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REVIEW ARTICLE

Possibilities of modern radiological modalities in the diagnosis of complicated diabetic foot syndrome

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ABSTRACT

The issue of establishing the diagnosis and differential diagnosis of diabetic foot syndrome (DFS), including at the early stages, is of great relevance, which can be achieved by expanding information on current trends in the visualization of this frequent and severe complication of diabetes mellitus. The authors analyzed, systematized and summarized the modern pilot data on the use of high-tech medical imaging methods in DFS mainly over the past 7 years. An expert analytical assessment of the possibilities of molecular pathogen-specific visualization of pathological processes in DFS using modern methods of SPECT and PET is given. To solve the fundamental and applied aspects of diagnosing DFS, the possibilities of using high-energy radionuclides in bacterial infection were analyzed. The most important literature data of foot perfusion in patients with diabetes mellitus and limb ischemia using new modalities of MRI and hybrid diagnostic methods (SPECT/CT and PET/CT) are systematized, which contributes to a new understanding of the response to revascularization and healing of foot ulcers. This article is aimed at substantiating the multiparametric approach for DFS, as well as the selection, development and implementation of innovative diagnostic strategies in diagnosing DFS and its complications as part of the development of personalized medicine.

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INTRODUCTION

Diabetic foot syndrome (DFS) at the present stage is not only a medical but also a social problem due to its increasing prevalence, early disability, high mortality and serious economic costs [1]. The pathogenesis of DFS includes two mutually aggravating links - angiopathy and neuropathy, contributing to the development of ulcerative-necrotic lesions in about 15% of patients and the addition of an infectious inflammatory process of soft tissues and bones in half of the cases [2]. Charcot osteoarthropathy with or without concomitant infection is another complication of DFS, accompanied by an imbalance in the activity of osteoblasts and osteoclasts and the initiation of intense osteolysis, which also causes irreversible disability [3].

The duration of treatment for patients with a complicated course of DFS is long, and the prognosis and treatment are difficult, since 80% of patients are hospitalized as part of emergency care in the on-duty surgical department at the stage of pronounced and irreversible clinical and morphological changes [4]. In addition to frequent relapses, osteomyelitis, which develops when infection of the soft tissues of the feet is not detected in time, is the main cause of amputations of the lower extremities in patients with DM [5]. The high cost of treating patients with complicated DFS and significant costs due to disability require the use of diagnostic methods that effectively and accurately distinguish soft tissue infection from osteomyelitis and Charcot foot, including the early stages, and allow assessing the therapeutic response and prognosis recovery [6].

Identification of the complicated course of DFS is carried out using radiological and laboratory research methods. Although the gold standard for diagnosing infection in DFS is still isolation of the pathogen by bone biopsy or ulcer cultures, these approaches are often invasive and carry the risk of sample contamination. Therefore, imaging plays a crucial role in diagnosing an infectious process and assessing its prevalence, providing important information for choosing a patient treatment strategy [7]. A wide range of modern radiological modalities should provide accurate and timely detection of foot pathogenetic processes, as well as identify emerging complications [6]. However, the problem of radiological diagnostics of the complicated course of DFS remains relevant. Thus, significant difficulties arise in the differential diagnosis of neuropathic disorders and purulent-necrotic processes, including the use of standard magnetic resonance imaging, which is considered by a number of authors as an informative technique [8]. The problem of topical diagnosis of inflammatory changes against the background of DFS using radionuclide diagnostic methods that determine functional changes in purulent-necrotic processes at the molecular level needs to be solved [6]. Along with the obvious problem of detecting intraosseous inflammation in patients with DFS, the importance of assessing the condition of the nerve trunks and blood flow in the feet is indisputable. Also of particular importance is the problem of early diagnosis of osteomyelitis in patients with DFS, which will contribute to effective and timely treatment, as well as disease prevention. This article will review and systematize the current data on visual methods for providing information about DFS and its complications, which will contribute to the solution of the above problems, as well as the selection of an appropriate therapeutic strategy for an individual patient with this syndrome.

