries, infections, and immobilization. One group of patients who are particularly predisposed to the development of DVT are injection drug users (IDUs). Below we report five

cases of patients diagnosed with VTE where the main risk factor was venous or subcutaneous tissue injection of drugs. All presented patients were diagnosed with viral infections that co-existed with drug addiction: either human immunodeficiency virus (HIV) or hepatitis B (HBV) or C viruses (HCV), or co-infections. The cases of these patients have been presented to share our observations on this specific disease course, which is slightly different from the classical one and to highlight the challenges associated with treating these particular patients. The authors would also like to attract the attention of communities that care for drug addicts, experts involved in the treatment of addictions, as well as experts dealing with VTE in order to convey the seriousness of this public health issue, which is marginally

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or not at all addressed in most studies and guidelines. All patients presented here were hospitalized in the Department of Angiology of the Regional Specialist Hospital in Wrocław, Poland, in the years 2010-2016. Every year the unit admits approximately 800 patients, 10% of whom are VTE patients.

## Description of cases

### Case 1

A 39-year-old man was admitted to the accident and emergency department (A&E) with pain, swelling, and cyanosis of his right lower limb; he was diagnosed with proximal DVT based on the clinical picture and ultrasonography. Because the patient did not give consent for hospital treatment, low molecular weight heparin (LMWH) was prescribed for outpatient treatment. The patient returned to the A&E unit after a week. As it turned out, he did not follow the prescribed treatment, and the disease symptoms had intensified. This time he was admitted to the Angiology Department, a Doppler echocardiography was again performed, confirming the presence of thrombus with mixed echogenicity that had completely filled the distal part of the common femoral vein and the femoral and popliteal veins; no blood flow was detected. A medical history revealed infection with HIV and long-term active drug addiction by means of injections, with recent administration of ephedrine intravenously (mixing the popular tablets used for a runny nose with readily available chemicals) and previous use of the so-called "compote" (Polish heroin) which was injected into the vein or subcutaneous tissue, most often within the thigh area. Six months earlier, the patient had ceased treatment at the acquired immunodeficiency and drug rehabilitation clinics. Moreover, in recent months he had been treated for a right thigh abscess. In the physical examination the advanced features of lipoatrophy, especially to the face, buttocks, and limbs attracted particular attention. The abdominal palpation revealed an enlarged liver and spleen. Single crackles at the lung base were identified. Enlarged peripheral lymph nodes were also observed. The right lower limb was swollen and livid, with visible dilated superficial veins; there was increased consistency and soreness of the soft tissue. On the skin of both lower limbs, numerous discolorations were visible, i.e., along the saphenous vein (Fig. 1). Scars and minor ulcers covered with dry necrosis were located on the lower limb and along the saphenous vein (Fig. 2). Moreover, confluent subcutaneous hematoma and petechiae could be seen in the distal area of the right lower limb (Fig. 3).

Laboratory tests showed: high C-reactive protein level (CRP) — 185 mg/L, white blood cells count

(WBC) — 13.4 K/uL, low hemoglobin (Hb level 7.5 g/dL), elevated D-dimer level (4661  $\mu$ g/L), hypokalemia and hyponatremia, and positive serological tests for HCV. Hepatosplenomegaly was evident with abdominal ultrasound, and on the chest X-ray, micronodular lesions in the left apex and the sub-apical zone were observed, which had progressed compared with the X-ray performed a year earlier.

Anticoagulant therapy was initiated (enoxaparin — 1 mg/kg of body weight every 12 hours) in addition to the lower limb elevation and compression therapy. Metamizole and paracetamol were also administered due to fever (up to 40°C). The entire clinical picture suggested a diagnosis of acquired immunodeficiency syndrome (AIDS), which is associated with specific pulmonary lesions. The patient was referred to the Infectious Diseases Unit. It was recommended that class II compression stockings be used, as well as a minimum of three months of anticoagulation treatment with enoxaparinum 1.5 mg/kg of body weight, once a day. The information received from this Unit confirmed the diagnosis of pulmonary mycobacteriosis.

### Case 2

A 43-year-old male professional driver was admitted to the Department of Angiology on a scheduled basis for diagnostic purposes in connection with a history of DVT in the left lower extremity seven months prior. A medical history upon admission revealed intravenous drug dependence in the past (13 years earlier), presence of HCV infection, and current treatment with an anticoagulant (rivaroxaban). In the physical examination, skin lesions on the lower limbs were noted; on the left thigh, there was a scaly tattoo (Fig. 4), and on both extremities, numerous scars, small scattered ulcers covered with necrotic scabs with local skin/subcutaneous tissue infections around them, and irregular, spread discolorations within the calf area (Fig. 5). Lesions in the lower limbs suggested active injecting of narcotic drugs. During the few days of hospitalization, attempts were made to establish a reliable medical history of addiction. On the last day of hospitalization, the patient admitted he was still taking drugs by injection (amphetamines, ephedrine), even when the thrombosis had been diagnosed. He also reported that his attempt to disguise the problem was due to the fear of losing his family.

