

## Limb Salvage in Diabetic Patients: The Italian Experience

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### Abstract

Diabetes is rapidly increasing worldwide and diabetic foot is the main cause of non-traumatic lower limbs amputation. However epidemiological data report a reduction of amputee's rate in different European countries and in USA. Also in Italy there were excellent results related to the improvement of treatment strategies. The aim of this commentary is to describe the Italian model analyzing the reasons that have contributed to this success.

**Keywords:** Diabetes; Diabetic foot; Non-traumatic; Amputation

### Commentary

Diabetes can be considered a fast-growing epidemic disease that currently affects 346 million people with a prevalence of 6% in the general population [1]. It is well known that diabetic foot (DF) is a typical and common complication of diabetes. The most recent epidemiological data report that a lesion appears in 15% of cases during the life of a diabetic patient [2-4]. Furthermore DF is the main cause of hospitalization and non-traumatic lower extremity amputation [3-5]. If we considered that the prevalence of major lower limb amputation affects more than 1 million of people between diabetic patients (4,8%), it is obvious the strong impact of this disease on the society in terms of quality of life and economic costs [6,7].

Currently the worldwide incidence of lower limbs loss is high with significant differences reported by various studies. In 1989, the Saint Vincent Declaration marked an important step with the aim to reduce the incidence of lower extremity amputations improving the healthcare measures for DF complications [8]. From this date several studies revealed significant improvements in the incidence of major amputation of lower limbs [9-14]. Amputees rate among the different countries are extremely variable and this odds could be explained by the heterogeneity of the population analyzed and the not standardized strategy to treat DF [15-21]. Also social, geographical and economics factors may influence the possibility of certain patients to access to necessary treatment for their disease, restricting the possibility of care for these group of people [22]. Overall in the European context there is a trend of reduction of major amputation that can be related to the reinforcement of multidisciplinary approach and the implementation of podiatry service [19-21].

In this scenery, Italy has a prominent role for the significant results obtained in terms of limb salvage in diabetic patients affected by peripheral arterial disease (PAD) complicated by diabetic foot ulcers (DFU) and critical limb ischemia (CLI).

Also in Italy the prevalence of diabetes is progressively increasing. According to the epidemiological analysis of the year 2012, 3.000.000 persons are affected by diabetes with a prevalence of 5.5% in the general population ([www.epicentro.iss.it/igea/en/FactSheet.asp](http://www.epicentro.iss.it/igea/en/FactSheet.asp))

Italian data were reported in a recent study where the period 2001-2010 was analyzed. In these years, a mean annual of 11,639 subjects were amputees and 58,6% of whom had diabetes. The risk of major and minor amputation in patient with diabetes was respectively 6,4 and 11 times higher compared to patients without diabetes. In 2010, 2,47 for 1,000 people with diabetes had an amputation of the lower limbs. Overall it is documented a progressive reduction of amputations rate for major amputations among persons with diabetes (-30.7%), while the rate of minor amputations was stable (-4.6%) [23]. Therefore this recent Italian analysis reflects the framework of some European countries and USA characterized by a significant reduction in the rate of major amputations [11,20,24-30]. In this regard Italian model can be considered as a reference for the approach to DF disease. The main reasons of Italian success may be found both in the improvement of diabetes therapy and in the knowledge and approach to DF, especially in the treatment of lower limbs arterial disease with the implementation of endovascular approach that now guarantees a treatment for almost all patients affected by CLI [31-35]. It is well known that infection and ischemia show a rapid evolution and these conditions are the main risk factor for major lower limb amputation [36,37]. In relation to the necessity for identifying and treating a DFU with a high risk to be amputee, recent Italian papers implemented the role of the multidisciplinary approach and the need to establish a protocol of diagnosis and treatment for critical diabetic foot (CDF). Caravaggi et al. designed a new system of Diabetic Foot Triage to identify a diagnostic flow chart to stratify the severity of infectious process and to establish a surgical integrated protocol in case of emergency [38]. In our recent paper we defined the conditions of CDF and we have consolidated the main four point that must be treated in condition of emergency: 1) extensive surgical debridement to remove infected tissues, 2) aggressive antibiotic therapy, 3) immediate revascularization in case of ischemia, 4) careful management of general conditions [39].