DISCUSSION

Radionuclide diagnostics in DFS

Methods of radionuclide diagnostics are widely used to assess the feet in patients with diabetes mellitus with suspected purulent-inflammatory processes. From the point of view of nuclear medicine, the “gold standard” for visualization of infectious complications of DFS continues to be radiolabeled leukocyte (WBC) scintigraphy, provided that it is performed in accordance with the EANM recommendations. In 2018, the European Society for Nuclear Medicine (EANM) developed results interpretation criteria and study protocols to standardize the leukocyte labeling procedure. The availability of closed and disposable kits has simplified the separation and labeling of leukocytes, making all steps safer for the operator [9]. To visualize in vivo the physiological process of granulocyte migration to the site of infection, it is recommended to perform the study at three time points - 1 hour after injection, 3 hours (delayed image) and 20 hours (delayed image). In the case of osteomyelitis, the accumulation of radiopharmaceuticals on delayed images (20 hours) will be equal to or greater than the accumulation of radiopharmaceuticals in the area of interest on 3 hours images. Moreover, in the case of an aseptic inflammatory process, leukocyte hyperfixation on a delayed image will be lower than that of an early image. Calculations of the accumulation of the drug are made with a correction for the natural decay of ^{99m}Tc [10].

According to a review article by Lauri et al. the best set of indicators of diagnostic efficiency was demonstrated by scintigraphy with [^{99m}Tc]Tc-HMPAO-labeled leukocytes, the sensitivity of which is 91%, and the specificity is 92% [11]. Some authors note that scintigraphy with [^{111}In]In - oxime-labeled leukocytes is informative as a control of response to treatment. The infrequent use of this method is associated with a higher radiation exposure and lower availability, including economic factors. The diagnostic efficiency indicators of this technique do not differ significantly from the results obtained using [^{99m}Tc]Tc-HMPAO [12].

The advantages of scintigraphy with labeled leukocytes are low radiation exposure and high sensitivity, and the main reasons for the decrease in the specificity of this technique are low anatomical spatial resolution, as well as hyperfixation of labeled leukocytes at the site of an aseptic inflammatory process in patients with Charcot foot due to increased hemopathic activity of the bone marrow, secondary in relation to chronic inflammation. In addition, this method is not optimal for patients with reduced leukocyte counts [13]. To overcome these limitations, it is proposed to perform additional bone marrow scintigraphy using nanocolloids [9]. In the case of using a dual technique, two criteria for the diagnosis of OM in Charcot's arthropathy have been described: (1) capture of labeled leukocytes without corresponding activity on bone marrow scintigraphic images and (2) spatially incongruent distribution of two radiopharmaceuticals [9, 14]. In addition, an increase in the specificity of scintigraphy with labeled leukocytes is possible when combined with a modality that is highly informative in terms of imaging anatomical structures.

The effect of long-term antibiotic treatment on the sensitivity of leukocyte-labeled scintigraphy is still a matter of debate. A number of studies have shown that leukocyte-labeled scintigraphy retains high sensitivity and specificity while maintaining the inflammatory process, regardless of antibiotics. The optimal time to perform WBC scintigraphy after antimicrobial therapy is not clearly stated in the literature, but this diagnostic procedure is usually performed 2 weeks after the end of therapy. The literature data on therapy monitoring in DFS are based on small samples and do not allow to draw definite conclusions, but, judging by preliminary data, allow the use of radiolabeled leukocytes in this situation, even in the presence of false negative results [10, 12].