In the laboratory analyses, the serological tests for HCV infection were positive, and mild anemia was found (Hb 11.4 g/dL). Genetic studies for thrombophilia showed homozygous mutation of the homocysteine gene (MTHFR C677T) with normal homocysteine concentration. Ultrasound of the veins showed an obstruction in the distal part of the iliac vein, the common femoral vein (without recanalization characteristics);



**Figure 1.** Discoloration and scarring along the saphenous vein; the so-called "track marks"



**Figure 2.** "Track marks" in addition to minor ulcers covered with dry necrosis are visible



**Figure 3.** Confluent subcutaneous hematoma and petechiae of the right lower limb

mural thrombi with mixed echogenicity were also observed in the femoral vein, popliteal, and saphenous veins (moderate recanalization).



**Figure 4.** Small, scattered ulcers covered with necrotic scabs, the so-called "skin popping", are visible, with local skin/subcutaneous tissue infections around them. Tattoo on the left thigh (it has been blurred to prevent identification of the patient)



**Figure 5.** Numerous scars, as well as small, scattered ulcers covered with necrotic scabs ("skin popping") are visible, with local skin/subcutaneous tissue infections around them

Considering the patient had received over six months of anticoagulant therapy and reported active injection of narcotic substances, anticoagulants were discontinued and the patient was advised to use class II compression stockings and to book into a drug rehabilitation center.

### Case 3

A 42-year-old man was brought by ambulance to the A&E department because of swelling and cyanosis of the right lower limb. A medical history revealed HIV and HCV infections. In the past, the patient had been addicted to intravenous drugs (heroin), and he was currently undergoing methadone treatment. The patient had experienced an episode of acute renal failure as a result of a drug overdose. A physical examination revealed right lower limb swelling, soreness and increased calf consistency, cyanosis of the skin, and widening of the superficial veins. In the area of the right groin, local skin and subcutaneous tissue thickening was visible, in addition to subcutaneous hemorrhage and scarring (Fig. 6). Ultrasound examination showed an occluding thrombosis of the common femoral vein, the femoral vein, and the popliteal vein. The vein lumen was filled with thrombotic material of mixed echogenicity, and was non-collapsible in the transverse compression testing, with no signs of blood flow. Additionally, we observed the presence of a tumor with mixed echogenicity compressing the femoral veins at the site where they join, suggesting local inflammation/hematoma.

The patient denied active intravenous use of narcotic drugs. However, he was behaving peculiarly and repeatedly changed the information he was providing. He tried to explain the “thickening” as a groin injury or wrong body positioning during sleep. At the end of the hospitalization, he confessed to returning to drug use and to administering heroin multiple times in the same location (common femoral vein).

Laboratory tests for D-dimer (1611 ug/L) and CRP (15.9 mg/L) were performed. There were no significant changes found in the chest X-ray. Abdominal ultrasound showed an enlarged liver with a homogeneous, slightly increased echo texture.



**Figure 6.** Subcutaneous hematoma in the right groin (location of administration of heroin, at the location of the common femoral vein); a “blown vein”

Treatment with anticoagulants (enoxaparinum 1 mg/kg of body weight every 12 hours), compression therapy, and lower leg elevation were initiated, as well as empirical antibiotic therapy (amoxicillin with clavulanic acid). The patient was discharged with instructions to take enoxaparin 120 mg every 24 hours for 12 weeks, as well as to use class II compression stockings, and to book into a local drug rehabilitation clinic. A follow-up visit to the Angiology Clinic was scheduled after three months, which the patient did not attend.

### Case 4

A 29-year-old man came to the hospital emergency unit with increasing swelling, and pain in the left lower limb. At the time of admission to the Department of Angiology, the patient experienced respiratory dyspnea at rest. Ultrasound showed an occluding thrombosis of the following veins: popliteal, femoral, and common femoral with a clot tail in the external iliac vein. In the past, the patient had been treated for external left iliac artery pseudoaneurysm. The medical history revealed a five-year addiction to intravenous psychoactive substances (specifically, heroin). In the physical examination, swelling of the right lower limb, cyanosis, and numerous enlarged and tender lymph nodes in the groins were noted. Furthermore, in the region of the greater saphenous veins, numerous skin indurations were observed (lesions from injections), as well as scarring and inflammatory changes in the lower leg and in both groins. During the patient’s stay on the ward, he ran a fever. The laboratory tests revealed high markers of inflammation — CRP 242 mg/L, WBC 26 K/L, elevated D-dimer level 1889 ug/L, mild anemia (Hb 11.2 g/dL), hyponatremia, and positive serological tests for HCV infection.