In the Italian way of approaching to limb salvage, the management of vascular disease plays certainly a key role. In our country, the endovascular treatment of lower extremity disease is a steady approach and our results have validated this strategy to treat diabetic ischemic foot. In this regard, Italy has a prevalence of amputations among the lowest in Europe [40] and the Eurodiale study, where 14 European tertiary reference centers for the treatment of DF were included, reported that Italian centers had the best outcomes in terms of wound

healing and amputation [41,42]. According to this concept, in 2013, the Italian Society of Diabetes (SID, AMD), Radiology (SIRM) and Vascular and Endovascular Surgery (SICVE) published the Italian guidelines for the treatment of PAD in diabetic patients. In this consensus document the role of angioplasty is emphasized. Several studies showed the effectiveness, the feasibility, the high rate of limb salvage and low operative risk of endovascular treatment [43-49]. Even if in certain conditions surgical revascularization allows a higher long-term patency if compared to angioplasty [50,51], several reasons justify the widespread use of percutaneous transluminal angioplasty (PTA) to treat PAD in diabetic patients. Usually a large part of diabetic patients affected by CLI are elderly with several comorbidity. Therefore they can't tolerate a surgical procedure for the high operative risk and secondly it is often no possible to pack a by-pass because of the absence of a suitable vein and due to the presence of a local infection that may not guarantee an adequate anastomosis site [43,45,46,52-55]. In these fragile patients the endovascular approach can be considered the only option for its minimally invasiveness because it does not require general anesthesia and has few contraindications in patients with existing heart or kidney disease [32,43,46]. Moreover the lower limbs angioplasty can be divided in different times, performing a second procedure only after appropriate clinical and instrumental assessment which shows the need for other treatment. In this way it is possible reduce the surgical stress and the amount of contrast medium that can determine a contrast induced nephropathy or worsen the condition of renal failure in patients with already compromised renal function. Angioplasty can be easily repeated and it must be underlined that in the last years there was a significant growth of instrumental and alternative techniques which also allow the treatment of distal and aggressive lower limbs vascular disease [56]. Farther, a close collaboration between physicians who manage the clinical foot problem and interventional radiologist has now established. This cooperation allowed to design the road map for diagnosis of CLI and the best endovascular approach. Particularly, it is currently stronger the concept of "wound related artery", defined as the target revascularization addressed to the artery that perfuses the wound area [57,58]. Moreover, the treatment of the angiosome involved by the lesion seems to show best results in terms of limb salvage and wound healing if compared to not target revascularization [59,60]. All these considerations have consolidated the concept of angioplasty first approach to treat the PAD in diabetic patients with CLI andDFU [61]. In relation to the incidence of major amputation, a separate discussion should be done about the dialyzed diabetic patient. In fact, in diabetic patients under dialysis treatment affected by ischemic foot lesion, the rate of amputation reaches the 44% as documented in several studies [62]. In our recent paper, we found that dialyzed patient showed worse results if compared to the other classes. Therefore our analysis confirmed that renal replacement therapy implies a high risk of amputation. However, we found a higher limb salvage rate and a reduced major amputation and death if compared to literature data; furthermore our patients were unselected. We retain that the explanation of these results could be related to endovascular approach. In fact the angioplasty is much less invasive than traditional by-pass and therefore more feasible in these patients with poor clinical conditions. Even more we did not find significant differences between the different chronic kidney disease classes and the positive outcomes for all groups despite the worse conditions could be justified by our less invasive approach and the strict follow-up [63].

## Conclusion

In conclusion, even if the data collection of several studies can sometimes be affected by many variables, overall there is a reduction of the incidence of amputations in USA and in some European countries. In this special ranking Italy has a considerable position and we retain that Italian approach to DF and limb salvage can be considered as a reference model.

The reasons for this success achieved in recent years can be attributed to the improvement of diabetes therapy, the definition of a systematic approach in case of CDF with a high risk of limb threatening, the consolidation of the endovascular treatment in case of CLI, the implementation of multidisciplinary approach particularly in the collaboration between diabetic foot specialist and interventional radiologists.

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