An alternative to radiolabeled leukocytes can be monoclonal antibodies (MoAbs) directed against specific antigens or antibody fragments (Fab) expressed by activated granulocytes. Due to the high molecular weight of whole antibodies, these methods have a number of disadvantages. Radiopharmaceuticals have a long half-life from blood plasma, limited distribution to the focus of the inflammatory process, and their nonspecific accumulation in inflamed areas of various origins has also been recorded. In addition, the role of monoclonal antibodies and Fab fragments in assessing the complicated course of DFS has not been widely studied, and at the moment there are no standardized protocols for collecting data and interpreting research results, and the world literature presents data mainly only on small groups of patients [9].

Due to the unique ability of bacterial molecular imaging to monitor the treatment of patients with DFS complicated by infectious processes, the latest research has been carried out to develop highly specific biomolecules and new agents. Ankrah et al. report on the evaluation of the results of using a number of isotope indicators in this category of patients, in particular: [^{18}F]F-FDS, [^{99m}Tc]Tc-UBI 29-41, [^{68}Ga]Ga-NOTA-UBI, which do not require manipulations with blood and are able to differentiate inflammatory and infectious processes with high specificity [15]. However, further evaluation of the sensitivity of these agents in larger clinical trials is required, especially in chronic infections with lower bacterial load [16].

Scintigraphy with labeled antibiotics can visualize the infectious process, as well as differentiate between septic and aseptic inflammation, however, when analyzing this method in patients with DFS, ambiguous results have been obtained. The most commonly used radionuclide-labeled antibiotic is ciprofloxacin, however, this drug ([^{99m}Tc]Tc-ciprofloxacin) has lower diagnostic performance compared to radiopharmaceuticals with labeled leukocytes, which is probably due to a non-specific accumulation mechanism. Therefore, and due to some inconsistencies in its synthesis procedures and lack of beta-lactamase activity, [^{99m}Tc]Tc-ciprofloxacin, which is specific for bacterial imaging, has not yet been used in the clinical setting. Also, the disadvantage of this drug is its accumulation in dead bacteria, which leads to the appearance of false positive results [6]. However, Kozminski et al., after synthesizing and evaluating the physicochemical and biological properties, consider the combination of ciprofloxacin with [^{68}Ga]Ga-DOTA to be promising for creating a radiopharmaceutical suitable for diagnosing DFS using PET, a technique characterized by higher sensitivity, spatial and temporal resolution [17].

In 2019, a group of researchers led by Ahmed N. published the results of labeling with [^{99m}Tc]Tc-ceftizoxime, a third-generation cephalosporin with a broad spectrum of action compared to ciprofloxacin [13]. The applied antibiotic did not change its properties after the labeling procedure and showed its effectiveness in a small sample of patients with osteomyelitis of the feet in comparison with classical scintigraphy with [^{99m}Tc]Tc-methyldiphosphonate. The authors note the prospects for further study of the resulting radiopharmaceutical based on ceftizoxime and plan to evaluate the diagnostic efficiency of the method in a larger sample of patients [13].

Several radiolabeled antibiotics have been studied to date, but the least studied are inhibitors of bacterial cell wall synthesis, such as the 99mTc SPECT indicator vancomycin, which has shown affinity for S. aureus infectious foci. [^{99m}Tc]Tc-vancomycin labeled with [^{99m}Tc]Tc-HYNIC confirmed this observation with a threefold increase in uptake at the site of S. aureus infection compared to control. Studies using fluorescently labeled vancomycin have also shown promising results, although isotopically labeled vancomycin has a high absorbance [18]. A SPECT radiopharmaceutical containing this antibiotic may be of value in the clinical management of complications of DFS, and the development of an indicator for PET with vancomycin may provide better image resolution [6].

Identification of the pathogen or multiple pathogens causing infection in DFS and their antibiotic susceptibility is very important for selecting appropriate antimicrobial therapy, especially when multidrug-resistant organisms are likely to be present. However, one recent publication indicates that PET imaging using radiolabeled antibiotics has not yet been investigated in the context of diagnosing DFS. Because infections and other conditions can alter drug metabolism, and infection-related inflammatory responses and critical ischemia can interfere with antibiotic penetration, the authors suggest using antibiotic-labelled PET in patients with purulent inflammation associated with DFS to assess drug penetration at the site of infection, which could increase the effectiveness of the treatment of this pathology [16].

