Case Report

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Percutaneous Transluminal Angioplasty Using Carbon Dioxide Contrast in Chronic Limb Threatening ischemia Patient with Renal Failure

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Abstract

Background: At present times, it is estimated that more than 202 million patients suffer from peripheral arterial disease (PAD) worldwide. Chronic limb-threatening ischemia (CLTI) represents the end stage of PAD, which often needs lower extremity amputation, and the aftermath can be worse. For patients with CLTI and chronic kidney disease (CKD) who need endovascular therapy, iodinated contrast may enhance the risk of contrast-induced nephropathy (CIN). CIN is an acute renal injury and may lead to irreversible loss of renal function. In high-risk patients who were allergic to iodinated contrast material and for those with renal insufficiency Hawkins in the 1970s pioneered the intra-arterial application of carbon dioxide (CO2) gas angiography to reduce the volume use of iodinated contrast.

Case Illustration: A single case was presented in this report. An 80-year-old man was referred to National Cardiovascular Center Harapan Kita with the chief complaint of independent rest pain and a nonhealing wound in his left forefinger, in accordance with the criteria CLTI. The duplex ultrasound examination shows total occlusion at the left anterior tibialis artery. The patient then underwent a percutaneous transluminal angioplasty (PTA) procedure using a CO2 contrast agent and the Plain Old Balloon Angioplasty (POBA) technique for revascularization. The flow to the distal of the left anterior tibialis artery returned using only 30 ml of Iodinated contrast. The follow-up of this patient shows there is no increase in serum creatinine level and eGFR.

Summary: Endovascular therapy in patients with CLTI with a high risk of operation could be performed in patients with CKD using the carbon dioxide contrast agent in order to minimize the usage of iodinated contrast avoiding further loss of renal function. In this case report, the procedure was performed successfully without an increase in serum creatinine and a decrease in GFR.

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Keywords: *CLTI, Carbon dioxide Contrast, Endovascular Therapy.*

Introduction

CAt present times, it is estimated that more than 202 million patients suffer from peripheral arterial disease (PAD) worldwide. The prevalence of peripheral arterial disease (PAD) in individuals aged ≥ 40 years is 4.3%, and for individuals aged ≥ 70 years is 14.5%.[1] The prevalence of peripheral arterial disease (PAD) in Indonesia is 9.7%, as shown in A Global Atherothrombosis Assessment (AGATHA) study.[2,3]

Chronic limb-threatening ischemia (CLTI) represents the end stage of peripheral arterial disease that often needs lower extremity amputation, and the aftermath can be worse. In a German registry involving more than 40,000 patients with peripheral arterial disease, two-thirds of the patients with chronic limb-threatening ischemia and major tissue loss underwent limb amputation within 4 years after diagnosis.[3] PAD patients with end-stage renal disease (ESRD) have worse patency after revascularization due to restenosis and thrombosis and mid- and long-term increased need for repeat revascularization and unplanned amputations.[4] The goal of treatment of CLTI is to relieve pain, heal wounds, preserve a functional limb, and improve the quality of life. Along with the control of the infection and other medication, revascularization is key in the therapy, in which without revascularization the amputation rate reaches more than 40%. The method performed for the revascularization could be bypass surgery or endovascular therapy. In patients with High surgical risk, limited life expectancy, minor tissue loss, discrete occlusive disease (stenoses or short occlusions), or inadequate autogenous vein, endovascular therapy is the best option available for revascularization.[5]

For patients with CLTI and chronic renal disease (CKD) who need endovascular therapy, iodinated contrast may enhance the risk of contrast-induced nephropathy (CIN). CIN is an acute renal injury and may lead to irreversible loss of renal function. In percutaneous cardiovascular intervention therapy, CIN

