ULCUS CRURIS VENOSUM

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Abstract

The article presents the definition of venous ulcers as the terminal stage of chronic venous insufficiency. The medical, socioeconomic, and epidemiological significance of this disease is discussed. The theories of the origin of venous ulcerations are presented, as well as original etiopathogenic concepts. It has been found that there are two types of venous ulcers caused by surface and perforator insufficiency (which are less extensive and have satisfactory therapeutic results), and ulcers due to reflux or obstruction of the deep system (which are accompanied by more severe microcirculatory and tissue changes and are refractory to most known therapeutic agents). The use of individual therapeutic modalities is presented (local and general measures, compression bandaging, and medicamentous and surgical therapy). Data on the results and indications for surgical treatment are also presented (crossectomy, stripping of surface trees, ligation and other procedures on insufficient perforators, saphenopopliteal anastomosis, femoro-femoral crossover anastomosis, interposition of venous trees, and other interventions on deep veins). The immediate and remote results of treatment depend on the etiological assessment of the disease and precise indication criteria.

Keywords: venous ulcers, etiology, diagnosis, clinical state, treatment

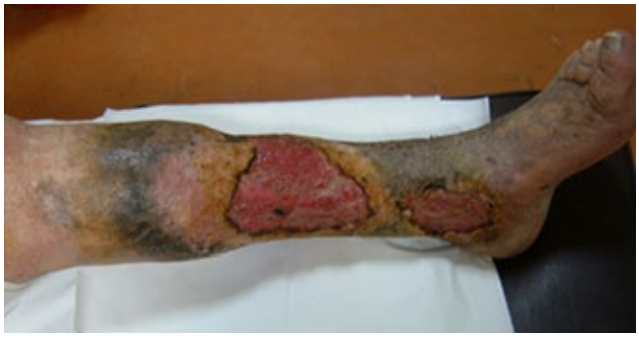
Introduction

Ulcus cruris (ulcer) is a wound or sore on the lower leg caused by a pathological process that has not healed for the past 6 weeks[1]. Various pathological conditions can lead to the development of ulcers, including stenotic occlusive arterial diseases, inflammatory and occlusive lymphatic diseases, certain hematological diseases, certain neurological conditions, or a combination of different conditions (mixed etiology). The most common cause (around 80-85% of all ulcers) is terminal chronic venous insufficiency, and these ulcers are called venous ulcers or *Ulcus venosum cruris*. Venous ulcers affect 1-3% of the Western European and US[2] populations. This condition is more common in women than in men (3:2)[3-5]. All diseases with leg ulcers are associated with high disability, and significant costs of prevention, diagnosis, and treatment, which indicates their significant socioeconomic importance[6].

Chronic venous insufficiency (CVI) is a progressive venous congestion of blood flow through the superficial, perforating (communicating), and deep veins of the lower extremities, resulting in venous hypertension and complex hemodynamic and local metabolic disorders (lipodermatosclerosis and venous ulceration). In recent years, the CEAP (Clinical, Etiology, Anatomy, and Pathophysiology) classification of CVI has been widely accepted: C - clinical manifestations of different degrees (0 - no changes, 1 - telangiectasias or reticular veins, 2 - varicose veins, 3 - edema, 4 - hyperpigmentation and other skin changes, 5 - intermittent ulceration, 6 - constant ulceration), E - etiology (congenital - primary or secondary), A - anatomical distribution (superficial, perforating, deep veins), P - pathophysiological findings (reflux or obstruction)[6]. Incompetence (valvular insufficiency) or obstruction of the veins in the lower extremities leads to progressive CVI and venous ulcers.

Venous leg ulcer, also known as *Ulcus venosum cruris*, is defined as ulceration or defect of the epidermis and dermis resulting from weakness in the venous system and is most commonly located in the lower part of the leg, in the region of the medial malleolus (image 1), but can rarely occur in other locations[7], including the upper part of the leg. The causes of venous ulcers include isolated incompetence of superficial veins (10-25% of patients), incompetence of

Image 1. *Ulcus venosum cruris* (Stage 2 ulceration on the lower part of the leg with surrounding dermatosclerosis and hyperpigmentation of the skin) due to post-thrombotic occlusion of the popliteal-crural deep veins



DOI: 10.5937/Galmed2306054M

perforating (communicating) veins (15%), and most commonly, post-thrombotic valvular insufficiency (reflux) or occlusions of deep veins[4, 7, 8].