Hybrid methods of radiological diagnostics and positron emission tomography in DFS

A method useful according to Ahluwalia et al. for functional and structural imaging, both in suspected osteomyelitis of the foot and in the evaluation of patients with suspected Charcot foot, is SPECT/CT, since even at stage 0 Charcot foot there is bone pathology that requires appropriate emergency treatment [19]. However, a broader prospective approach is needed to study SPECT/CT as a method for identifying predictors of Charcot foot formation, especially considering the advantages over MRI in detecting fractures and cysts, as well as in those patients with contraindications to MRI [10].

Vouillarmet et al. reported on the use of WBC-labeled SPECT/CT to predict remission after a 6- or 12-week course of antibiotic therapy in the case of conservative treatment of foot osteomyelitis in DM [20]. It is clarified that if after 6 weeks of taking antibiotics, there were no clinical signs of inflammation in the foot and the SPECT / CT scan is negative, there would be no recurrence of the disease in the next 12 months. The ability to predict the absence of a probable recurrence as soon as possible using this hybrid technique will avoid unnecessary long-term use of antibiotics. These results suggest that scanning with [^{99m}Tc]Tc-HMPAO-labeled leukocytes can accurately predict remission near the end of antibiotic treatment. Moreover, based on reports using [^{111}In]In-labeled leukocytes, this scanning procedure appears feasible for monitoring the response of patients with osteomyelitis in DFS to antibiotic therapy over time, as abnormal scans turn to normal within two to eight weeks of successful initiation of antibiotic therapy [6]. However, Jeffcoate etal., based on a number of publications in 2016-2017 on comparing the effectiveness of clinical and diagnostic (instrumental) monitoring of the condition of patients with complicated DFS, notes that the use of this hybrid technique can be overestimated, and the method itself, even with increased use, does not have a great impact on everyday clinical practice [21].

[^{18}F]FDG PET provides non-invasive 3D imaging of the feet with higher spatiotemporal resolution and high sensitivity compared to SPECT and MRI [22]. Although coexisting conditions such as hyperglycemia and peripheral arterial disease and the use of antibiotics make direct comparisons difficult, some preliminary studies suggest that mild hyperglycemia does not affect the diagnostic performance of [^{18}F]FDG [23]. The disadvantage of the method is low specificity: PET cannot differentiate between infection (e.g., osteomyelitis), neoplastic process, or aseptic inflammation (eg, Charcot's foot). In addition, glucose uptake may remain impaired for 3–4 months after surgery or injury [16].

Ruiz-Bedoya et al. note that molecular imaging of the bacterial class at the site of infection facilitates the selection of appropriate empiric antimicrobial therapy [16]. A drug similar to [^{18}F]FDS (^{18}F-

fluorodeoxysorbitol), which selectively targets the Enterobacteriales group of bacteria, according to the authors, can be used in combination with a broad-spectrum imaging marker (for example, ^{11}C-para-aminobenzoic acid) for PET indication of infection and differentiation of gram-positive and gram-negative bacteria. However, these molecular imaging techniques have now been tested in animals and, in the case of [^{18}F]FDS, in a group of healthy volunteers. Their use in DFS complicated by infectious processes is considered as a perspective for PET imaging.

