ORIGINAL ARTICLE

IMPACT OF OPEN AND ENDOVASCULAR CASELOAD IN LOWER LIMB AMPUTATION IN PORTUGAL – AN ANALYSIS FROM 2000 TO 2015

Filipa Jácome* [1,2], Alberto Freitas[3], Sérgio Sampaio[3], Marina Dias-Neto[1,2], Ricardo Castro-Ferreira[2,4]

[1] Department of Angiology and Vascular Surgery, Centro Hospitalar Universitário de São João, Porto, Portugal
[2] Department of Surgery and Physiology, Cardiovascular R&D Unit, Faculdade de Medicina da Universidade do Porto, Portugal
[3] Centro de Investigação em Tecnologias e Serviços de Saúde (CINTESIS), Porto, Portugal
[4] Centro Hospitalar de Vila Nova de Gaia e Espinho, Vila Nova de Gaia, Portugal

* **Corresponding author**: filipacjacome@gmail.com

Abstract

Objectives: *Effective revascularization is the cornerstone of limb salvage in chronic limb threatening ischemia. In recent years, less invasive endovascular revascularization techniques have supplanted surgical bypass as the primary mode of revascularization. The real impact of this transition is being increasingly questioned. This study aims to evaluate the endovascular evolution, and how it impacted the amputation rates nationwide since de beginning of the century.*

Methods: *Patients admitted to Portuguese public hospitals with peripheral arterial disease between 2000 and 2015 were selected. Of these, patients that underwent to limb revascularization and/ or limb amputation were evaluated. The information was obtained through the National Health Service administrative database. Three time periods (2000-2004, 2005-2009, 2010-2015) were considered to evaluate the evolution in amputation rates and type of revascularization.*

Results: *The global number of revascularization episodes consistently increased along the 15 analyzed years. There were 25252 admissions for revascularization (55.1% open and 44.9% endovascular). The mean incidence of endovascular procedures significantly increased 5.8 times ($p<0.01$), and open surgery increased 1.3 times ($p<0.01$) when comparing the three time periods. 34633 limb amputations (65.3% major vs 34.7% minor) were realized along 15 years. The mean incidence of lower limb amputations increased by 1.5 times thanks to minor amputation, whose mean incidence increased two-fold while with the incidence of major amputations remained stable. Additionally, mean hospital mortality associated with revascularization episodes decreased from 10.6% to 8.2% ($p<0.01$), on 15-year follow-up.*

Conclusions: *There was a significative increase in revascularization episodes over the 15 years, suggesting better access to health services and/or better diagnostic accuracy. Endovascular procedures were the most practiced. This was along with an increase in the minor limb amputation, a stabilization in major amputations incidence. This nationwide study adds to the increasing body of knowledge in the ever-pertinent discussion of revascularization types and their benefits.*

Keywords: *Incidence; Amputation; Lower extremity; Peripheral arterial disease; Endovascular Procedure*

INTRODUCTION

Lower-extremity peripheral artery disease (PAD) affects >200 million adults worldwide, and its prevalence seems to be increasing[(1)]. Approximately 11% are likely to develop chronic limb-threatening ischemia (CLTI), resulting in persistent foot pain, skin ulceration and gangrene[(1)]. According to studies, nearly 25% undergo lower limb amputation within 1 year[(1)], that entails a significant morbidity and mortality and represents a high social impact and poor clinical prognosis as well as considerable financial implications for health care systems.

