

# POSTTRANSPLANT DIABETES MELLITUS. CASE REPORT OF A PATIENT WITH DIABETIC FOOT AFTER A HEART TRANSPLANT

## Potransplantačný diabetes mellitus. Kazuistika pacienta s diabetickou nohou po transplantácii srdca

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### Abstract

Heart transplant represents a vital surgery and an established treatment for patients with an end-stage heart failure. However, is accompanied by many associated complications, of which posttransplant diabetes mellitus (PTDM) and its complications are very important and frequent. We present the case of a patient suffering from diabetic foot caused by PTDM successfully treated by multidisciplinary cooperation (Fig. 8, Ref. 10). Text v PDF [www.lekarsky.herba.sk](http://www.lekarsky.herba.sk).

**KEY WORDS:** heart transplant, posttransplant diabetes mellitus, diabetic foot.

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### Abstrakt

Transplantácia srdca predstavuje životne dôležitú operáciu a zavedenú terapiu pre pacientov s konečným štádiom srdcového zlyhávania. Sprevádzajú ju mnohé pridružené komplikácie, z ktorých je veľmi dôležitý a častý potransplantačný diabetes mellitus (PTDM) a jeho komplikácie. Prezentujeme prípad pacienta s diabetickou nohou, spôsobenou PTDM, úspešne liečenou multidisciplinárnou spoluprácou (obr. 8, lit. 10). Text v PDF [www.lekarsky.herba.sk](http://www.lekarsky.herba.sk).

**KLÚČOVÉ SLOVÁ:** transplantácia srdca, potransplantačný diabetes mellitus, diabetická noha.

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### Introduction

Solid organ transplantation is often followed by PTDM. Furthermore, the majority of recipients after the transplantation are present with impaired glucose tolerance during hospitalization. The pathophysiological mechanism is different from diabetes mellitus (DM) type 2. The risk factors of PTDM development correlate with preexisting diabetes risk (age >40, Body Mass Index >25 kg/m<sup>2</sup>, Hepatitis C Virus infection, non-caucasian ethnicity, family history of DM and metabolic syndrome). However, the major role is attributed to immunosuppressant medications whereas the variation between the regimen, emphasis on high-dose steroids, is associated with the highest incidence rates (1).

Long-term survival rate has improved significantly, mainly due to advanced immunosuppressive regimens now available. However, their diabetogenic effects contribute to the increase in the incidence of PTDM.

International Society of Heart and Lung Transplantation (ISHLT) Registry states the prevalence of DM to be 23% at one year increasing to 37% at 5 years after heart transplant (2).

The goal of this case report is to highlight the importance of prevention of PTDM. Patients after heart transplantation are fragile and hard to manage. Mortality risk is twice as high in transplant recipients with pre-existing and post-transplant diabetes compared to patients without it (3). In order to prevent PTDM, use of insulin in the immediate postoperative period is advised as it was associated with a 73% lower probability of developing PTDM (4).

We present the case of a polymorbid patient suffering from right foot little finger wet gangrene. Patient was managed promptly and after almost a year of treatment the wound is healed, and patient's state improves day by day.

### Case report

The patient is a 69 year old polymorbid man suffering from biventricular heart failure NYHA class III; grade 3 arterial hypertension, type 2 DM with multi-organ complications, stage 3 chronic kidney disease, chronic obstructive pulmonary disease GOLD 2B, cholelithiasis, hypothyroidism, peptic ulcer disease, hyperuricemia, exogenous obesity (current BMI 48 kg/m<sup>2</sup>, at time of transplantation 36 kg/m<sup>2</sup>), hyperlipoproteinaemia, chronic venous disease of the lower extremities, with a history of left common and superficial femoral vein thrombosis and deep proximal profunda femoral and popliteal vein thrombosis. He is a former smoker, started smoking in 1975, 20–30 cigarettes daily, stopped smoking after heart transplantation.

Initially, he had multiple risk factors predisposing to heart transplantation, including coronary artery disease, extensive anterior myocardial infarction, heart failure with reduced ejection fraction, atrial fibrillation, implantable cardioverter-defibrillator, all of which led to heart transplantation in April 2010. The initial medications for the heart transplant included high-dose corticosteroids, mycophenolate mofetil and cyclosporine. Subsequently, DM was newly diagnosed in October 2010, the patient was treated with dietary therapy, later with antidiabetic agents with transition to insulin in 2015, currently on intensified insulin therapy.

