

EFFECTIVENESS OF THE FAST-TRACK PATHWAY FOR THE MANAGEMENT OF PATIENTS WITH DIABETIC FOOT THROUGH THE NETWORK BETWEEN SECOND AND THIRD LEVEL CENTERS

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ABSTRACT

Diabetic foot is one of the most serious and expensive complications of diabetes. It requires prompt treatment in order to avoid the amputation of the foot, lower limb or even death of the patient.

The aim of this study is to evaluate the effectiveness of the Fast Track Pathway (FTP) between level I, II and III diabetes centers in the Lazio Region for the treatment of diabetic patients with injuries in order to reduce the rate of amputation and mortality.

A retrospective observational study was performed from January 2020 to December 2020. We enrolled 23 diabetic patients presenting injuries and Diabetic Foot Ulcers (DFUs) belonging to a level I and II di-abetic foot care center and were divided according to the type of DFUs into uncomplicated, complicated and severe; and when necessary, sent to a specialized center for the care of level III diabetic foot. The following outcomes were evaluated: healing, healing time, minor amputation, major amputation, and survival.

Healing occurred in 15/23 patients (65.2%). Healing time averaged approximately 7 ± 5 weeks. The minor amputation rate was 17.4%. The major amputation rate was 0. The survival rate was 95.6%.

The preliminary data collected allow us to state that the FTP path guarantees excellent management of the diabetic patient with DFUs between the territory and a second and third level diabetes center.

INTRODUCTION

Diabetic foot is one of the most serious and costly complications of diabetes, the result of interactions of various etiopathogenetic factors which, if not well diagnosed and treated in a timely manner, can lead to foot amputation, limb amputation and in more serious cases patient death (Bus & Ph, 2017).

The correct prevention and management of all its complications plays a key role in the ideal implementation of this strategy to reduce complications related to diabetic foot.

Of primary importance is the timing with which this pathology is treated, as often cited “Time is Tissue” (Lepántalo et al., 2011).

Ulcer grade and severity are important predictors for healing time (Smith-str et al., 2017) and the treatment of complications such as ischemia and infection always requires urgent treatment (Lepántalo et al., 2011). For example, a delay in the surgical debridement of an abscess in the deep space of the foot increases the level of amputation (Faglia et al., 2006). Given the complexity of the management of diabetic foot ulcers (DFUs), it is essential to implement a multidisciplinary approach where each professional figure, while interacting with the others, maintains a differentiated role to best guarantee the achievement of the set objectives.

In this regard, it is important to build a local network for the management of DFUs in order to reduce amputation rate, reduce healing time, and improve the patient’s quality of life.

The proper approach is the one proposed in the Fast Track Pathway (FTP) (Meloni et al., 2019) which aims to identify an action strategy for the treatment of diabetic patients with DFUs (Graph 1).

It is ideal to implement the FTP on a regional level that not only serves to indicate the appropriate management of the patient, but that also creates a network between the various diabetic structures that are currently divided into levels of assistance with different skills and characteristics. Below is Table 1, published within the IWGDF of 2019, which identifies the different levels of assistance and specifies the specialists involved (Jakosz, 2019).