Effective revascularization is the cornerstone of limb salvage in CLTI patients. In the last decades, the treatment of this pathology has progressed from an exclusively open surgical approach to one that includes percutaneous options. Owing to the reduced invasiveness and definitely lower perioperative complication rate, morbidity and mortality

compared with open surgery, endovascular interventions have gained increased acceptance by physicians and patients[2, 3]. In some countries endovascular therapy for PAD has surpassed open surgical revascularization as the dominant treatment modality[4]. However, restenosis and necessity of long-term reinterventions still is the Achilles heel of endovascular procedures[5]. The BASIL trial, a randomized clinical trial that compared bypass surgery-first versus balloon angioplasty-first treatment strategy in patients with severe limb ischemia, did not find a significant difference in amputation-free survival or overall survival between both strategies in the first 2 years of follow-up. However, patients who live more than 2 years are probably better served by a bypass-first strategy, preferably with vein, because in the longer run, open surgery seems to be associated with a significant increase in overall survival and a also nonsignificant increase in amputation-free survival[6]. Also, the cost of a first endovascular treatment for CLTI has been estimated to be >$15,000 per patient, with 86.8% of this cost being attributable to hospitalizations, which is a burden in public health services accounts[4,6]. The real impact of this transition to a new endovascular era is being increasingly questioned.

This study aims to evaluate the endovascular evolution and how it impacted the amputation rates in Portuguese Health Care Services between 2000 and 2015.

METHODS

This is an observational retrospective study. All patients were included were identified through the National Health Service (SNS) administrative database, formerly designated as Diagnosis Related Groups (DRGs) database. This database was provided by the Portuguese Central Health System Administration (ACSS) and contains a registry of all hospitalizations (retrospective consecutive case entry) occurring in mainland Portugal public hospitals. Each registered hospital episode includes information about diagnoses and medical or surgical procedures, both coded using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). The manuscript follows the RECORD statement[7], extended from the STROBE statement[8].

Data collection

Such database includes clinical data (such as diagnosis, type of surgery, length of stay in the hospital) in all Portuguese hospitals. The primary diagnosis of an episode represents the main condition investigated or treated during that hospital stay. In this study, all admissions considered to have a primary diagnosis with specific ICD-9-CM code for peripheral arterial disease (443.9) were included. Amputation procedures were categorized as major amputation (that includes above-knee, through the knee and below-knee amputations) and minor amputations (such as toe and foot

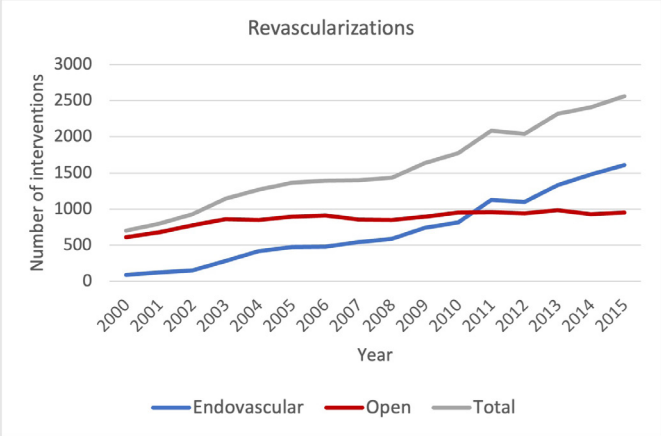

Figure 1 *Trend in revascularizations realized in Portuguese hospitals from 2000 to 2015, by type of revascularization and by year.*

