

DETECTION AND MONITORING OF TISSUE ISCHEMIA DUE TO ACUTE ARTERIAL OBSTRUCTION IN THE LIMBS OF PATIENTS WITH QUANTITATIVE VIOLATIONS IN CONSCIOUSNESS, PERIDURAL ANESTHESIA

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ABSTRACT

Background: Traced and interpreted is the dynamic and correlative relations between the values of certain biochemical parameters of the homeostasis connected with cell metabolism in skeletal muscles so a verification of tissue ischemia (TI) and ischemic tissue lesion (ITL) can be performed. **Aim:** To detect the tissue ischemia that is due to acute arterial obstruction in the limbs. **Methods:** The target group is patients with quantitative violations in consciousness and peridural catheters placed for anesthesia, with the suspicion that an acute arterial obstruction in the limbs (AAOL) has occurred, or one has already been verified. Test of the serum levels of CK; CK (MB); ASAT; ALAT and Myoglobin were initially performed and were monitored in dynamic. A valuation of the ASAT/ALAT index in close correlation with the other parameters and clinical course of the disease was also performed. **Results:** We found an severe elevation of the enzyme activity of CK; CK (MB) and ASAT in the case of AAOL which generated TI. In cases with unsuccessful, late or impossible revascularization and transition to TI and ITL (ischemic rhabdomyolysis) we found progressive elevation in the levels of the parameters being monitored, including ALAT and Myoglobin. The registered values, in the patients who were not operated, before death, were 900 times above for CK, and CK (MB) did not exceed 5% of CK. The ASAT/ALAT index is extremely positive in the group with ITL. The registered values of serum Myoglobin reached up to 70 times above the reference range. In cases with ischemic gangrene the ASAT/ALAT index from extremely positive in the beginning (>3.0-5.0) progressively decreased due to the rapid elevation of the values of ALAT with permanently high ASAT. **Conclusion:** The significant changes and correlative relations of the monitored parameters have distinct differences in cases with reversible TI and irreversible ITL, forming typical laboratory constellations in all of the controlled cases. This gives sufficient reason to believe that the implemented approach can form the basis of an objective method for early detection and monitoring of TI and ischemic tissue damage in AAOL in the target patient population for good clinical practice.

KEYWORDS: Acute arterial obstruction in the limbs; detection and monitoring of tissue ischemia, violations of consciousness; peridural anesthesia.

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DOI:10.5455/ijsm.ischemia-arterial-obstruction

First Received: November 06, 2016

Accepted: November 15, 2016

Manuscript Associate Editor: George Baitchev (BG)

Editor-in Chief: Ivan Inkov (BG)

Reviewers: Giulio Illuminati (IT)

Introduction

Acute arterial obstruction, acute arterial insufficiency in the limbs (AAOL) is a frequent complication in patients with the poor general condition, admitted in intensive care and resuscitation departments due to serious diseases.

A significant percent are intubated, contact with them is impossible or severe, because of the quantitative and quality violations of consciousness.

In other cases, the patients had a peridural catheter for a long lasting anesthesia of the lower limbs. Acute vascular incidents (AVI) are a diagnostic problem. Usually, a lack of arterial pulse in one of the places used for examination, temperature deviations in different areas of the skin, changes in the color of the skin of the limb, edema, and trophic changes, are found by accident.

Information for the changes in superficial and deep sensibility, mobility, rigidity, pain and others is impossible to acquire from the patient. In cases with no trophic changes, we cannot verify on the spot, whether the lack of pulse is due to a chronic or AAO, which is of the utmost importance for our clinical behavior and outcome from the treatment. Existing to date scales to assess the severity of arterial insufficiency is inapplicable due to lack of contact with the patient or because of impaired sensation in extremities. Clinical assessment methods are too subjective and dependent on the experience and training of clinician. Imaging diagnostics only establish the number, type, and level of arterial lesion. They do not verify the presence of TI and ITL as a clinical manifestation of AAIL and do not motivate our choice of therapeutic approach. The problem with the verification of TI and transitional and irreversible ITL has been a subject of study for a long time.