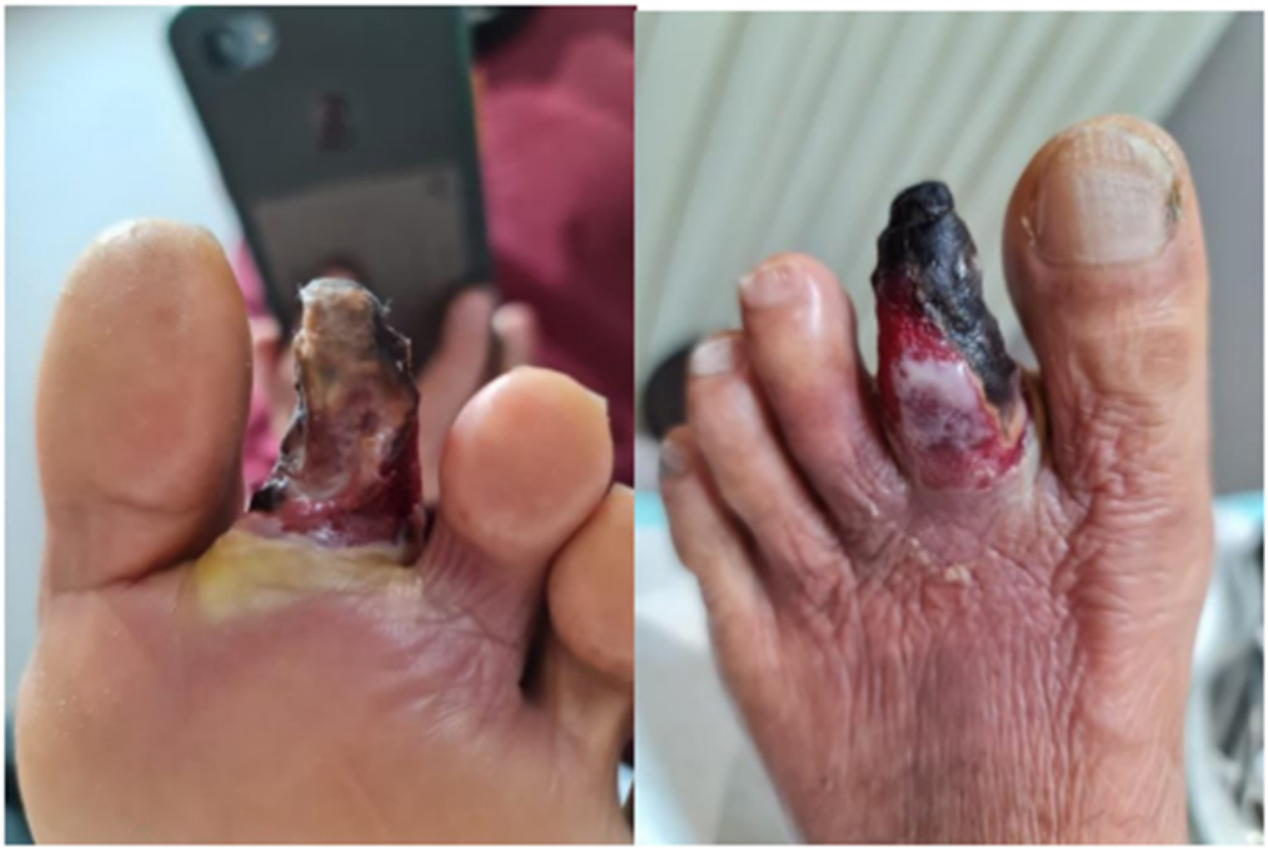

Figure 1. Clinical picture of patient's left forefinger.

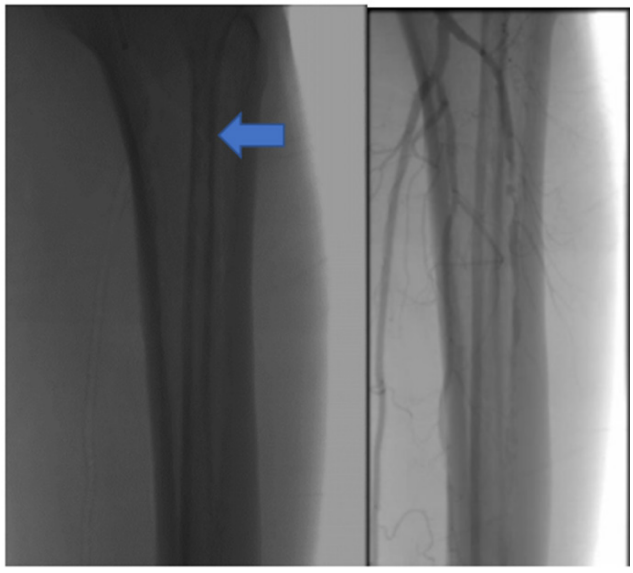

Figure 2. Percutaneous transluminal angiography procedures on this patient shows occlusion in anterior tibialis artery with carbon dioxide contrast (left) and Iodized contrast (right).