Risk factors for the development of venous ulcers include[7, 9]: age over 55 years, positive family history of chronic venous insufficiency (CVI), elevated body mass index (BMI), prior history of pulmonary embolism or superficial and/or deep vein thrombosis, congestive heart failure, bone and joint disorders and injuries of the lower part of the leg, lower leg edema, multiple pregnancies, physical inactivity, professions involving prolonged sitting or standing, i.e. prolonged static effort, prolonged systemic corticosteroid therapy, lipodermatosclerosis, and venous reflux, etc. Poor prognostic signs include: ulcer duration over three months, initial ulcer size over 10 cm, peripheral arterial disease, and older age. Clinical signs of CVI and premonitory signs of venous ulcers include: varicose veins, edema in the ankle and foot region, venous dermatitis, and darker pigmentation of the skin (interstitial hemosiderosis) of the lower extremities. Complications of venous ulcers include: local infection, cellulitis, edema, secondary lymphatic obstruction, contact allergic dermatitis, eczematous reactions, ankle joint ankylosis, periostitis, osteomyelitis, and even malignant transformation. All of these significantly reduce the quality of life of patients[10].

The etiology of venous ulcers

There are several theories about the etiology of venous ulcers. Homans and de Takats[12] proposed a hypothesis that venous stasis and tissue hypoxia are the main etiological factors in the development of venous ulcers. However, Blalock[13], Piulachs, and Vidal Barrequer[14] discovered elevated oxygen levels in the venous blood of patients with CVI and ulcers, leading to the theory of arteriovenous fistulas[15] and subsequent tissue hypoxia. Browse and Burnand[16] have also contributed to the etiopathogenesis of venous ulcers by proposing a hypothesis about pericapillary fibrin accumulation, which blocks the capillary exchange of gases and nutrients, leading to cell death and the formation of venous ulcers. Another hypothesis suggests that leukocytes block the exchange by adhering to the endothelium and releasing toxic free radicals[17]. All of these theories suggest that precise etiopathogenic mechanisms have not yet been discovered.

Original etiopathogenetic research[7, 18, 19] was conducted on 16 patients before and during surgical treatment for unilateral venous ulcers who were divided into two groups of 8 patients each based on clinical and Duplex scanning findings: CV group (C_{5-6}EpsAspPr classification) - venous ulcers with an ultrasonically established presence of incompetence of superficial and communicant veins and normal flow through the deep system, and DV group (C_{5-6}EpsAdpPro classification) - venous ulcers with an ultrasonically established presence of post-thrombotic lesions of deep veins and incompetence of communicant veins with reflux through perforators due to valvular insufficiency or obstruction of deep veins. The results showed that hypoxemia and hypercapnia were present in the CV group, while no significant accumulation of anaerobic metabolites (lactate and pyruvate) was detected[18], whereas, in the DV group, hyperoxemia and significant accumulation of lactate and pyruvate after static load was present.

Pathomorphological examinations[7, 19] have shown the presence of phlebosclerosis with the accumulation of connective tissue and significant obstruction of small blood vessels in the ulceration region. Electron microscopic studies have shown the presence of pericapillary accumulation of abundant fibrin deposits, lesions of endothelial cell organelles, and thickening of the basement membrane with extravasation of erythrocytes, as well as progressive dermato-phlebosclerotic disorders with severe ischemic changes and irreversible cytolysis, karyolysis, scarring, and hyalinization in the region of CV and DV ulceration[7, 18, 19]. Hypoxemia and hypercapnia lead to the formation of venous ulcers that are not accompanied by the accumulation of anaerobic tissue metabolites. Such findings support the theories of Homans[11] and de Takats[12]. Venous stasis caused by post-phlebothrombotic damage to deep veins (reflux or obstruction) has greatly impaired capillary dynamics[11] and significant interstitial changes with the accumulation of anaerobic metabolites during static load. These findings confirm the correctness of the hypotheses of Blalock[13], Piulachs, and Vidal Barrequer[14]. In such conditions, although the blood is rich in oxygen (hyperoxemia), it cannot "release" oxygen or "collect" carbon dioxide from the surrounding tissue, resulting in severe trophic changes accompanied by a local increase in anaerobic metabolites during patient static load[19]. This supports the theories proposed by Browse and Burnand[16] and leukocytes entrapment (Coleridge Smith and colleagues)[17].