Based on a computed tomography angiography (CTA) of the lungs, PE was excluded. Treatment with anticoagulants was initiated (initially intravenous unfractionated heparin was administered, controlled by activated partial thromboplastin time; then, enoxaparin, 1 mg/kg of body weight every 12 hours), as well as compression therapy and limb elevation. Empirical antibiotic therapy was also administered. Inflammatory lesions on both lower limbs transformed causing abscesses (with ulceration on the left side, debridement of which resulted in evacuation of bloody-purulent content). The patient’s condition improved, and the fever subsided. The patient was discharged, with instructions to take classic heparin subcutaneously 2 x 5000 IU/0.2 ml (due to lack of medical insurance, this treatment was the most appropriate due to the costs). Class II compression stockings or flexible bandages were also recommended. The patient was referred to a local substance abuse treatment center.



### Case 5

A 28-year-old woman, hospitalized twice in the Department of Angiology, reported a total of three episodes of thrombosis in an 18-month period. During her first stay in the hospital, ultrasonography revealed an occluding external iliac vein and a femoral vein thrombosis, all on the right side. Subsequent incidents involved the left lower limb; the femoral, popliteal, and deep thigh veins. The medical history revealed a 10-year addiction to intravenous psychoactive drugs, mostly heroin, in addition to HIV and HCV infections. Further, a healed suppurating right groin fistula (Fig. 7) and a chronic suppurating right foot ulcer (Fig. 8) were reported.

Anticoagulant therapy (enoxaparin, 1 mg/kg of body weight every 12 hours), compression therapy, and lower limb elevation were used, as well as empirical antibiotic therapy (ciprofloxacin during one stay; amoxicillin with clavulanic acid during the subsequent visit). Ulcers were debrided and bandaged. The recommendations following hospital discharge on each occasion did not differ and included anticoagulant treatment (enoxaparin, 1.5/kg of body weight, one abdominal injection daily), class II compression stockings, and bandages for skin lesions. The female patient was booked in for a thrombophilia test, which she did not attend.

### Discussion

Drug addiction has been a major global social issue for many years. Based on data from 2015 [2, 3], it is estimated that there are 10.2 to 23.7 million IDUs aged 15–64 years in the world; these are people who are addicted to psychoactive substances. Among many complications, one issue that continuously poses not only a diagnostic but also a therapeutic challenge is lower limb DVT. The lack of clear guidelines for anticoagulation therapy in this group of patients, who are at high risk of bleeding, as well as their psychosocial problems, prove extremely challenging. The complex psyche of these patients, and their sense of social exclusion, brings about a negative attitude toward medical care and treatment. As such, this results in a late diagnosis of the disease, as well as a lack of cooperation between the patient and the doctor. The proportion of IDU patients without health insurance ranges from 50% to even 70% [4, 5], and one of the most common explanations for “not seeking” medical attention is financial problems. Among the cases described here, only the first patient admitted openly active drug addiction. In all other cases, it was the frequent conversations of doctors with the patients that helped to determine the real cause of current DVT. At this point, it is worth mentioning that a thorough physical examination and knowledge of



Figure 7. A healed right groin fistula



Figure 8. Oval, suppurating ulcer of the right foot dorsum

characteristics of the clinical course can lead clinicians to a correct diagnosis. Publicly available information shows that DVT in IDUs is more common among:

- young or middle-aged people, usually under the age of 40 years [6]
- men; depending on the source, the male: female ratio is reported to be 11.5:1, 7:1 and 2.8:1 [7–9]
- patients with a previous episode of DVT, especially if relapse occurred within the first six months [10].



In the physical examination, the following symptoms should raise suspicion:

- lesions in the form of tumors, abscesses, or groin fistulas that are leaking or bleeding
- linear, discolored indurations and scarring along the veins, so-called “track marks”
- purulent infections of superficial veins
- scattered scars on the skin and subcutaneous tissue, with necrotic foci; so-called “skin popping”
- skin and subcutaneous tissue inflammation
- accompanying fever.

The clinical picture often does not resemble the typical course of DVT, and it is common to identify a septic type DVT. This requires administration of empirical antibiotic therapy as soon as possible while the purulent lesions often require surgery. The infections are usually caused by Gram-positive bacteria, most often the staphylococcus aureus.

Injection drug use is responsible for a growing number of HIV infections. The percentage of IDUs infected with HIV exceeds 40% in some countries [2, 11]. On the other hand, HIV infection is considered a risk factor for venous thromboembolism, and it is estimated that HIV-positive people carry a 2–10 times higher risk of DVT than the general population [12]. Globally, it is estimated that 52.3% of IDUs are HCV-antibody positive, and 9.1% are HBV surface antigen positive [2].