Most agents for imaging infection in DFS are still in preclinical testing. A significant part of the developed indicators are labeled with ^{99m}Tc, but given the advantages of PET over SPECT imaging, it is recommended to study and develop PET equivalents of indicators that are potential for imaging infectious agents. Thus, by using new labeling options, there is the potential to replace ^{99m}Tc with ^{18}F in most indicators at the preclinical level. The use of radiometals, such as the one produced by the ^{68}Ga generator, offers more possibilities for labeling, especially peptides. Radioisotopes with longer half-lives, such as ^{64}Cu and ^{89}Zr, can also be a good alternative for labeling peptides currently labeled with ^{68}Ga. These relatively longer-acting radioisotopes will enable delayed imaging, which is a requirement for imaging infections, including DFS. The half-life of ^{64}Cu is 12.7 hours, but its use in clinical practice is limited due to the difficulty of producing this radioisotope. ^{89}Zr's long half-life of 78 hours also makes it an attractive label for large proteins such as antibodies, but the diagnostic value must be balanced against the radiation burden the patient is exposed to with the long-lived radioisotope. Radioimmunotherapy with antibiotics using nanoparticles labeled with new isotopes for drug delivery may offer new opportunities, in particular to reduce the duration of antibiotic therapy and to target resistant microorganisms [15].

In recent decades, hybrid technology such as [^{18}F]FDG-PET/CT has gained an important role in the diagnosis of infection and inflammation, since [^{18}F]FDG has several advantages over classical scintigraphy, especially in the evaluation of the forefoot. Most of the available publications demonstrate the diagnostic advantages of [^{99m}Tc]Tc-HMPAO-labeled leukocyte scintigraphy compared to hybrid diagnostic methods, which has led to recommendations for the use of PET/CT only as an alternative to leukocyte-labeled scintigraphy, especially when it cannot be performed, as well as attempts to creation of specific radiopharmaceuticals for labeling leukocytes with subsequent use in PET/CT [24]. Although it is noted that [^{18}F]FDG-PET/CT is still an alternative to scintigraphy, nevertheless, data from the literature show conflicting results, mainly due to the lack of unambiguous criteria for the interpretation of PET images, which is often carried out based on personal experience researcher without standardization of this hybrid technique, which affects the differences in the indicators of diagnostic efficiency of the method obtained by different scientific groups [7, 10]. Thus, some authors note the lower sensitivity of the hybrid technology in diagnosing a complicated course of DFS compared to MRI, while the specificity and accuracy of the PET/CT are significantly higher than magnetic tomographic indicators [25, 26]. Moreover, there are still many concerns about the criteria for interpreting [^{18}F]FDG-PET/CT performed during antibiotic therapy, especially when comparing a scan with a baseline study to assess the effectiveness of treatment [7].

When performing [^{18}F]FDG-PET/CT, a semi-quantitative analysis of the maximum standardized absorbance value (SUVmax) is promising. Therefore, Lauri et al. report statistically significantly higher SUVmax values in the presence of osteomyelitis in DFS compared to the same indicator in the presence of Charcot foot and uncomplicated DFS, which indicates the significance of the SUVmax parameter for the differential diagnosis of these pathological processes [14]. Although Diez et al. also concluded that the SUVmax indicator can be a useful parameter for differentiating pathological processes in the foot in DM, some authors did not find statistically significant differences when comparing this indicator in patients with Charcot foot and osteomyelitis and believe that its role for evaluation of inflammation therapy is still unclear [7, 25]. Such conflicting data may be due to practical and technical factors, as well as the lack of standardization in the definition of this quantitative parameter. Thus, the literature data are not sufficient to address the issue of introducing a quantitative assessment of the maximum standardized absorption value into a wide clinical and diagnostic practice for the differential diagnosis of a complicated course of DFS. While assessment of CT data simultaneously with PET is useful for accurate anatomical localization of the pathological process in the bones of the feet, it does not provide the necessary information about soft tissues and does not fully resolve the issue of differential diagnosis.

A common disadvantage of SPECT/CT and PET/CT is the higher cost of diagnostic equipment, while noting a significant reduction in the cost differential between SPECT and SPECT/CT in recent

years. In addition, the disadvantages of hybrid techniques, which were identified in the study of patients with DFS, today include difficulties in combining the distal parts of the feet associated with the small size of the metatarsal bones and toes, as well as the impossibility of an adequate assessment of soft tissue structures and bone marrow [14]. Patients receiving an additional dose of radiation is not currently considered a significant obstacle to the introduction of hybrid techniques for examining the condition of the feet, since the additional level of radiation when using low-dose CT techniques usually fluctuates around 0.1 mSv.