was observed in 8–15% of total patients and 40–50% of high-risk patients. The strategy used for this patient profile is rehydration and reducing the use of iodinated contrast to as little as possible. In high-risk patients who were allergic to iodinated contrast material and for those with renal insufficiency Hawkins in the 1970s pioneered the intra-arterial application of carbon dioxide (CO_2) gas angiography to reduce the volume use of iodinated contrast.[6]

In this case presentation, we present a 80 years old patient with CLTI and CKD who underwent percutaneous transluminal angioplasty at the National Cardiovascular Center Harapan Kita using CO_2 as contrast media aiming the reduce iodinated contrast usage and prevent the further loss of renal function. This case presentation will describe the clinical course of the patient and discuss the clinical properties of CO_2 as contrast media in the PTA procedure.

Case Illustration

An 80-year-old male was referred to the National Cardiovascular Center Harapan Kita from Abdi Waluyo Hospital, with the chief complaint of pain in his left leg for the past 3 months. The pain is getting worsened with walking activity and persists even during resting state, especially during bedtime. The patient could still move his left leg but felt a diminished sense of touch on his left leg. There was also a non-healing wound in his left forefinger, for the past 2 months before admission, the finger shrunk and blackened (Figure 1). The patient was also treated for his hypertension and type II diabetes mellitus with oral antidiabetics and oral antihypertension. From the previous hospital, the patient's laboratory test shows renal dysfunction with an estimated GFR=23 ml/min/1.73m.[2]

The patient underwent a Duplex Ultrasound examination at the referring Hospital resulting in total occlusion at the left anterior tibialis artery and calcification at the left common femoral artery without significant stenosis, there is no deep vein thrombosis in both legs. The CT angiography was not done in the case of the patient's renal condition. The patient then prepared for a Percutaneous Transluminal Angioplasty procedure at the National Cardiovascular Center Harapan Kita.

TConsidering the patient's renal function, we planned to do the PTA procedure using as minimal iodinated contrast as possible, therefore we decided to use Carbon Dioxide contrast in this procedure. In the PTA procedure, from angiography, we found the totally occluded left anterior tibialis artery and used the Plain Old Balloon Angioplasty (POBA) technique for revascularization (Figure 2). The flow to the distal of the left anterior tibialis artery returned using only 30 ml of Iodinated contrast. After the procedure, we do a renal function examination for the patient resulting estimated GFR of 30 ml/min/1.73m^2. The patient was then observed for any perioperative complications before being referred back to the previous hospital.

Discussion

Critical Limb-Threatening Ischemia

CLTI, a manifestation of PAD that is characterized by chronic, inadequate tissue perfusion at rest, is associated with decreased quality of life and substantial morbidity and mortality. In contrast to acute limb ischemia (ALI), chronic limb-threatening ischemia (also called critical limb ischemia, chronic critical limb