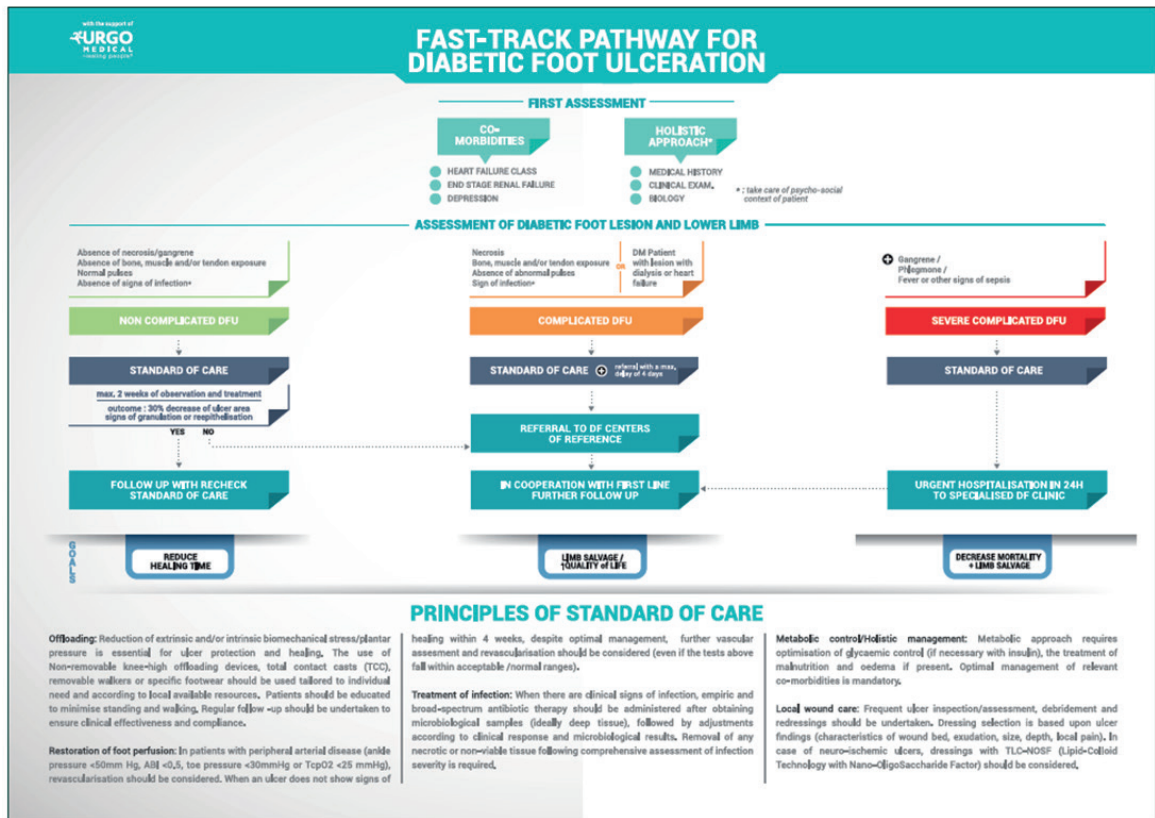
This relationship between structures of different levels would guarantee an adequate management of the patient with reduction of costs, improvement of the patients’ quality of life, reduction of amputations and fewer deaths.

Objectives

Evaluate the effectiveness of the management of diabetic patients with DFUs through the creation of a “Fast-Track Pathway” between level I, II and III diabetes centers in the Lazio Region.

MATERIALS AND METHODS

A retrospective observational study was carried out from January 2020 to December 2020. All patients diagnosed with type I and II diabetes mellitus, aged 18 to 90 years, of both sexes, who belonged to both the Diabetology UOSD of II level of the San Camil-



Graphic 1 - Fast-Track Pathway

lo De Lellis Hospital in Rieti both at a level I center (Podiatry Studio - Poggio Mirteto) which presented uncomplicated, complicated and severe DFUs. These patients who presented these characteristics and required level III specialist care, were sent to the Diabetic Foot Unit at the Tor Vergata Hospital - Rome. It is important to denote: the centers that participated in this study are all located in the Lazio Region. Uncomplicated DFUs were defined as superficial, uninfected, and non-ischemic wounds. Patients who did not show healing or improvement within 2 weeks of treatment (30% area reduction or absence of granulation tissue formation or signs of re-epithelialization) were referred to a specialized diabetic foot care center (Meloni et al., 2019). Complicated DFUs were defined as ischemic and/or infected or deep wounds (tendon or bone exposure) or any type of lesion present in patients with heart attack (not heart attack, but heart failure), or on dialysis. These patients had to be referred to the specialized diabetic foot care center within 4 days (Meloni et al., 2019). Severe DFUs were defined

when wet gangrene and/or abscess/phlegmon were present or the patient had a fever and/or showed signs of sepsis. Such patients needed urgent hospitalization within 24 hours in a specialized diabetic foot care center (Meloni et al., 2019).