An important problem that remains unresolved is the choice of appropriate treatment for DVT among IDUs. When introducing a therapy, we need to bear in mind the presence of active drug dependence, and thus, an increased risk of hemorrhagic complications. The choice is usually between LMWH and oral anticoagulants; the former is usually favored. This choice has been confirmed by the opinions of experts [13]. Apart from the risks of bleeding disorders, which are difficult to manage, oral medications can also interact with narcotic drugs, and thus, there is a need for regular and appropriate monitoring. According to the general guidelines, the therapy should last up to 12 weeks [14]. Compression therapy should also be recommended to patients, with graduated compression stockings or elastic bandages, as well as a referral to a drug rehabilitation center. The patients described here were scheduled for a follow-up visit at the Angiology Outpatient Unit, which they did not attend. Therefore, it is difficult to determine how long, if at all, these patients adhered to the recommended treatment after leaving the hospital. IDUs have been found to have three times more frequent recurrence of thrombosis in the first six months after an episode in comparison to the general population [10, 15]. This suggests that IDUs tend to deny the problem, and therefore, discontinue therapy early. This leads to the risk of further complications, including frequent,

severe post-thrombotic syndromes, and formation of hard-to-heal wounds.

In conclusion, it should be emphasized that the problem of DVT in intravenous drug users requires special investigation, as well as a holistic approach. Each patient should be treated individually, taking into account all aspects of the disease, including thrombosis, frequent co-existing characteristics of bacterial infection, accompanying viral diseases and their treatment, drug dependence, and their complex psychosocial problems.

## Conflict of interest

None.

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# Type 2 endoleak embolization and utilization of non-contrast-enhanced magnetic resonance angiography (NCE-MRA) as a non-invasive imaging follow-up method

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## Abstract

*Endovascular aneurysm repair (EVAR) is a minimally invasive technique widely used in abdominal aortic aneurysm treatment. The most common complications after EVAR are endoleaks, with type 2 endoleak (T2EL) being the most prevalent. T2EL detection and surveillance require imaging techniques such as computed tomography angiography (CTA), contrast-enhanced magnetic resonance angiography (CE-MRA), Doppler ultrasound, or digital subtraction angiography (DSA). However, these modalities are associated with numerous limitations, including exposure to ionizing radiation, contrast media administration, or operator dependency, as in the case of ultrasonography. A non-contrast-enhanced (NCE-MR) could be a substitute non-invasive method for endoleak monitoring.*

*Our case report describes an 83-year-old female patient with type 2 endoleak and enlarging aneurysm sac detected on a CT scan. Despite the enormous aneurysm size, the patient underwent endovascular treatment owing to multiple comorbidities. Due to challenging feeding vessel anatomy, catheterization of the aneurysmal sac was impossible. Attempted polymerization of the aneurysmal sac with Glubran-2 partially sealed the sac and obliterated the feeders' inflow. Unfortunately, a non-targeted embolization resulted in the loss of patency of the right feeder and adjacent communicating branch.*

*The patient underwent follow-up imaging that included non-contrast-enhanced as well as contrast-enhanced MRA. The examination revealed the presence of a small residual endoleak, a freshly formed thrombus, and areas of old thrombi. The NCE-MR appeared to be a valuable tool in endoleak detection and provided a detailed clot morphology.*

**Key words:** endoleak, EVAR, magnetic resonance angiography, stent graft

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## Introduction

Type 2 endoleak accounts for the most prevalent type of endoleak following endovascular aneurysm repair (EVAR) of the abdominal aortic aneurysm (AAA) and affects about 10% of patients after EVAR [1, 2]. It results from a retrograde filling of the aneurysmal sac by the feeding vessels. The most common culprit feeders include inferior mesenteric, lumbar, and internal iliac arteries. The less common ones are accessory renal or median sacral arteries. Most type 2 endoleaks (T2ELs) have a mild clinical course and do not require urgent intervention; however, approximately 1% of these endoleaks result in aneurysm sac rupture [3]. Despite the relatively high prevalence and availability of effective management, the routine treatment of type 2 endoleaks remains challenging and controversial [1, 4–5].

Based on the time of onset and duration, T2ELs are categorized as early (onset < 12 months after EVAR) or late/delayed (onset > 12 months after EVAR), and transient (resolved  $\leq$  6 months) or persistent (resolved > 6 months) [3]. As described by Pineda et al., early-onset T2ELs resolve without treatment in 75% of cases, while late-onset T2ELs self-resolve in only 29% of cases [6]. Furthermore, persistent T2ELs are associated with an increased risk of sac expansion, aneurysm rupture, re-interventions, and conversion to open surgical repair [7]. According to the Society of Vascular Surgery practice guidelines, T2EL treatment decisions should be based on the following criteria: the expansion of the aneurysm by  $\geq$  5 mm, the type and size of feeders, and the appearance of symptoms [4]. However, the European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines suggest that an enlargement of sac diameter by  $\geq$  10 mm, found during follow-up imaging on comparable scans, may be considered a valid threshold for significant sac growth and hence require re-intervention [3]. Primary treatment options include transarterial T2EL embolization and embolization via direct sac puncture. Transvenous, transcaval, transarterial perigraft, and transarterial transgraft account for other embolization approaches. Laparoscopic ligation of the supplying vessels and open surgical treatment are considered the last resort [1, 8].