In-depth studies were made in the 90s of last century, but they do not solve the problem.[1] In the USA over 150 methods have been patented, mostly invasive for detection of TI, have not found the clinical application.[2] Only impedance spectroscopist (colorimetric method) used for a particular period, but because of the expensive and sophisticated equipment and inadequate information in the clinical aspect, it was implemented only in experimental conditions.[3] In the preliminary phase is immunological methods Immunofluorescence with mouse monoclonal antibody.[4] The scale for the assessment of tissue ischemia by indirect indicators (ABPI; TP) offered by TASK2 in the treatment of peripheral arterial disease (PAD) and diabetic foot is applicable for the determination of the stage of chronic arterial insufficiency and partially controlling the effect of the treatment. It does not answer the fundamental question, which determines the therapeutic approach immediate risk and expected output.[5]

It necessitates the application of objective, a non-invasive and affordable method for early detection and monitoring of TI and the transition from TI to irreversible ischemic rhabdomyolysis. Objectification TI, free of ITL requires urgent revascularization with good postoperative results. Objectification of ITL imposes different volume amputations of limbs. Failed, delayed revascularization or impossible optimal level amputation in high aortic and iliac obturations end with death. Infrainguinal obturations with verified ITL or experienced gangrene require different to a significant volume amputations of the lower limbs. Early detection of organ dysfunction in cases with ITL generates a multidisciplinary problem and requires necessary interdisciplinary therapeutic procedures. Late objectification of TI, ITL and organ dysfunction in these cases leads to expensive medi-

cal procedures, prolonged hospital stay in intensive clinics and characterized by an exceptionally high degree of disability and death. This determines the high socio-economic importance of the problem. The possibility for early detection and monitoring of ischemic tissue suffering allows us to control the effect of revascularization or amputation. In the target group AAO and manifestation of TI in one or more limbs, we observed typical dynamics in the levels of cytoplasmic and mitochondrially presented substances closely related to the metabolism of the muscle cell. Active control and the correct interpretation of the correlational relationship between the enzyme activity and serum creatine kinase (SCK), SCK-MB, transaminases, ASAT / ALAT index and levels of myoglobin in serum are an instrument in the hands of the clinician for good clinical practice. The monitored patients were divided into groups according to clinical course and clinical manifestations of AAO. The goal is to demonstrate proof of the significance of the monitored parameters and their correlational relations for the verification of the unique pathophysiological processes in muscle cells during ischemia with verified anaerobic metabolism. The transition towards cell ischemia and ischemic cellular destruction verified. The effect of revascularization or amputation is controlled.

Materials and methods:

In this article patients admitted for treatment in intensive care and resuscitation departments, which in one way or another, due to serious diseases are intubated, have quantitative disturbances in consciousness and are not contactable, are presented. Some of the patients were with peridural catheters or prolonged analgesia. In all of the cases, AVI occurred with compromised arterial blood flow in one or more limbs (arterial embolisms or thrombosis). Due to the lack of contact or permanent analgesia and anesthesia, they have discovered accidentally. All they have developed AAIL leading to TI or ischemic tissue lesion, followed by severe debilitating operations (different volume amputations of limbs), AHVI, ABVI or multiple organ failures with fatal outcome.

Diagnosed and monitored 18 patients, including 11 women and seven men. With quantitative changes in consciousness and impossible contact were 13, and with peridural catheters for analgesia 5. In all of the patients in the group acute arterial accidents occurred with loss of arterial pulse (pulse loss) in one or two of the limbs, with the development of AAI and TI or an existing one has already engulfed wide areas as a result of the propagation of the thrombus and deepening of the ischemic tissue suffering. Two received severe reperfusion complications of the type "no-reflow phenomenon" in entirely satisfied but late revascularization with the presence of a peripheral pulse. (Table 1)

Group 1: Five patients admitted for planned vascular surgery developed postoperative complications associated with acute reobturation of a native vessel or an obturation of the graft, with delayed or unsuccessful revascularization with catheters placed for lasting analgesia or intubated. The indicators for monitoring, TI in AAIL were tested immediately after verification of postoperative ACVA (acute cerebrovascular accident) and three times on the day of the attempted revascularization. Once a day to the final amputation or death. The Amputees were monitored once a day for four days. The values of monitored parameters are compared with the initial which were within the normal range. Group 1 is very demonstrative because the patients placed on

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Table 1

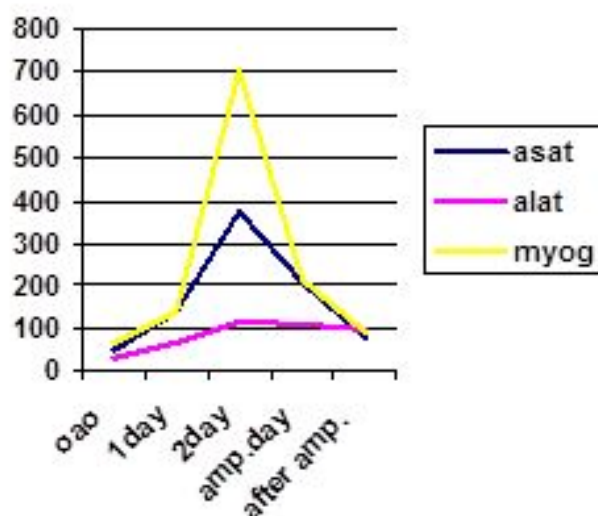
	Infrainguinal AAO	Suprainguinal AAO	Amputated	Reamputated
Intubated	0	13	4	2
Peridural catheters	2	4	4	4
Death	1	12	2	0