With the development of hybrid techniques, some publications began to appear on the possibilities of using PET/MRI in assessing the state of the bone marrow and the possibility of monitoring the course of the disease in patients with DFS with the subsequent prospect of solving the problem of differentiation of soft tissue structures [25, 27]. A number of authors believe that PET/MRI, compared with PET/CT, can potentially improve the accuracy of diagnosing a diabetic foot infection by improving the differentiation of osteomyelitis proper and soft tissue infections [7, 24]. To date, there are SPECT/MRI machines for animal studies and work is underway to create hybrid SPECT/MRI systems for use in clinical practice. Along with the high resolution of PET/MRI, these devices have a potential advantage in the case of the creation of multimodal contrast agents, in which paramagnetic and radioactive labels will be simultaneously combined with a pharmaceutical agent.

The development of PET indicators for use in PET/MRI opens up wide opportunities for visualization of foot infections, for pre- and intraoperative evaluation of the complicated course of DFS requiring surgical intervention, which can become an effective visualization tool for these patients from a metabolic and anatomical point of view [15].

There is also the potential for any hybrid volume imaging and SPECT/MRI in particular using workstation software as well as free software. In publications on the use of programmatically combined SPECT/MRI, high diagnostic indicators of the studied technique are noted, which were further confirmed by comparison with other diagnostic modalities. The disadvantage of the technique was the impossibility of accurate alignment of the distal parts of the feet, which in the future can be eliminated by combining SPECT/CT and MRI, where CT data will be used as anatomical landmarks [28].

A few foreign articles describe various approaches to the quantitative/semiquantitative assessment of visual data in patients with DFS and the creation of clinical diagnostic scales. So, a variant of the scoring system is presented by Meacock et al. with data from a study of patients with Charcot foot who underwent MRI to identify the presence and severity by visualizing the prevalence of the process of this disease. The presented semi-quantitative scale was based on such MRI findings such as bone marrow edema and the presence of a fracture of the affected bone. However, the authors note that further research is needed to establish this scoring system as a clinical tool for monitoring treatment and evaluating outcomes in this category of patients [29].

In diagnostic practice, Udodov et al. (2018) patented and described in the dissertation work a scoring system for assessing programmatically combined SPECT/MRI in patients with DFS and suspected osteomyelitis, which at this stage is the only one of its kind. This scoring system includes a number of MR symptoms of inflammatory processes in DFS and two radionuclide symptoms based on the results of scintigraphy with labeled leukocytes. Based on the results of the ROC analysis, a threshold value for the presence of osteomyelitis in the presence of DFS was obtained with a total score of existing visual symptoms of more than 12. This quantitative criterion is highly specific and sensitive (Se=95.5% Sp=100.0%, AUC=99.5%) and may become promising in the clinical diagnostic evaluation of feet in patients of this category.

Radiological diagnosis of the state of foot perfusion in DFS

A significant problem in patients with DM is endothelial dysfunction and capillary microangiopathy, which develop as a result of impaired tissue perfusion. These phenomena can lead to critical ischemia with a high incidence of lower limb amputations and high mortality [16, 30]. An important solution for targeted treatment of ischemic non-healing foot ulcers is the angiosomal theory of foot blood supply [31]. The results of a comparative study of direct (angiosome directed) and indirect (nonangiosomal) revascularization showed that the former can lead to a significantly higher rate of wound healing and a decrease in the risk of large limb amputations in patients with peripheral arterial disease (PAD) [30].