Diagnosis, surveillance, and post-treatment follow-up of type 2 endoleaks require medical imaging. The most commonly used modalities encompass computed tomography angiography (CTA), contrast-enhanced magnetic resonance angiography (CE-MRA), digital subtraction angiography (DSA), Doppler ultrasound, and contrast-enhanced ultrasound (CE-US) [3–4, 9]. Unfortunately, these aforementioned techniques are associated with numerous limitations. CTA and DSA require exposure to ionizing radiation and iodine

contrast media administration, which carries a risk of renal injury, life-threatening allergic reactions, or thyrotoxicosis [9]. Regarding CE-MRA, gadolinium deposition in the brain and the bones was recently described [11, 12]. Furthermore, in patients with renal insufficiency performance of contrast-enhanced studies may be unfeasible [13, 14]. That is true for both MR and CT examinations since they possess similar eGFR level restrictions. Doppler and CE ultrasound are heavily operator-dependent, difficult to reproduce, and limited by patients' body habitus [9, 10]. Additionally, a comparison of aneurysmal geometry using these studies is challenging, especially considering variable aneurysm growth.

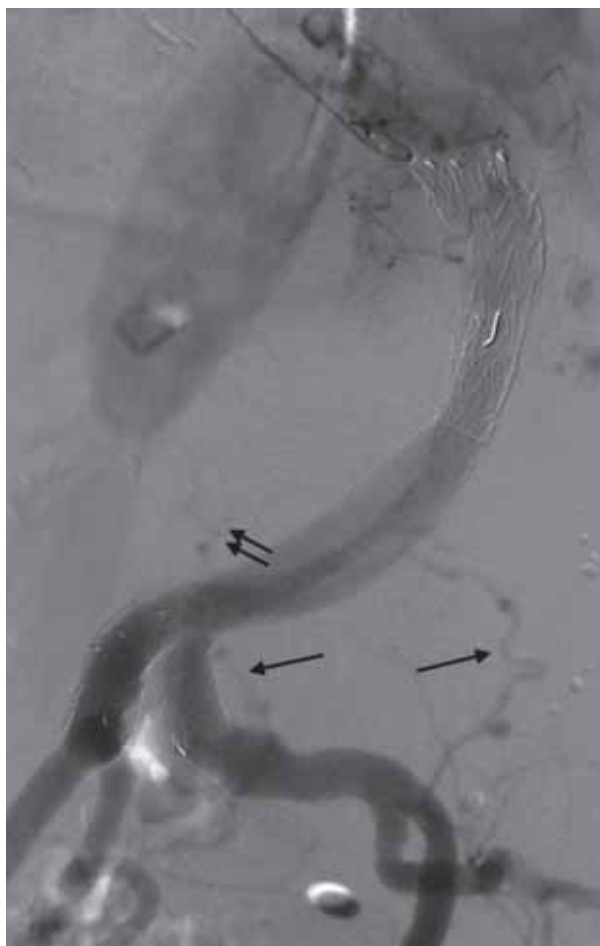
Hence, a non-contrast-enhanced (NCE-MR) could be an optimal, non-invasive imaging method practical for both diagnosis and surveillance of endoleaks [10].

## Case report

An 83-year-old female patient presenting with abdominal pain and increasing abdominal circumference was referred to our clinic due to evidence of aneurysmal sac expansion detected on contrast-enhanced CT.

The patient had undergone EVAR of the AAA with Excluder stent-graft implantation seven years earlier (in 2015). The aneurysmal sac measurements preceding implantation with regard to the largest diameter and surface area were around 60,1 mm and 2427,3 mm<sup>2</sup>, respectively (CE-CT in 2014). The same aneurysm sac parameters at the time of symptomatic enlargement measured about 152,2 mm and 12521,8 mm<sup>2</sup> (CE-CT in 2022). After the EVAR, the patient was under ultrasound surveillance, although the control examinations were quite unsystematic. The CT findings on admission were equivocal regarding the endoleak feeding sources, and the surgical repair was ill-advised owing to multiple patient comorbidities, which prompted an endovascular intervention to precisely localize and treat the endoleak. DSA confirmed type 2 endoleak supplied by two tortuous branches originating from the right and left internal iliac arteries and measuring about 3 mm in diameter (Fig. 1). The feeders exhibited a communicating branch and a shared inflow to the aneurysmal sac.