active monitoring, and the lack of pulsatile blood flow in the native vessel or graft discovered relatively early. The monitored parameters immediately tested. The obturations were in the iliofemoral segment, i.e. areas affected by TI are large and close in volume.

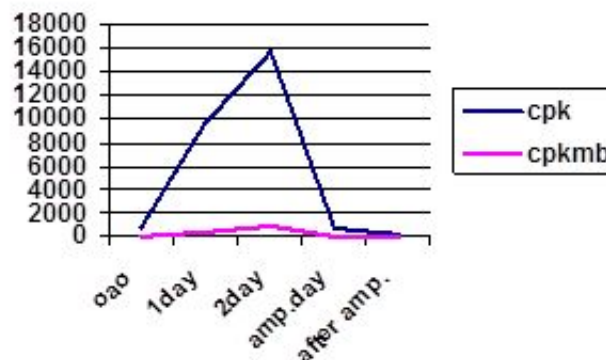
Group 2: Patients with infected allografts. Two in the arthroiliac, one in the iliofemoral and one in the femoropopliteal segment. One with extra-anatomical axilobifemoral bypass. All had surgery to eliminate the infected vascular prostheses and prevention or management of acute bleeding from a lesion on graft without the possibility of subsequent revascularization. Three with epidural catheters for postoperative analgesia, two were intubated. This group is very demonstrative because TI is expected and develops immediately postoperatively. Monitoring is conducted three times in the operating day and twice in the coming days. The values of the monitored parameters compared with the initial which were tested preoperatively and were within the normal range.

Group 3: Patients who developed AAIL, as a severe complication, during their stay in intensive care and resuscitation clinics due to another serious disease, intubated, without the possibility of contact, in which accident found the complication. Two with embolism of the lower limb, two with embolism of the upper limb, and three patients with multifocal embolism as a complication of rhythmic cardiac violations or infective endocarditis (IE). The indicators were tested immediately after the verification of arterial obstruction, once a day after emergency surgery or death.

Group 4: Admitted by emergency, four patients with symptomatic AAIL as a result of acute embolism of the two iliac arteries. Three operated and successfully revascularized. Two were with epidural anesthesia catheters and the remaining intubated. Two developed acute reperfusion complications type of "no-reflow phenomenon" in the next two days, in the conditions of present and kept throughout central arterial flow without local changes. One was successfully vascularized and intubated, with a subsequent ABVI and fatal outcome. Unoperated with bilateral iliac embolism, intubated patient with acute ischemic zone expansion, due to upward thrombosis which obturated AA subsequent lethal outcome. The monitored indicators were tested initially, after the revascularization and once a day until hospital discharge or fatal outcome.



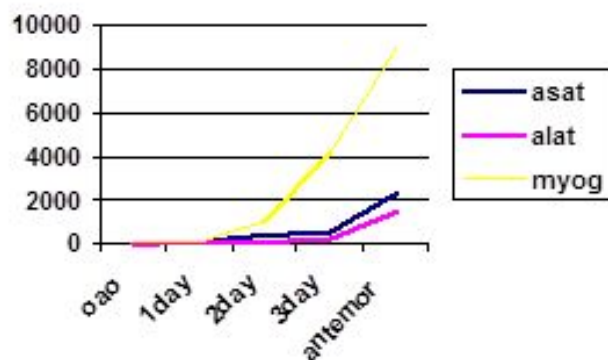
Group 1: Graph 1 and 2 showed averaged values of CPK; CPK(MB); ASAT; ALAT; Myoglobin. Measured on the day of AAO, in following days to amputation and after amputation.



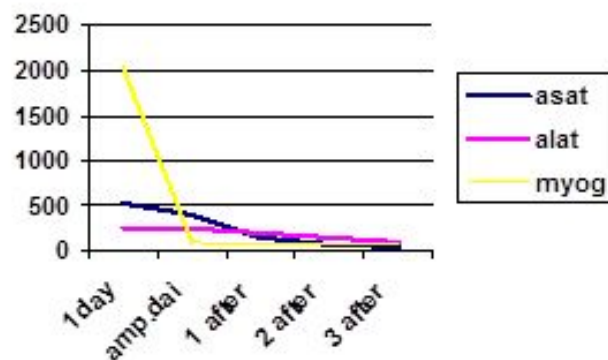
Group 1: Graph 1 and 2 showed averaged values of CPK; CPK(MB); ASAT; ALAT; Myoglobin. Measured on the day of AAO, in following days to amputation and after amputation.