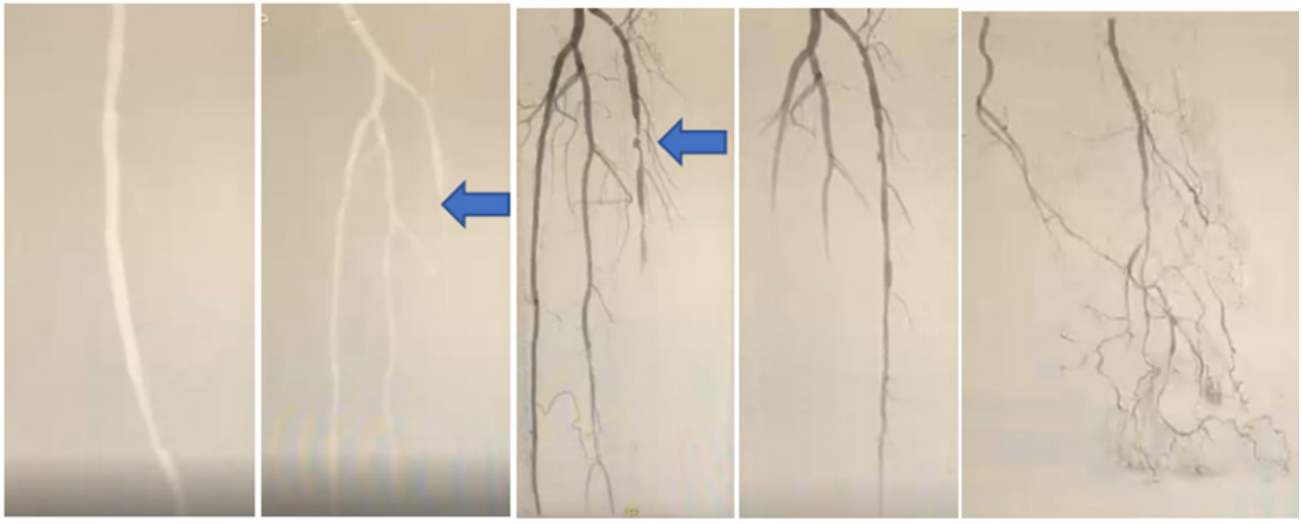

Figure 3. (A) Injection of CO2 contrast at SFA shows no stenosis or occlusion, (B) The contrast can not fill the ATP due to occlusion, (arrow) (C) Angiography before POBA and (D) After POBA, and (E) The flow to the distal of the run off artery after POBA.

ischemia, or severe limb ischemia) is characterized as ischemic pain in the foot while a person is at rest with pain lasting 2 or more weeks, nonhealing wounds, or gangrene that is attributable to objectively proven arterial occlusive disease.[5]

Our patient was an 80-year-old male with a chief complaint of pain in his left leg for the past 3 months. The pain is categorized as an independent rest ischemic pain with the onset of more than 2 weeks (3 months). There was also dry gangrene on his left forefinger as shown in Figure 1. With the data we obtained from the history taking we diagnosed the patient with CLTI with gangrene in Digiti-2 of left foot. The patient also has a history of CKD, diabetes, and hypertension with the current result of HbA1C of 8,0 % and eGFR of 24 before the PTA procedure.

The diagnostic methods suggested by ESC guidelines for PAD include Ankle Brachial Index (ABI), Duplex Ultrasound (DUS), Digital Subtraction Angiography (DSA), Computed Tomography Angiography (CTA), and magnetic resonance angiography. The method suggested is used to describe the anatomy and focal lesion of the diseased vascular and the prognosis of the patient we treat.[7]

We obtained the DUS examination result from the previous hospital resulting in total occlusion at the left anterior tibialis artery and calcification at the left common femoral artery without significant stenosis, there is no deep vein thrombosis in both legs. From the DUS examination and considering the angiosomal concept of the wound, we determined the culprit occlusion is in the left anterior tibialis artery. We did not perform CTA on the patient considering his renal condition to avoid further loss of his renal function. At the current hospitalization, we did not have a chance to perform an ABI examination as the patient has CKD, and the result of ABI cutpoints are not well defined despite of increased prevalence of high ABI attributed to arterial stiffness.[8]

Other examinations suggested by guidelines for patients with CLTI are Toe systolic BP, toe-brachial index (TBI), and transcutaneous oxygen pressure (TcPO2). TBI had good performance in patients with diabetes, claudication, and those at risk of Low Extremity Arterial Disease (LEAD). Toe pressure and TcPO2 are useful for CLTI assessment and are often used to determine the healing capacity after amputation. If TcPO2 is 40 mmHg, wound healing capacity is good after minor amputation. For values in between (10–40 mmHg), provocation tests allow better stratification. For a provocation test, TcPO2 is measured 7 in addition to the supine position, when the patient breathes 60% oxygen (O2) or when the patient's leg is elevated. The following results in provocation tests may predict sufficient wound healing capacity and minor amputation should be attempted if there is no possibility of revascularization:

increase in TcPO2 >10 mmHg or >_ 50% from the baseline value when the patient is breathing O2 or a decrease of < 10 mmHg when the leg is elevated.[7] Thus, for our patient we suggest performing a TcPO2 test after the revascularization from the outpatient clinic.