Despite multiple attempts, catheterization of the aneurysm sac via both feeding branches was unsuccessful. The reason was predominantly significant tortuosity and critical stenosis of the vessels. At this point, the typical onyx embolization was not achievable. That led to an effort to polymerize the sac via the right feeder using Glubran-2. The administration of a 16% mixture of cyanoacrylate glue and lipiodol resulted in partial polymerization of the aneurysmal sac and closure of the endoleak inflow site (Fig. 3). Additionally, given



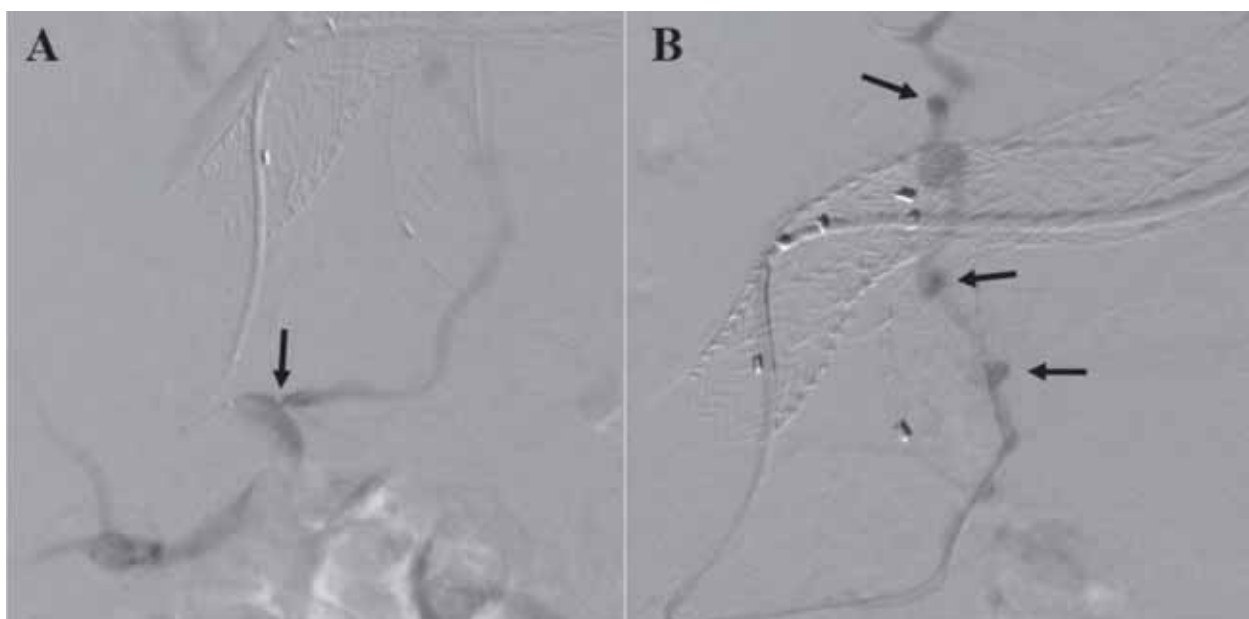
**Figure 1.** Endoleak feeding branches originating from the right and left internal iliac arteries (single arrows) and communicating branch connecting the right and the left feeder (double arrows)

the technical difficulties of using endovascular glue, the embolic agent obliterated the right feeding artery and the communicating branch connecting both feeders.

Four days following the embolization, the patient underwent MRA of the abdomen and pelvis using SIGNA Artist 1,5T GE. The sequences included 3D IFIR, FIESTA fs, 3D Heart, and LAVA, pre- and postcontrast administration. The NCE-MRA accurately visualized the size of the aneurysmal sac and the morphology of its contents. The largest diameter and surface area of the sac post-embolization were around 144,2 mm and 10466,4 mm<sup>2</sup>, respectively. Multiple hyperintensity



**Figure 3.** Non-target embolization of the right feeding artery and the adjacent communicating branch. Arrows point to an embolic agent polymerized inside the aneurysm sac



**Figure 2.** Challenges encountered during the catheterization of the feeding vessels. Arrow indicates stenosis of the feeder (A). Arrows indicate tortuosity of the feeding branch (B)

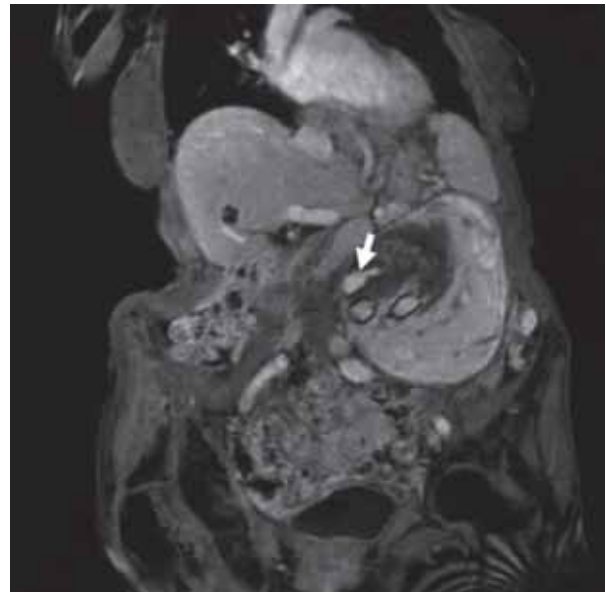


areas visible within the aneurysm sac on the 3D Heart sequence represented old thrombi. A hypointense area detected inside the sac on the 3D Heart sequence corresponded to a fresh thrombus with residing cyanoacrylate glue particles. Additionally, the non-contrast sequences allowed for the visualization of a small residual endoleak (Fig. 4).