Results

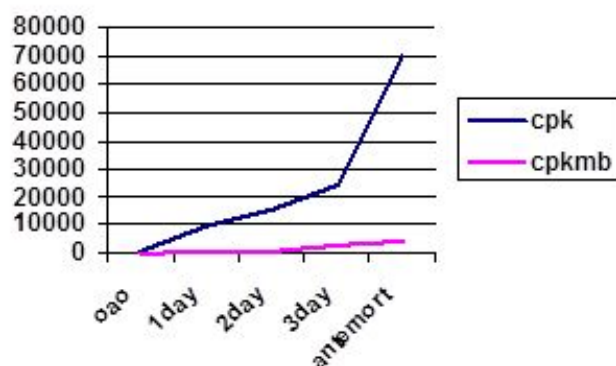
Group 1: Graphics



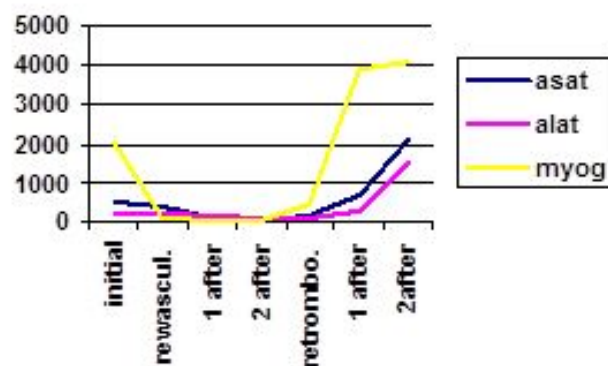
Group 2: Graph 3 and 4 demonstrated a significant elevation in values of monitoring determinants to fatal outcome of the patients.



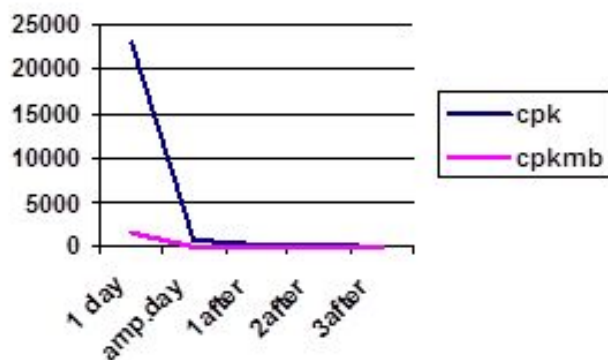
Group 3: Dynamics on graphs expressed critical decrease in values of monitoring determinants on the day of the amputation and after that.



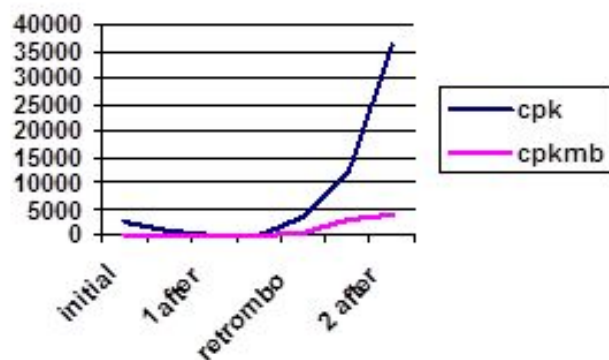
Group 2: Graph 3 and 4 demonstrated a significant elevation in values of monitoring determinants to fatal outcome of the patients.



Group 4: Graphs showed a critical reduction of determinants after successful revascularization and significant elevation after acute reobturation to a lethal outcome.



Group 3: Dynamics on graphs expressed critical decrease in values of monitoring determinants on the day of the amputation and after that.



Group 4: Graphs showed a critical reduction of determinants after successful revascularization and significant elevation after acute reobturation to a lethal outcome.

Discussion

AAIL diagnosis in patients with whom contact is difficult or impossible because of the quantitative and qualitative disor-

ders of consciousness or because of locoregional techniques for anesthesia and prolonged analgesia is a highly big problem.