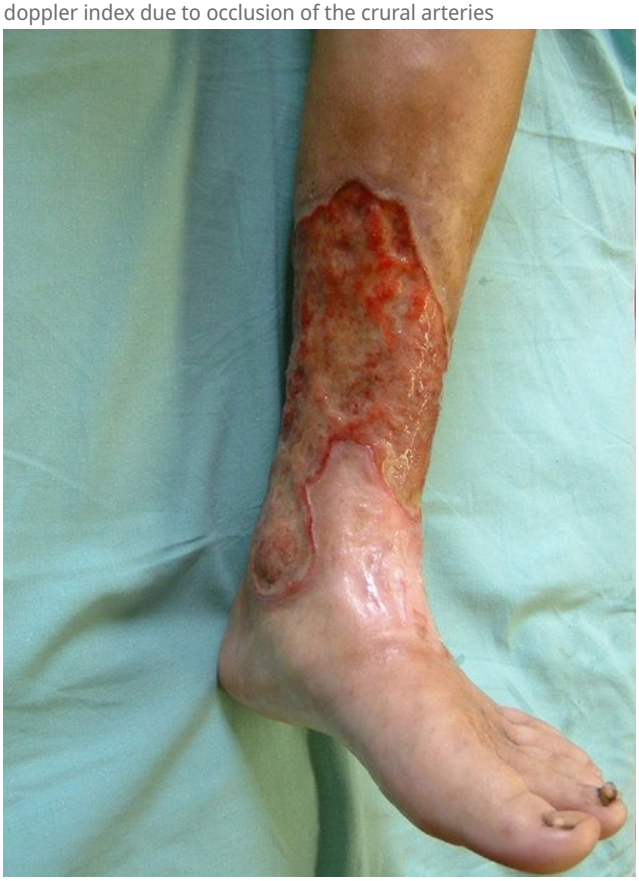
In practice, there are two mechanisms of venous ulcer development: hypoxic, in patients with stasis due to superficial and perforator vein insufficiency, and hyperoxemic, with capillary exchange blockage and extravasation of blood elements due to deep vein insufficiency or obstruction, which is also accompanied by anaerobic metabolite accumulation. Differentiating between these different etiological types is clinically, therapeutically, and prognostically important. The assumption of opening arteriovenous shunts in the pathology of venous ulcers was not confirmed by the original research.

Diagnosis of venous ulcers

The diagnosis of venous ulcers is established based on the medical history, clinical examination, and color Doppler ultrasound (examination of the superficial, perforating, and deep veins)[3, 7, 18, 20]. Rarely, phlebography or other methods are applied. Palpation of pedal pulses and measurement of

the ankle-brachial pressure index (ratio of the pressure in the *a. tibialis anterior* and *a. tibialis posterior* to the pressure in the brachial artery) are mandatory for differential diagnosis. It is important to detect mixed etiology ulcers (venous and arterial) that can be extensive and very resistant to most therapeutic procedures (image 2).

Image 2. *Ulcus venosum et arteriosum cruris* (mixed etiology): ulceration affects the entire circumference of the distal half of the lower leg. The patient has been diagnosed with post-thrombotic occlusion of the popliteal and crural deep veins and significantly reduced doppler index due to occlusion of the crural arteries



Anamnesis of venous ulcers is typical: positive family history and present risk factors. Clinical signs of CVI (extent of ulceration, feeling of heaviness and tension, pain, venous claudication, hyperpigmentation and other skin changes, edema, and secondary lymphedema) are more pronounced in the group of patients with deep vein insufficiency (DVI) than in patients with superficial and communicant vein (CV) insufficiency[3, 7].

Non-invasive assessment of the venous system can be achieved by using plethysmography, strain gauge plethysmography, and air plethysmography (measuring blood flow and limb volume depending on venous competence). Similarly, photoplethysmography (measuring light absorption by the skin in dermal venous plexuses) and light reflex rheography can be used[3, 21, 22]. However, in recent years, all of these methods have been replaced by Doppler ultrasound diagnostics. Doppler ultrasound is widely used in angiology. Johann Christian Andreas Doppler[23, 24] showed that the frequency of the reflected wave from a moving object differs depending on the speed of that object. Franklin[24] was the first to apply this effect to the study of blood flow.