The patient has a history of a healed left foot defect but presents to emergency department of the University Hospital on April 29<sup>th</sup>, 2023, with a right foot defect. He is unable to state the time of the foot trauma or the approximate duration of the defect. He is aware of oedema and pain progression, fever and is being treated with peroral antibiotics (lincosamides) by his general practitioner. On admission to surgical clinic, the patient's CRP level is 229.42 mg/L, creatinine 257.5 µmol/L, leukocytes 12.65x10<sup>9</sup> cells/L, haemoglobin 92 g/L. Objectively, there is a localised oedema of the right foot with phlegmon of the foot and forelimb, necrosis of the fifth metatarsal on the lateral side of the foot, wet gangrene of the fifth finger and no pulses of the posterior tibial and dorsalis pedis arteries (PTA, DPA). We decide to perform a right foot x-ray (Fig. 1), which shows osteomyelitis of the fifth metatarsal and the proximal phalanx of the fifth finger.

A cardiologist of transplant centre is contacted due to surgery planning, and it is recommended that immunosuppressive medication be stopped during the stay at the surgical clinic. Oral antibiotics are changed to intravenous antibiotics, the patient receives a blood transfusion. After that, on 30<sup>th</sup> April, the fifth ray amputation was performed in foot block anaesthesia with two abscess cavities on the sole, a sample was taken for microbial culture (result: *Enterococcus faecalis* + *Proteus mirabilis* + *Morganella morganii*), two incisions were made with pus drainage, a surgical glove drain was inserted, perioperatively the patient received one blood transfusion.

Figure 1. Osteomyelitis of the fifth metatarsal and proximal phalanx of the fifth finger.



After surgery, the patient's general condition slowly worsens, inflammatory markers elevate, the stump does not heal adequately. Technique imaging methods are performed. Colour Doppler ultrasound of right lower limb (Fig. 2) shows calcified plaques of common and superficial femoral artery (CFA, SFA) which do not significantly invade the lumen, medial calcinosis of the forelimb. Triphasic spectral waveforms of CFA, SFA, popliteal artery (PA), biphasic spectral waveforms of PTA, DPA are present. There is no significant stenosis of the right lower limb arteries. Ankle brachial index is limited due to mediocalcinosis, toe brachial index is not performed due to technical issues. Venous Duplex ultrasound shows no obstruction in deep venous system, no insufficiency in superficial venous system of the right lower limb, but past femoral vein thrombosis of the left lower limb, superficial femoral vein with partial recanalization. Digital subtraction angiography is not performed due to high levels of creatinine.