Since it was our first attempt to use NCE-MR as a surveillance method after endoleak embolization, the examination was supplemented by contrast media administration. CE-MRA confirmed the leak of the contrast media into the aneurysm sac corresponding to the inflow of fresh blood, as identified on NCE-MR (Fig. 5). In our opinion, the NCE-MRA allowed for the depiction of the morphology of the aneurysmal sac contents, especially the distinction of the age of the thrombus. The patient was scheduled for an NCE-MR follow-up to track the progress of aneurysmal sac clot formation.

## Discussion

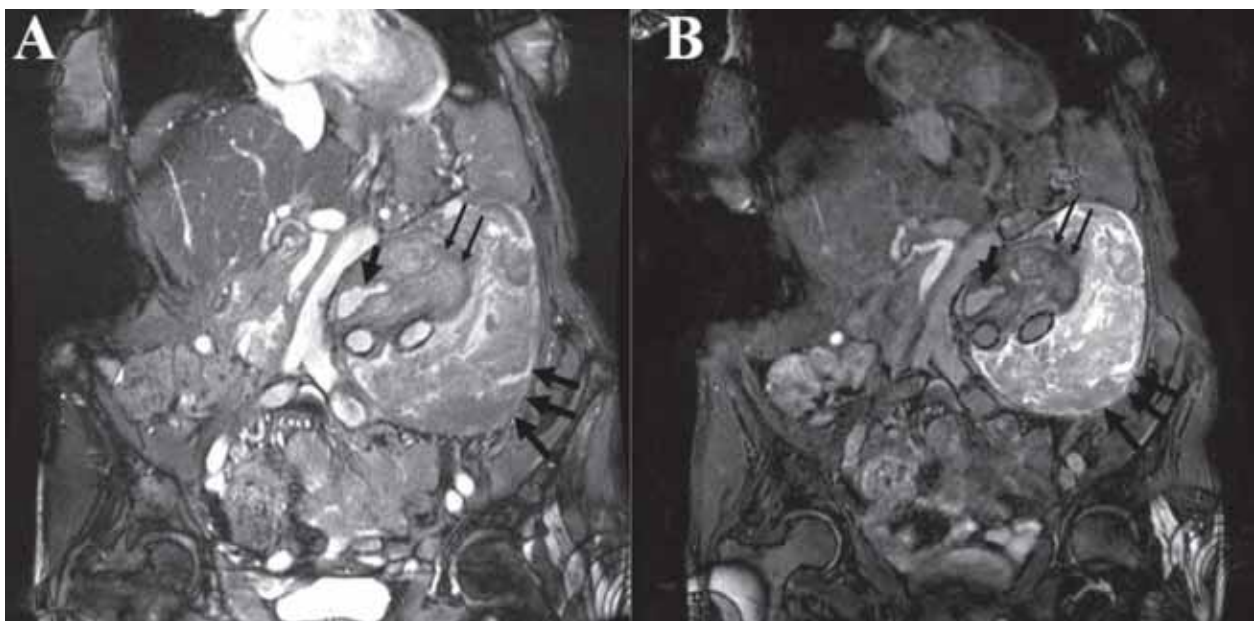
Type 2 endoleak embolization may prove exceedingly challenging due to unpredictable feeding vessel anatomy. Troublesome characteristics of feeders may include variable origin, tortuosity, or critical stenosis. Moreover, access through internal iliac arteries compared to the one through the arc of Riolan makes manipulation of the catheter more difficult due to multiple acute angles that need to be passed. Thus, catheterization and satisfactory embolization of the aneurysm sac may not always be achievable. Ideally, the obliteration would involve



**Figure 5.** The T1-weighted CE-MRA sequence visualized contrast leakage into the aneurysm sac, proving the presence of the residual endoleak (corresponds to fresh blood inflow area visible on NCE-MRA; see Fig. 4 A, B)

the liquid part of the sac and both inflow and outflow sites of the endoleak. Unfortunately, such a situation is often impossible.