The following were excluded from the study: all diabetic patients who did not have lesions, patients who had a shortened life expectancy (<6 months) for whom conservative therapy was carried out, patients unable to travel between the various diabetes centers. Demographic and clinical characteristics of all participants were recorded: age, gender, type of diabetes, duration of diabetes, glycosylated hemoglobin (HbA1c), ischemic heart disease (IHD), hypertension (arterial), peripheral arterial disease PAD), distal symmetrical sensory motor polyneuropathy (Diabetic Peripheral Neuropathy - DPN), chronic renal failure in dialysis, dyslipidemia, presence of previous amputation, type of access to the referral center.

The following outcomes/primary outcomes were assessed:

| Level of care | Interdisciplinary specialists involved |
|---------------|---|
| Level 1 | General practitioner, podiatrist, and diabetes nurse |
| Level 2 | Diabetologist, surgeon (general, orthopaedic, or foot), vascular specialist (endovascular and open revascularisation), infectious disease specialist or clinical microbiologist, podiatrist and diabetes nurse, in collaboration with a shoe-technician, orthotist or prosthetist |
| Level 3 | A level 2 foot centre that is specialized in diabetic foot care, with multiple experts from several disciplines each specialised in this area working together, and that acts as a tertiary reference centre |

Tab. 1 - Level of care and interdisciplinary specialist involved

- healing, understood as complete re-epithelialization of the DFUs;
- healing time, understood as the time elapsed between the appearance of the lesion and complete healing;
- minor amputation, amputation performed below the ankle joint;
- major amputation, amputation performed above the ankle joint;
- survival.

The following secondary outcomes were then evaluated:

- ulcer regression > 50% of the initial surface;
- recurrence of the ulcer or the formation of a new ulcerative wound;
- resumption of walking, the patient's ability to walk independently without the use of aids (such as canes, crutches, walkers, wheelchairs).

Only patients with a minimum follow-up of 3 months were considered. Patients were divided into 3 groups corresponding to the type of injury reported (uncomplicated, complicated, severe). The following characteristics of DFUs were evaluated: ulcer location, size and depth, presence of ischemia, infection and gangrene. All patients were treated in accordance with the 2019 IWGDF guidelines for the treatment of ischemia, infection, offloading, local treatment of the wound and management of comorbidities (Jakosz, 2019). The diagnosis of PAD was made through the palpation of the peripheral arterial pulses (pedial and posterior tibial artery) and through the ABI (Ankle brachial Index) calculation. However, most patients with PAD and foot ulcers may have autonomic neuropathy that causes calcification of the middle layer of the arteries (Mönckeberg's sclerosis) in the lower limbs, which negatively affects the usefulness of this test (Gentile et al., 1990). There are insufficient studies to recommend a single test to reliably rule out PAD in a patient with DFUs. For this reason it was necessary to perform a second test such as the evaluation of Doppler waveforms (Forsythe et al., 2020) and the evaluation of transcutaneous oximetry (TcPO₂) (Brownrigg1 et al., 2016). Accurate identification of peripheral artery disease in these patients is important in order to carry out timely management and plan the most appropriate type of intervention, including revascularization in case of critical ischemia (Aiello et al., 2014; Jakosz, 2019).