Surface and deep veins can be examined using a handheld linear Doppler probe (flow, fluctuation flow depending on respiratory movements, and distal manual compression). Increased retrograde flow is detected in venous reflux. Tourniquets are used to determine the presence of reflux in the superficial, perforator (communicating), or deep systems[25].

Duplex ultrasound scanning with the help of an additional transducer or a phased array transducer provides a better image and more information. This allows more precise vascular examination with measurement of velocity and direction of flow (surface, perforating, and deep veins)[26]. Flow is accelerated by manual compression of the calf. Practically all veins below the inguinal ligament can be visualized using this technique, allowing the assessment of valve competence[27]. Duplex scanning is in good correlation with venography in the assessment of venous reflux and deep vein thrombosis[28-30]. Color duplex scanning is the gold standard in the evaluation of patients with venous pathology. It provides accurate anatomical and significant functional data on the veins of the lower extremities.

Phlebography (venography) of the lower extremities is an invasive method that involves injecting contrast into a vein in the leg or foot to visualize the superficial, perforating (communicating), and deep veins[3]. Nowadays, venography (ascending, descending, and varicography) of the lower extremities[7] is used only in the preoperative diagnosis of specific conditions. There are other invasive and non-invasive diagnostic methods available (laser Doppler fluxmetry, transcutaneous oxygen pressure, capillary microscopy, measurement of skin perfusion using radioactive tracers, etc.) but they are rarely used[3].

Treatment of venous ulcers

Effective treatment of CVI and venous ulcers should be based on etiopathogenetic principles and the CEAP classification. To achieve good immediate and long-term results, it is usually necessary to simultaneously or successively apply two or more therapeutic options.

General therapeutic measures include treating associated and accompanying diseases (hypertension, diabetes mellitus, anemia, etc.), eliminating risk factors and harmful habits, and encouraging daily physical activity and movement. Specific therapeutic procedures include local hygiene and periodic elevation of the limbs, graduated compressive bandaging, physical therapy, medication (pentoxifylline, phlebotropic drugs), and surgical methods (removal of superficial postphlebitic venous branches, ligation of incompetent perforating veins, and reconstruction (interposition,

bypass procedures, intraluminal dilations) of insufficient or occluded deep veins.

Local wound care of venous ulcers is performed using mild antiseptics and topical agents. There are a large number of pharmaceutical dressings used for dressing ulcers (hydrocolloid, hydrofiber, hydrogel, collagen, etc.) with or without bactericidal additives. However, their therapeutic effect is limited, and their defect is that they are expensive. This method is usually combined with other methods (graduated compression bandage).

External compression therapy has been used in the treatment of venous diseases since the time of Hippocrates[31]. The main mechanism of action is the reduction of edema. Graduated compression is a type of compression where the highest pressure is achieved in the region of the medial malleolus (30-40 mmHg), and the compression pressure decreases upwards, thus imitating the function of the venous pump[32, 33]. This is achieved using commercially available elastic stockings or by applying elastic bandages. The advantage of bandages is that they are cheaper, but they require skill in a placement to be effective. Therefore, stockings are increasingly being used, although some on the market may be of questionable quality. Before use, it is necessary to determine the compression level and size of the stocking for each patient. The benefits of multicomponent, high compression are greater than *single* low compression, and short stretch bandages are less effective[34]. Indications for compression therapy are conditions where there is deep venous reflux or a combination of deep and superficial venous reflux through perforating (communicating) veins. It has been shown that this therapy slows down lipodermatosclerosis and promotes the healing of venous ulcers, so it is indicated either as a standalone or adjuvant therapy for CVI and venous ulcers. In some inoperable ulcerative conditions[31, 34], this therapy may be the only form of treatment. Contraindications for the use of compression therapy are reduced Doppler, ABI indices below 0.8, infected ulcers with pronounced exudation, cellulitis, metabolic edema, and heart failure.