Medical Treatment

The therapeutic approach to patients with PADs includes two aspects. The first is to address specific symptoms of any localization and the risk related to a specific lesion. The second aspect of management in these patients is related to their increased risk of any CV event. In symptomatic low extremity artery disease (LEAD), the therapy suggested to prevent MACE and CV death is single antiplatelet therapy (SAPT). SAPT is indicated only if LEAD patients are symptomatic or have undergone revascularization. Clopidogrel is the preferred antiplatelet drug in LEAD patients.[7] Chronic anticoagulation therapy is given only if there is a concomitant indication and may be combined with SAPT when there is a recent revascularization procedure.[8]

Our patient was diagnosed with CLTI with gangrene in Digiti-2 of left foot, CKD stage IV, type II Diabetes Mellitus, and controlled Hypertension. Thus we continue the medication of CKD and T2DM with gliclazide 60 mg twice daily,[16] Units of insulin at night, and atorvastatin 20 mg once daily. The patient also has amlodipine 10 mg once daily candesartan 8 mg once daily and carvedilol 3,125 mg for his hypertension. For the antithrombotic therapy, we use clopidogrel 75 mg once daily and aspirin 80 mg once daily.

Observational studies of smoking cessation, antihypertensive therapy, antiplatelet therapy, statins, and improved glycemic control have shown improved limb-related outcomes in patients with symptomatic peripheral arterial disease. So we determined to optimize the hypertension and diabetes mellitus treatment while antiplatelet agents, statins, and angiotensin-converting-enzyme inhibitors were prescribed unless contraindicated.[5]

Revascularization

Along with the control of the infection and other medication, revascularization is key in the therapy, in which without revascularization the amputation rate reaches more than 40%. The method performed for the revascularization could be bypass surgery or endovascular therapy. In patients with High surgical risk, limited life expectancy, minor tissue loss, discrete occlusive disease (stenoses or short occlusions), and inadequate autogenous vein, endovascular therapy is the best option available for revascularization.[5]

Our patient was sent from the previous hospital after getting medication for pain relief with intravenous paracetamol and antibiotics as the bacteria culture suggested. After obtaining the culprit lesion we prepare the patient for revascularization. The patient is 80 years old and has CKD, diabetes, and hypertension, therefore we categorized the patient with an increased risk of surgery. Based on the algorithm suggested we choose the endovascular therapy to be performed in the patient.

After the procedure we need to configure the risk of amputation of the patient, A new classification system (WIfI) has been proposed as the initial assessment of all patients with ischaemic rest pain or wounds. This classification includes three primary factors that constitute and contribute to the risk of limb threat wound (W), ischemia (I), and foot infection (fI).[7] As for our patient, the wound is at category 2 which is non-extensive gangrene and the foot infection can be categorized as level 2 with infection deeper than the skin. We are not performing the Ischemic test at the moment but with only the data we obtain, the risk of amputation of this patient can be considered moderate-high.

Carbon Dioxide Contrast in Endovascular Therapy

Iodinated radiographic contrast media may cause kidney dysfunction, particularly in patients with preexisting renal impairment associated with diabetes. This dysfunction, when severe, will cause CIN. CIN occurs within 24–72 hrs after the intravascular injection of iodinated contrast media. The mechanisms underlying CIN might be due to several factors, including renal ischemia, the formation of reactive oxygen species (ROS), reduction of nitric oxide (NO) production, and tubular epithelial and vascular endothelial injury.[10]

Carbon dioxide (CO_2) to conventional iodinated contrast, particularly in situations where there are contraindications to iodinated contrast or where a less viscous or cheaper imaging contrast can be used to the

operator's advantage. The main benefits of using CO_2 for angiography are that CO_2 has no adverse effects on the kidneys or the immune system and that it is the least expensive contrast medium.[11] In a prospective study for patients with CKD undergoing peripheral angioplasty procedures, the incidence of CIN was significantly higher in the iodinated contrast medium group (29%) compared with the carbon dioxide group (14%).[12]