When deemed necessary, revascularization surgery was performed in order to improve the perfusion of the foot. The TcPO₂ measurements were repeated about 3-4 weeks after the surgery in order to evaluate the effectiveness or lack thereof of this procedure. A clinical diagnosis of soft tissue infection was made, based on the presence of local and/or systemic signs of infection or symptoms of inflammation. Patients with severe infections associated with the presence of other comorbidities were hospitalized. The "Probe-to-bone" test and radiography (RX) were performed for subjects with suspected osteomyelitis (Aragón-Sánchez et al., 2011; Jakosz, 2019). In case of diagnostic doubts, second level investigations were carried out (MRI, CT). In the event of infection, empirical antibiotic therapy was administered and culture examination of infected tissue was carried out and in cases in which the tissue resulted positive, a more specific antibiotic therapy was prescribed, targeting the pathogen identified in the culture. In the presence of a soft tissue infection, antibiotic therapy was administered for 1-2 weeks and subsequently modulated as reported in the guidelines (Jakosz, 2019); in the presence of severe infections, parenteral antibiotic therapies were performed. Topical antibiotic therapies were not used. The cleansing of the wound was carried out with a solution containing polyhexanide and betaine (Bellingeri et al., N.d.) and carried out when necessary mechanical debridement. The uninfected neuro-ischemic DFUs were treated, in accordance with the IWGDF 2019 guidelines (Jakosz, 2019), with dressings consisting of TLC (Technology lipido-colloid) combined with NOSF (Nano-oligosaccharide Factor), an innovative, patented technology. TLC-NOSF interacts with the wound microenvironment of the wound, preventing the negative effect of Matrix Metallo protease (MMP), which in excess in chronic wounds creates a continuous degradation of the extracellular matrix (Lázaro-Martínez et al., 2019). In the presence of neuropathic or neuroischemic plantar ulcers of the forefoot and midfoot, a non-removable knee relief device (TCC or non-removable walker) was prescribed as a first choice intervention. Removable relief devices, both at the knee and at the ankle, were used as a second choice, in relation to patient compliance (Lazzarini et al., 2020). For the management of all comorbidities, the intervention of a multidisciplinary team with optimization of metabolic compensation and

| Variably | Group (n=23) |
|-----------------------------------|--------------|
| Age | 73±10 |
| Gender | 15 (65.2%) |
| Diabetes type (2) | 22 (95.6%) |
| Duration of diabetes (years) | 19.5±9.5 |
| Glycated hemoglobin (%) | 7.5±0.6 |
| Hypertension (n) | 23 (100%) |
| Dyslipidemia | 21 (91.3%) |
| Ischemic heart disease | 14 (60.9%) |
| Chronic renal failure in dialysis | 0 (0%) |
| Chronic obstructive bronchopathy | 8 (34.8%) |
| N. comorbidities | 3.5±0.9 |

Tab. 2 - Demographic and clinical characteristics of all participants

| Variably | Group (n=23) |
|--|--------------|
| DFUs classification according the Fast-Track Pathway | 2 (8.7%) |
| - 1 | 17 (73.9%) |
| - 2 | 4 (17.4%) |
| - 3 | |
| Ischemia | 16 (69.5%) |
| Infection | 18 (78.3%) |
| Sepsis | 1 (4.3%) |
| Dimension > 5 cm ² | 9 (39.1%) |
| Deep wounds (up to the bony plane) | 17 (73.9%) |
| Gangrene | 9 (39.1%) |

Tab. 3 - The characteristics of the DFUs

control of cardio-vascular risk factors was necessary.

■ RESULTS

24 patients were selected for the study. Only one patient was lost (excluded) for not having continued treatment in the reference centers. Of the 23 patients included, 15 were male, 8 were female. The average age of the patients was 73 ± 10 years. 22 (95.6%) patients had type 2 diabetes mellitus and only one patient had type I diabetes mellitus. The mean duration of diabetic disease was 19 ± 9.5 years. Patients had a

mean glycated hemoglobin of $7.5 \pm 0.6\%$. They had various comorbidities including: all patients had arterial hypertension, 21 (91.3%) had dyslipidemia, 14 (60.9%) ischemic heart disease, 8 (34.8%) chronic obstructive bronchopathy. None had chronic renal failure undergoing dialysis treatment. This overview, which includes all the comorbidities examined, allows us to state that on average the patients presented 3.5 ± 0.9 (Table 2).