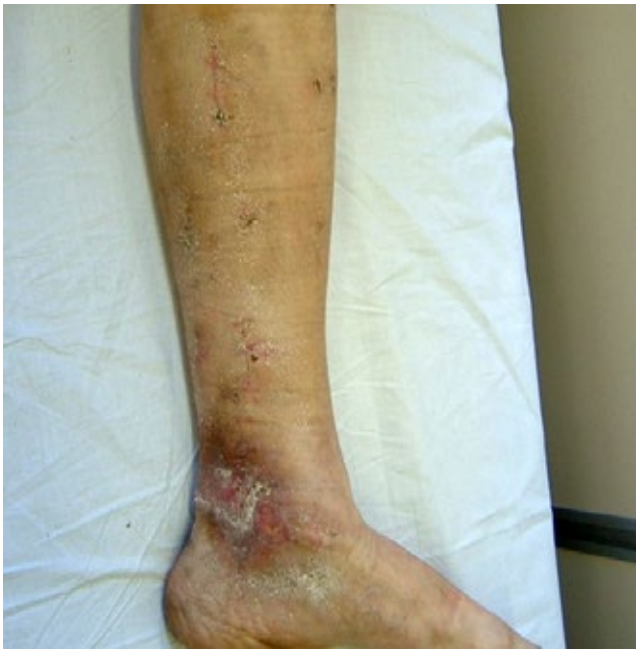
The use of medications in CVI is often promoted by the pharmaceutical industry, but this therapy should be rational and based on established microcirculatory disorders. Edema in CVI is most often due to increased capillary permeability, where the edematous fluid is rich in proteins[3]. Treatment of these edemas is more effective with an elevation of the leg and compression therapy than with diuretics. Antibiotics are indicated only in cases of cellulitis and sepsis. Hydroxyethyl rutosides, flavonoids from plant glycosides, reduce the rate of capillary filtration in patients with CVI, which is accompanied by a decrease in edema and clinical improvement[35]. However, there is no solid evidence for the beneficial effects of these drugs on venous ulcer healing. As microcirculatory impairment is significant in patients with CVI and venous ulcers, the use of pentoxifylline is justified for its hemorheological properties[36]. How this agent affects erythrocytes (promotes flexibility) and leukocytes (reduces adhesion to endothelium)[37, 38], its use may lead to ulcer healing. The adopted concept of diffusion barrier caused by pericapillary fibrin deposits has led to investigations of the use of profibrinolytics (stanozolol) in venous ulcers, but the number of patients is still small and satisfactory results have not been achieved[39]. Similar are the initial results of prostaglandin therapy. Previously used therapy with zinc sulfate is now practically abandoned.

Sclerotherapy involves injecting hypertonic or other agents into the venous vessel to induce local sclerosis of the vein, after which the entire limb is bandaged for 2-6 weeks[40]. The procedure is performed in strictly selected patients and should not be applied near the main, especially deep veins, to avoid thrombophlebitis, phlebothrombosis, thromboembolism, or skin necrosis. In recent years, endovenous ablation of insufficient branches using various (thermal, radiofrequency, laser) agents has been increasingly used[41].

Surgical treatment involves performing various procedures on incompetent superficial, deep, and perforating (communicating) veins. It is carried out according to strict indications to be directed towards the incompetent system. Operations should be performed systematically, patiently, and completely to prevent complications (intraoperative nerve and lymphatic injuries, extensive hematomas, etc.) and varicose ulcer disease recurrences[42-44].

Around 30-50% of patients with venous ulcers have only superficial vein disease[45, 46]. The surgical treatment for such patients consists of performing a saphenofemoral junction ligation and stripping of the superficial vein trunk, as well as the excision of varicosities (Babcock-Trendelenburg operation). In addition to surgical ligation of the junction and tributaries in the saphenofemoral region, radiofrequency or laser ablation is increasingly being used, while taking precautions to prevent thromboembolic complications. Perforator incompetence is often present in patients with damaged superficial main trunks ($C_{5\text{-}6}$EpsAspPr classification)[46, 47]. Disruption of pathological reflux through incompetent communicant veins (Cockett, Dodd, Boyd and others) can be performed above the fascia (Stenton, Sherman, Luke, and Myers procedures), at the level and below the fascia (Cockett's operation), or below the fascia with medial (Linton's operation), posterior (Dodd's operation), lateral (Felder's operation), or extensive (Sherman's operation) approaches. Subfascial blind dissection (Bassi, Cigoraga, Albanese, Edwards[48] with the introduction of a specially modified phlebotom in our case[7, 18]) is similar to endoscopic ligation of perforators. However, most of these procedures have been replaced by simpler approaches after preoperative precise ultrasound marking, which allows surgical access to perforators through small skin incisions. Such subfascial ligation of perforators leads to favorable immediate and long-term results[7, 18, 46-48] (image 3).