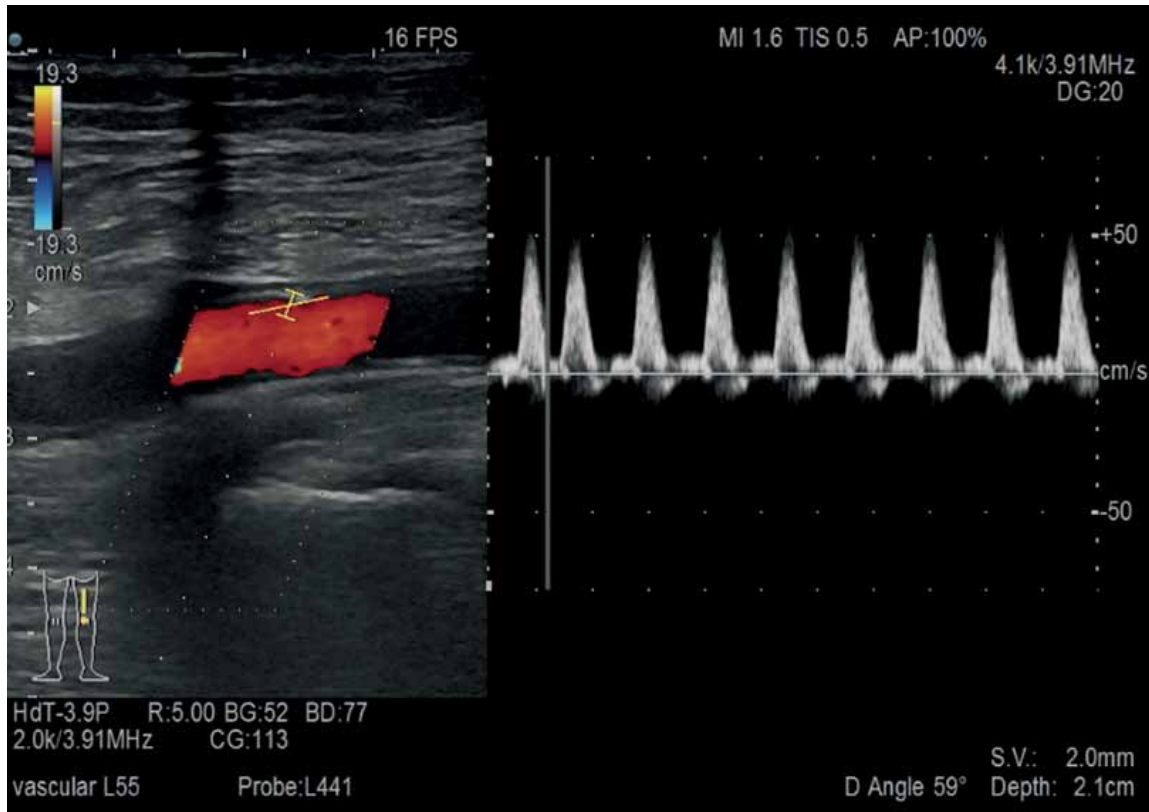
After these methods transmetatarsal amputation is indicated and then performed on 4<sup>th</sup> May (Fig. 3).

Residual limb heals as expected with no post-operative complications (Figs 4, 5), treated with dermal cream (sodium hyaluronan, silver sulfadiazine salt-sodium lauryl sulfate) and bandage.

On 16<sup>th</sup> May, the patient has a fever, shortness of breath, Ag-Covid test is performed with positive result. Pneumologist prescribes the medication for Covid-19 disease (Remdesivir), Chest X-ray is performed (Figs 6, 7).

When Covid-19 disease is cured, patient is stable, wound heals, the department of burns and reconstructive surgery is contacted, reconstructive surgeon recommends continuing in topical medication with his regular check-ups for future skin autotransplantation. On 25<sup>th</sup>

Figure 2. Color Doppler ultrasound of right lower limb.



May, the patient is discharged to the outpatient care of the transplant center including the management of immunosuppression.

The wound is closed with skin graft in October 2023, regularly being bandaged with dermal cream. Patient rehabilitates, starts walking again as prior to amputation, feels minimal pain and uses his immunosuppressive medication. When contacted in February 2024, the wound is healed (Fig. 8), although he feels weak and walks less than before the amputation.

Figure 3. Patient after transmetatarsal amputation.



Figure 4. Residual limb May 9<sup>th</sup>.



## Discussion

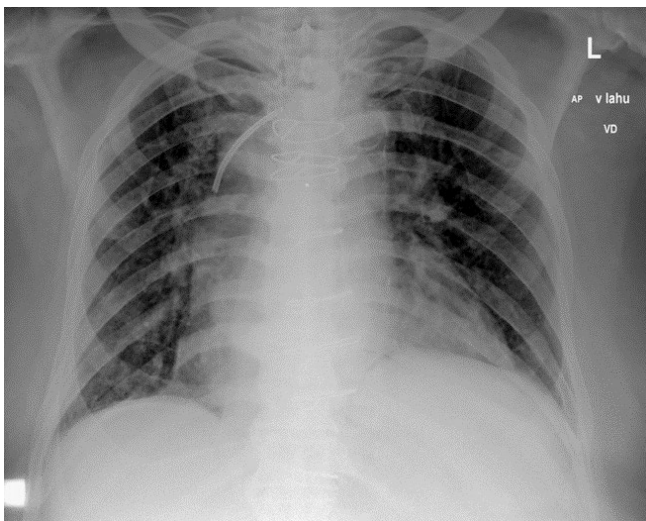
Diabetes mellitus may occur either pre-heart transplantation or as new-onset DM post-HT. PTDM has been recognized as a major complication of solid organ transplantation as it increases the risk for graft failure. High doses of immunosuppressants administered soon after transplantation to prevent acute rejection cause hyperglycemia and together with other risk factors, lead to PTDM. New-onset PTDM is common among heart transplant recipients and has been shown to be asso-

ciated with higher rates of renal dysfunction and death or re-transplantation (5, 6).