The characteristics of the DFUs are present in table 3. Of the 23 lesions, 2 (8.7%) were uncomplicated DFUs, 17 (73.9%) complicated DFUs, and 4 (17.4%) severe DFUs.

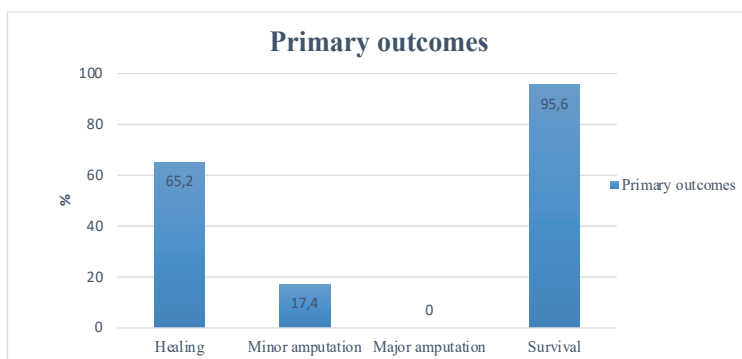
Ischemia was present in 16 lesions (69.5%), infection in 18 (78.3%) and only one patient had a septic condition. 9 (39.1%) lesions were larger than 5 cm² and 17 (73.9%) were deep wounds up to the bony plane. Only 9 (39.1%) patients had gangrene present.

Healing occurred in 15/23 patients (65.2%). Healing time averaged approximately 7 ± 5 weeks. The minor amputation rate, despite the complexity of the clinical picture, showed relatively low data: only 4 patients (17.4%) (Graph 2) underwent a minor amputation of the lower limb. The major amputation rate was 0. The survival rate was 95.6%.

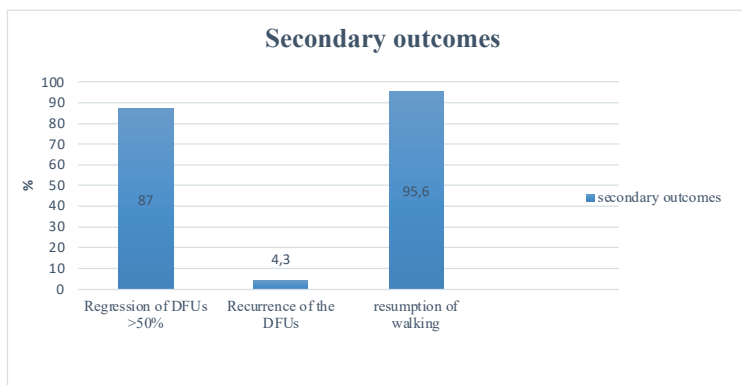
A regression of the ulcerative lesion greater than 50% was also observed in 20 patients (87%) and only one patient (4.3%) had a relapse on the contralateral foot, which required a new approach to revascularization of the limb. The resumption of walking was recorded in 22 patients (95.6%) (Graph 3).

■ DISCUSSION

In this study, all patients showed significant clinical complexity, presenting various pathologies in addition to the diabetic one. Cardio-vascular compromise was among the most important comorbidities. Furthermore, the population under examination presented an advanced age, which normally aggravates the general management of the patient. The local clinical



Graphic 2 - Primary outcomes



Graphic 3 - Secondary outcomes

picture showed some complexity in that most of the lesions (73.9%) were lesions defined by their “complicated” characteristics. Most of the lesions (78.3%) had infections. Only one patient experienced sepsis and this shows that there was excellent control of the infection, probably related to early management and referral. The state of the lesions was also aggravated in relation to depth of the same; most (73.9%) also involved bone tissue.