Arenas Azofra et al. studied technical and clinical success following T2EL transarterial embolization (TAE). The authors defined it as a lack of endoleak on control angiography (technical) and a lack of sac growth by  $\geq 5$  mm detected on contrast-enhanced CT



**Figure 4.** The NCE-MRA visualized the inflow of fresh blood into the aneurysm sac (single arrow), fresh thrombus inside the sac (double arrows), and organizing thrombus with retraction spaces (triple arrows). FIESTA (A). 3D Heart (B)

one year postembolization (clinical). The former was achieved in 71%, while the latter in 63% of cases. The re-intervention rate was about 36% [15].

Furthermore, Horinouchi et al. [16] suggested that an aneurysm sac diameter exceeding 55 mm at initial type 2 endoleak TAE is a significant predictor of aneurysm sac expansion. The authors advise performing TAE of the T2ELs before the sac reaches such a diameter. Moreover, the investigators concluded that T2EL TAE is not always an efficient way to prevent sac expansion, and further re-interventions may be necessary.

The mentioned earlier studies may prompt a conclusion that the availability of a reproducible, non-invasive, and precise diagnostic imaging modality is critical.

Presently, the gold standard for endoleak surveillance is a contrast-enhanced CT; however, observation of sac enlargement is possible using Doppler ultrasound, magnetic resonance imaging (MRI), or CT is possible without contrast media administration [3–4, 16]. Nevertheless, sac growth over 5 mm requires further evaluation by contrast-enhanced CT [4]. Notwithstanding, Habets et al. [17] implied that CE-MRA might be more sensitive in the detection of T2ELs in comparison to CE-CT.

A recent study by Salehi Ravesh et al. [9] proposed that NCE-MRA may yield better anatomical and functional insight into the distinct endoleak types than CTA or DSA. NCE-MRA provided a satisfactory evaluation of the aortic aneurysms, including their hemodynamic parameters and the contents of their sacs. Nonetheless, the study was limited by a small number of patients, different types of aortic aneurysms treated, high diversity of endovascular prostheses implanted, and variability of endoleaks detected.

In their study, including 46 patients with AAA and/or common iliac artery aneurysms treated with EVAR, Kawada et al. reported endoleak detection sensitivity, specificity, and accuracy of NCE-MRA endoleak detection as 77%, 92%, and 85%, respectively. This study's limitations included early post-operative NCE-MRA examination and different types of endoleaks identified. However, the authors concluded that NCE-MRA is a promising imaging technique for post-EVAR patient surveillance [10].

Similarly, the findings presented in our case report suggest that non-contrast-enhanced MRA may prove equally valuable in detecting residual endoleak post-TAE. In our experience, NCE-MRA allows for accurate evaluation of the aneurysmal sac size and enables a detailed analysis of the organizing thrombus.

As with any other imaging modality, NCE-MRA comes with its limitations. These mainly include classic contraindications to MR examination, i.e., the presence of implanted metallic and electronic devices or older

types of stent grafts with metallic components. The newer stent graft technology allows for safe MR imaging. According to van der Laan et al. [18], four out of the currently available stent grafts (Excluder, AneuRx, Talent, and Quantum LP) should not compromise MR imaging. Some (the metal Zenith and the Lifepath) show ferromagnetic properties, causing artifacts obliterating stent-graft lumen and adjacent structures. Evaluation of the MR images in the case of the Ancure graft may also be problematic.

In summary, non-contrast-enhanced MRA is a reproducible imaging method that does not require exposure to ionizing radiation or contrast media administration, which could prove particularly useful in patients with end-stage kidney disease. The NCE-MRA may ensure safe and precise T2ELs monitoring following Excluder stent-graft implantation, providing insight into thrombus morphology and its organization. Clinical studies, including prospective randomized controlled trials, are needed to implement an optimal NCE-MRA protocol for endoleak surveillance.

## Conflict of interest

None.

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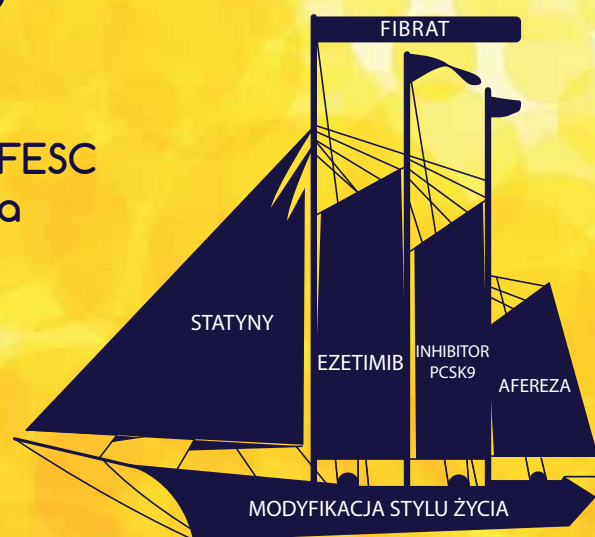
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