Acute arterial obturation is an underlying complication of other serious diseases. As a nosology with severe and fulminant clinical course it often becomes the cause of death, and in the best case leads to severe disability. The delayed diagnosis AAIL and the lack of a fast and affordable method for early objectification and monitoring of the TI and early detection of ITL generate problems in the clinical approach towards such complication. Existing scales to assess the severity of tissue ischemia of the limbs are subjective and are not applicable in the target patient population. Very often successful, but later realized revascularizations generate high risk for the life of the patient. Similar is the problem with late amputations. The performed observation announces a reliable approach for early detection and monitoring of TI in AAIL and early objectification of ITL. It based on the biochemical expression of the anaerobic metabolism and cell destruction in the muscle cell in AAIL. The first changes in TI occur in the SCK and SCK (MB). An elevation is registered immediately after AAO generating AAIL. SCK (MB) does not exceed 5-6% of the total enzyme activity during the whole period of monitoring.

In three digit SCK changes in ASAT and ALAT are not registered. They are within the normal range. ASAT / ALAT index is <2 . There is no dynamics in the values of Myoglobin in the serum. All successful revascularized patients with such laboratory constellation have retained their limbs and their function.

With the four-digit SCK, an elevation of the values of ASAT found. ALAT remains in the reference range. ASAT/ALAT ratio is ≥ 2 . The ASAT/ALAT index \geq than 2. Myoglobin in the serum in on the upper boundary or over the reference range, but it is two-digit. The successfully revascularized patients with similar lab constellation retained their limb. Disorders in function registered In these patients the values of the monitored indicators normalized for 1-2 days, and ALAT normalized for 3-4 days.

In patients with laboratory constellation in which SCK is five-digit, ASAT three digit with positive dynamics, ALAT above the upper limit, ASAT / ALAT Index > 2 and successful revascularization developed severe complications of the type "no-reflow phenomenon," with subsequent amputation of the extremities. Myoglobin in this group reached values up to 3850 ng/ml. The initially amputated lived. Histopathology examinations of the muscle tissue of the amputated limbs have identified cell destruction. The unoperated patients with extensive ischemic areas and the inability for amputation died within 36 hours. The cause of death for them is an acute renal failure with "renal arrest" and generalized intoxication. The monitored parameters in these cases showed drastic deviations, but with special correlative relations with all of the other cases, the subject of this study. With SCK values up to 900 times above the initial were registered. SCK (MB) did not exceed 5% of the total enzyme activity. The values of ASAT were up to 130 times above the initial. ALAT-increased over 100 times. The ASAT/ALAT index initially was extremely positive ($> \%$), before the lethal outcome it was near 1.0, with very high ASAT and a rapid elevation of the values of ALAT- bad prognostic sign. Myoglobin values were four-digit. The levels of this indicators and the period in which it remains in the circulation determine the outcome.

Conclusion

1. AAIL diagnosis of patients with disorders of consciousness and impaired sensation due to techniques for anesthesia and analgesia applied peridural's hard, most often it is found late and is a serious challenge. Existing approaches to assess the presence and the severity of AAO are subjective and unimplementable. There are no possibilities for the objectification of TI and ITL which can motivate therapeutic behavior and monitor the effects of its application. This leads to a very high percentage of disability and death in the target group.
2. AAIL is clinically significant; reversible TI is verified by the typical laboratory constellation in the first hour from the beginning of AVI. This is the most appropriate time for revascularization.
3. The transition from reversible TI to ITL characterized by a standard biochemical expression of the monitored indicators and the personal correlative connection between them in all of the surveyed patients. Revascularization is possible, but the risk of complications and severe reperfusion function laesa in the limb is very high.
4. The five-digit values of SCK and very high ASAT and ALAT, with ASAT/ALAT index extremely positive or close to 1.0 with permanently high ASAT and very elevated Myoglobin form a common laboratory constellation, which verifies the severe and irreversible ITL. Amputation is necessary and lifesaving. The mortality rate is very high
5. Successful (timely) revascularization or amputation at an optimal level and experienced gangrene lead to a rapid decrease of the values of the monitored parameters to reference levels for 3-4 days.
6. Very high mortality characterizes cases of unoperated patients and patients who were revascularized late or amputated late below the optimum level.
7. Non-vascularized or later revascularized patients with AAO in the aortoiliac and the iliofemoral segment or bilaterally infrainguinally with a verified ITL die within one day.

Abbreviations:

AAIL - acute arterial impossibility in the limb
AAO - acute arterial obstruction
AAI - acute arterial insufficiency
TI - tissue ischemia
ITL - ischemic tissue lesion
ACVI - acute coronary vascular incident
ABVI - acute brain vascular incident
AVI - acute vessel incident

Authors' Statements

Competing Interests

The authors declare no conflict of interest.

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