Evaluation of microcirculatory blood flow in the affected limb segments using quantitative indicators can be performed using CT perfusion, however, the limitations of the method are radiation exposure and the use of an iodine-containing contrast agent, which can cause an allergic reaction and is not always indicated in

patients with chronic kidney disease in diabetes [32]. PET and SPECT/CT, taking into account the angiosome theory, provide new approaches to accurately determine ischemic and viable areas in the lower extremities, to monitor the response of treatment with various methods of revascularization, and to determine the level of limb amputation [16].

Perfusion imaging by SPECT/CT using [^{99m}Tc]Tc-tetrofosmin is described in detail by Alvelo et al. The method allows assessing the qualitative and quantitative characteristics of foot microcirculation at rest, revealing perfusion defects in areas containing non-healing foot ulcers in patients with PAD and critical lower limb ischemia [30]. The lack of correlation between [^{99m}Tc]Tc-tetrofosmin uptake and the ankle-brachial index (ABI) in diabetic patients suggests that perfusion SPECT/CT imaging may be more sensitive than standard instrumental screening for PAD in diabetic patients. It should be noted that [^{99m}Tc]Tc-sestamibi, used mainly in cardiology, also showed high informative value and certain advantages at the preclinical and clinical levels of the study in the diagnosis of PAD and is considered as an alternative to [^{99m}Tc]Tc-tetrofosmin in future. While the relationship between SPECT/CT perfusion imaging and ankle-brachial index (ABI) has been assessed in the current work, the relationship between SPECT/CT and other measures, such as the index between the big toe and the shoulder region and transcutaneous oxygen pressure, should be evaluated in the future to establish the clinical relevance of the described imaging approach [30]. Summing up their research, Alvelo et al. pointed out that the use of SPECT/CT imaging to assess tissue perfusion in 3D angiosomes of the foot indicates a high potential for radionuclide imaging to improve the initial assessment of microvascular diseases in patients with PAD, which is especially important for patients with DM and critical limb ischemia [30]. The disadvantages of assessing perfusion of the diabetic foot using SPECT, however, include the impossibility of directly indicating the infectious process [16].

Chou et al., independently of previous scientists, developed and published a clinical imaging protocol in 2020, which also shows the potential of using hybrid SPECT/CT for vascular imaging of the feet in critical ischemia [33]. Using a hybrid method, data on tissue perfusion after revascularization were obtained, which were compared with the results of X-ray angiography, changes in the hemodynamics of the lower extremities based on ABI and toe-brachial indices (TBI). The authors concluded that it is reasonable to use SPECT/CT to quantify 3D angiosome perfusion in patients with DM and critical limb ischemia during planned lower limb revascularization as an additional method in relation to standard modalities, since ABI and TBI cannot assess perfusion based on concept of 3D angiosomes, and SPECT/CT allows one to consistently assess the perfusion response to peripheral angioplasty within the 3D angiosome of the foot containing a non-healing ulcer and intended for revascularization [33].

CONCLUSION

As the prevalence of diabetes mellitus increases, diabetic foot syndrome and its complications become a frequent clinical problem. Delay in making an accurate diagnosis contributes to an increase in patient complications, including non-traumatic amputations of the lower extremities. The complex pathophysiology of this disease and the suboptimal specificity of basic non-invasive imaging modalities make it difficult to diagnose its complications and respond to treatment. Key questions regarding the diagnosis of foot infection, its location and spread, type of pathogen, and response to treatment are still not fully resolved, as the accurate identification and differentiation of different types of DFS continues to be a challenge for clinicians. Moreover, current strategies for anatomical and molecular clinical imaging mainly target the patient's immune responses, without taking into account the assessment of the metabolism of the invading microorganism. Advances in imaging may lessen the impact of these problems and improve the evaluation of DFS. Systematized in this article, special methods for providing valuable information about DFS and its complications will contribute to a better understanding of the course of this disease and will allow planning the most appropriate clinical diagnostic strategy within the framework of personalized medicine.

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