Image 3. Venous ulceration in the region of the medial malleolus healed after multiple ligations of perforators at and below the fascia



Surgical treatment of DV ulcers (C_{5-6}EpsAdpPro classification) is achieved through different methods: direct and indirect valvuloplasty, interposition and transposition of venous trunks (saphenopopliteal and other anastomoses), femoro-femoral reconstruction (de Palma reconstruction), safenofemoral[48-50] and other reconstructive procedures[51] with or without temporary arteriovenous fistulas[3, 7].

The analysis of the original long-term results (1-10 years) of surgical treatment of CV (58 patients) and DV (17 patients) showed a similar incidence of recurrence of venous ulcers: 9 (15.5%) for CV and 3 (17.7%) for DV[7]. However, significant recurrence of varicose veins was also observed: 14 (24.1%) for CV and 3 (17.7%) for DV, as well as persistent hyperpigmentation and edema. Surgical treatment of CVI and venous ulcers resulting from changes in superficial and/or perforator veins is associated with good immediate results[3]. Although these methods lead to improvement of the muscle pump and healing of venous ulcers, these procedures are becoming increasingly rare due to poor long-term results[3, 7]. Interventions in the deep system due to venous hemodynamics are prone to early and late complications, so these methods are being abandoned more and more. The occurrence of a high rate of thrombosis after surgical corrections of reflux or obstruction of deep veins have been shown, so these surgical techniques are increasingly rarely used even in specialized centers[3, 7, 51]. Endovascular procedures (valvuloplasty, lumen dilatation, and stenting) of deep veins are increasingly being applied[52]. A better understanding of events at the level of microcirculation and macrocirculation allows for the examination of existing and new approaches to treatment, but ongoing monitoring of immediate and long-term results is necessary.

In summary, surgical treatment of patients with venous ulcers consists of operations on superficial veins (partial or complete stripping of the great saphenous vein or small saphenous vein), deep veins (bypass procedures, valvuloplasty, transposition of venous segments, etc.), and ligation of communicant (perforator) veins[53]. The basic premise in the treatment of CVI is to interrupt the pathological reflux of blood through incompetent perforators, which can be achieved by ligating perforators' suprafascially, at the level of the fascia, or subfascially. Color duplex scanning, precise preoperative localization of pathological reflux or obstruction, and determination of CEAP etiopathogenetic stage are prerequisites for the selection of the surgical method and good immediate and long-term treatment outcomes. Therefore, the choice of surgical procedure is often individualized for each patient. It is important to combine this treatment with other therapeutic modalities (graduated compression bandaging, medication therapy).

Conclusion

Venous ulcers represent the terminal stage of chronic venous insufficiency, which is a significant medical and socioeconomic problem. The risk factors for the development of venous ulcers are well-known, including age over 55, positive family history, obesity, congestive heart failure, bone and joint disorders of the lower leg, and static load. The clinical picture of these patients is complex, and the CEAP classification of the disease is used, which consider local clinical manifestations, etiology, anatomical localization, and pathophysiological findings. Significant microcirculatory and tissue changes occur in these patients. There are two types of venous ulcers: those caused by superficial and perforating vein insufficiency (C5-6EpsAspPr classification) and those caused by deep vein reflux or occlusion (C5-6EpsAdpPro classification), which are accompanied by a more severe clinical picture and the appearance of anaerobic metabolites. Diagnosis and differential diagnosis are established based on medical history, clinical findings, and the use of color Doppler ultrasound as well as

Doppler index measurements, and rarely other procedures. Treatment of venous ulcers requires the use of different therapeutic modalities, including local and general measures, compression bandaging, medication, and surgical therapy. Favorable immediate and long-term treatment outcomes can only be achieved through a multidisciplinary approach and respect for the specifics of each patient.

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Declaration of interest statement: None

Received: 26. 02. 2023.
Accepted: 04. 03. 2023.
Online: 01. 06. 2023.