Using Carbon dioxide contrast in PTA has some differences with iodinated contrast, regarding the property of the CO_2 itself. CO_2 is 28 times more soluble than O2 and 54 times more soluble than nitrogen. This high solubility of CO_2 allows its injection into the arteries below the diaphragm and veins without clinically significant gas embolism. When injected into a vein, CO_2 is carried by the blood to the lungs, then the gas is eliminated in a single pass. CO_2 should not be used as a contrast agent for imaging the thoracic aorta, the coronary artery, and the cerebral circulation because of its potential neurotoxicity and coronary artery gas embolism causing myocardial ischemia. The viscosity of a fluid or a gas is a measure of its resistance to flow. CO_2 is 400 times less viscous than contrast medium. Therefore, CO_2 in diagnostic quantities (15–30 mL) can be injected through a 3-Fr catheter. CO_2 does not mix with blood, and the gas bubbles remain undiluted, thus better visualizing peripheral vessels through collaterals. CO_2 contrast is viable in endovascular therapy, especially when the collateral exists, but in conditions where multiple or long stenosis or occlusion exist, or in the procedure of stenting and POBA, the iodinated contrast is superior.[13]

For our patient, we perform the PTA procedure with canulation in the left common femoral artery, we perform angiography with CO_2 contrast to view the vascularization of the artery above the knee, resulting there is no occlusion nor stenosis at the left femoral artery to left popliteal artery. The catheterization continued to the poplitea artery utilizing diagnostic catheter MPA2-5Fr and again we performed angiography with CO_2 contrast utilizing CO_2 injector tool connected to the diagnostic catheter. We did two CO_2 contrast injections with a total contrast of 25 ml. For a better view, we had to invert the color of the angiogram using an image processing method so the CO_2 contrast became more visible. From this angiography, we find that the CO_2 contrast could not fill the medial of the left anterior tibialis artery. To clearly define the lesion and begin the appropriate procedure, we used iodinated contrast utilizing a microcatheter and the angiography continued with the POBA procedure two times with 8 atm pressure for 3 minutes. After the POBA procedure, we commenced evaluation angiography with iodinated contrast find that the flow from the left anterior tibialis artery to the dorsal pedal artery returned (Figure 3).

To prevent CIN events, there are some methods available for a clinician, among those are monitoring renal function, removal of nephrotoxic drugs, choosing the less nephrotoxic radiocontrast agent, minimizing the iodinated contrast usage volume, and adequate hydration. Monitoring renal function is suggested to be done daily until the 5th day of the procedure. The increase in serum creatinine level should indicate nephrotoxicity. Adequate hydration will increase the infusion rate which may result in volume overload and trigger pulmonary edema in patients with predisposing cardiac conditions. In these patients, a rather low infusion rate of 1 mL/kg per hour has in general been recommended and used in clinical practice.[10]

Our patient underwent the PTA procedure with POBA using the CO_2 contrast to minimize the usage of iodinated contrast that can induce CIN and cause further loss of renal function. The procedure was performed successfully with total iodinated contrast usage of 30 ml, total CO_2 contrast usage of 25 ml, 20 ml of bleeding, and 16 minutes 2 seconds of fluorotime. The patient gets rehydration of 1 mL/kg per hour for 12 hours before and after the procedure. From the evaluation of renal function, we found there is no increase in the patient's serum creatinine level and eGFR. Creatinin level from the previous hospital is 2,8 mg/dL and eGFR 23 ml/min/1.73m^2 before the procedure. After the procedure, serum creatinine decreased to 2,04 mg/dL and eGFR increased to 30 ml/min/1.73m^2. The patient was then sent back to the previous hospital for further monitoring and evaluation.

Summary

Endovascular therapy in patients with CLTI with a high risk of operation could be performed in patients with CKD using the carbon dioxide contrast agent in order to minimize the usage of iodinated contrast avoiding further loss of renal function. In this case

report, the procedure was performed successfully without an increase in serum creatinine and a decrease in GFR.

List of Abbreviations

ABI	Ankle Brachial Index
ALI	Acute Limb Ischemia
AGATHA	A Global Atherothrombosis Assessment
CO_2	Carbon Dioxide
CIN	Contrast-Induced Nephropathy
CTA	Computed Tomography Angiography
CLTI	Chronic Limb-Threatening Ischemia
DUS	Duplex Ultrasound
DSA	Digital Subtraction Angiography
ESRD	End-Stage Renal Disease
LEAD	Low Extremity Artery Disease
POBA	Plain Old Balloon Angioplasty
PTA	Percutaneous Transluminal Angioplasty
ROS	Reactive Oxygen Species
SAPT	Single Antiplatelet Therapy
TBI	Toe-Brachial Index
TcPO2	Transcutaneous Oxygen Pressure

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