The percentage of healing, or 15/23 (65.2%) is a positive outcome. It should be considered that 2 patients (8.7%) did not recover because they were subjected to conservative therapy (for the general state of the patient where there is critical ischemia with vain attempt at revascularization) and one patient died during the study. For the first time a study entered the academic literature (Meloni, Izzo, et al., 2020) describing the characteristics of diabetic patients with DFUs unable to receive revascularization treatment (defined as “no-option critical limb ischemia”) and confirming that these patients show a reduced percentage of limb salvage and increased risk of major amputation and death compared to re-vascularized patients (Caetano et al., 2020). The healing rate in our study, not taking these last 3 cases into consideration, corresponds to 75%. Patients who did not show complete wound healing did however show a noticeable improvement in wound healing with > 50% regression of the lesion. We can state that 20 out of 23 patients (87%) showed a 50% regression of the DFUs surface.

Only one patient presented a relapse on the contralateral foot, which required a new approach to revascularization of the limb. The last secondary endpoint recorded, but not of minor importance, was the resumption of walking or the patient’s ability to walk independently without the use of aids. As many as 22 patients returned to ambulate, initially thanks to the aid of discharge devices and the achievement of healing owed to the use of secondary prevention footwear with custom-made foot orthotics (López-Moral et al., 2020). Considering that a patient is deceased, we can say that all patients returned to ambulate in full autonomy. In several studies, it has been confirmed that a delayed diagnosis and therefore a delayed treatment of diabetic patients with injuries contributes to several complications, which could lead to impaired healing, amputations and death (Gavan et al., 2016; Manu et al., 2018; Sánchez-Ríos et al., 2019). An early referral allows for better management of the diabetic patient with DFUs in terms of healing, healing time, minor and major amputation (Sung et al., 2020; Wise, 2016). The fast-track pathway is a useful tool for the management of these patients, ensuring multidisciplinary (Van et al., 2020) and differentiated specialist man-

agement in the various diabetes centers (Meloni et al., 2019). The correct diagnosis and timely referral of the patient (Smith-str et al., 2017) with complicated lesions that require adequate surgical and vascular management allows to reduce the risk of amputation strictly tied to an increased risk of death (Jupiter et al., 2015) and septic evolution of infected lesions.

The first multicenter study carried out in Italy (Meloni, Acquati, et al., 2020) confirms our argument and the same situation can be found in Europe (Manu et al., 2018). About 50% of patients were sent to the referral center one month later than the correct time for adequate management (Manu et al., 2018).

In particular, the Lazio region, where our study was carried out, shows an average delay compared to the other Italian regions, although it remains within the national average. It would be advisable to improve and speed up referral in the appropriate diabetes center, despite the fact that Italy still has the lowest rate of lower limb amputation compared to other European countries (Meloni, Acquati, et al., 2020). A well-defined path between the region and 3rd level hospital centers (Hinojosa et al., 2019) should be implemented to obtain positive outcomes as documented in this study.

Limits

A limitation of this study is the sample number, which is a small number of patients. It is also possible to understand the effectiveness of this study thanks to the data contained in the literature where it is known that the delay in the treatment of DFUs leads to a worsening of the lesion and to the general state of the patient, subjecting them to an increased risk of amputation and mortality. The small number of patients also does not allow accurate statistical analysis (multivariate analysis) to identify outcome predictors. Another limitation was the lack of a control group.

CONCLUSION

The preliminary data collected allows us to state that the FTP path guarantees excellent management of diabetic patients with lesions among the region and second and third level diabetes center. It can allow for a more rapid treatment of patients and their complications, avoiding the clinical worsening of lesions and of patients’ general conditions. It reduces the number of complications including major amputation and mortality. The different specialization of each center does not cancel out the specificity of the individual tasks, but guarantees the best approach and care in relation to the different degree of qualification. Further studies are needed to reinforce this data.

All authors declare that they have no conflicts of interest.

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