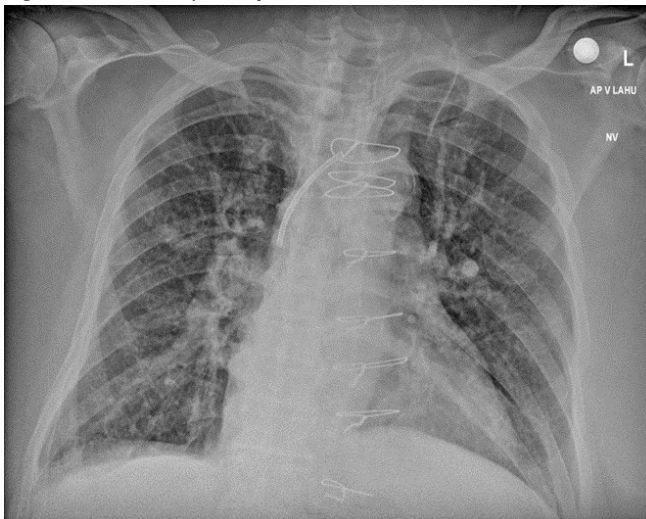
**Figure 5. Residual limb May 17<sup>th</sup>.**



**Figure 6. Chest X-ray when admitted.**



**Figure 7. Chest X-ray with positive Covid test.**



**Figure 8. Healed wound.**



As transient insulin therapy acts against hyperglycemia and improves  $\beta$ -cell function, Hecking et al. assessed whether basal insulin treatment postoperatively may be an effective strategy to control hyperglycemia in previously non-diabetic patients. They found 73% reduction in the odds of PTDM at 1 year (4).

Min Soo Cho et al. found out PTDM to be reversible in one-third of patients. The patients used insulin and/ or peroral antidiabetics. The most distinguishing and statistically significant characteristic was the time of PTDM development. Only early onset of PTDM, meaning less than 6 months from transplantation, was reversed (7).

DM is associated with macro and microvascular changes that can manifest in many ways, foot lesions being one of them. Diabetic foot ulcer (DFU) are rarely the results from a single pathological factor. To prevent diabetic foot and its complications, it is essential to know and understand the risk factors that put patients at high risk of ulceration. In addition to the benefits to patients and their quality of life, there are potential economic benefits to be gained from preventive strategies. The lifetime risk of a patient with DM developing a foot ulcer is estimated to be as high as 25% (8). Infection complicates over half of all DFUs with many patients eventually requiring some degree of amputation (9). Majority of all amputations caused by DM are preceded by DFU.

However, only a small number of studies have investigated PTDM after heart transplantation and its impact on possible development of diabetic foot. The existing studies are limited by small numbers of patients.

The incidence of DFU is greater in patients with DM and simultaneous chronic kidney disease. Wolf et al. demonstrated a negative correlation between DFU and estimated glomerular filtration rate. For every 10 ml/min increase in estimated glomerular filtration rate the odds for developing DFU decreased by 13% in patients with DM type 2. Dialyzed patients have even higher risk of amputation (10).

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## Conclusion

The diabetogenic effects of immunosuppressants are well known. The immunosuppressive regimen is recommended to be determined based solely on the best outcome for overall patient and graft survival, irrespective of PTDM risk (11). Studies show that the use of insulin in the immediate post operative period may reverse PTDM. This finding is important because long-term survival after a heart transplant has improved significantly in modern times. However, patients begin to suffer from the long-term consequences of heart transplantation, such as DFU. Preventing PTDM is therefore beneficial for patients' quality of life, but also for society in economic terms.\*

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**\*Compliance with Ethics Requirements:** The authors declare no conflict of interest regarding this article. The authors declare, that all the procedures and experiments of this research respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008 (5), as well as the national law.

**Conflict of interest:** The authors declare no conflict of interest.

**Informed consent:** Informed consent was obtained from all individual participants included in the study.

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