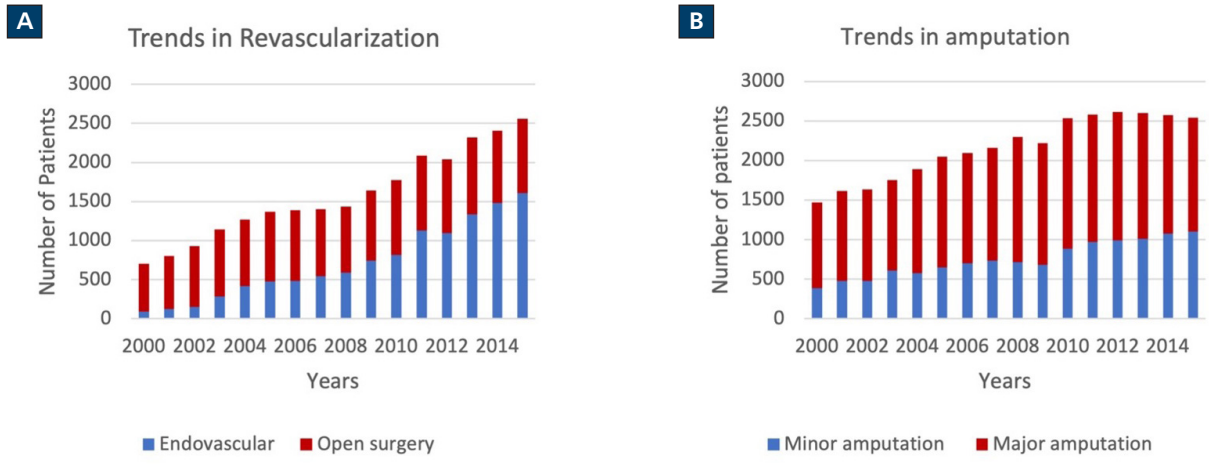

Figure 2 *Trends in revascularizations (A) and in amputations (B) Portuguese hospitals from 2000 to 2015.*

amputations). Also, revascularization procedures performed during the same period were categorized as open surgical procedures or endovascular procedures. Endovascular procedures include angioplasty, stenting, or atherectomy and open surgery includes endarterectomy and bypass. Hybrid revascularization procedures were excluded from the analysis and only isolated endovascular or open procedures were included. The intervention rate was calculated based on the episodes of care with the above-mentioned ICD-9-CM disease codes plus the ICD-9-CM procedure codes suitable for peripheral arterial disease treatment (Table S1).

Trends in the prevalence of amputations (major or minor) and revascularizations (endovascular or open) were the primary aims of the analysis.

Study outcomes

Our study aimed to evaluate the trend in the revascularizations and lower limb amputations in adult patients admitted by peripheral arterial disease (PAD) in Portuguese hospitals, between 2000 and 2015. We also compared the characteristics of patients summited to endo versus open revascularizations.

Statistical analysis

Data were calculated overall and for three periods (2000-2004, 2005-2009 and 2010-2015) to assess variations over time. Subgroup analysis was performed to investigate trend differences based on gender.

Continuous variables are presented as mean and standard deviation after histogram evaluation. Proportions were compared using the chi-square test. Changes in proportions over time were assessed using the chi-square test for trend. Normally distributed data were compared using one-way ANOVA. Bonferroni correction was applied to adjust for multiple testing. Additionally, for subgroup analysis, a significance level of $p < 0.01$ was considered. All statistical analysis was performed using SPSS for Mac version 25 (SPSS, IBM Corp., Armonk, NY).

RESULTS

A total of 51329 admissions were realized motivated by peripheral arterial disease (PAD) from 2000 to 2015 in Portuguese hospitals. The mean rate of admissions presented an increase of 75.1% between the periods of 2000-2004 and 2010-2015 (Table 1). The mean hospitalization time was 19.47±27.3 days. In our sample, 74.3% of patients were male. Comorbidities and characteristics of patients submitted to revascularization were presented in the Table 2.

Revascularization

In 25252 admissions, revascularization procedures were realized. The mean incidence of revascularization procedures increased 2.3 times from 2000-2004 to 2010-2015 (Figure 1/Figure 2A). In 11350 of these hospital admissions (44.9%), endovascular revascularizations were realized. The mean incidence of endovascular procedures significantly increased 5.8 times, comparing the first and the

Figure 3 *Trends in endovascular (in male patients (A) and in female patients (B)) and open revascularizations (in male patients (C) and in female patients (D)), by sex and by year.*

Table 1 **Incidence of hospital admissions by peripheral arterial disease, amputation and revascularization procedures in patients with CLTI across three time periods (2000-2004, 2005-2009 and 2010-2015) in Portugal.**

	2000-2015	2000-2004	2005-2009	*2010-2015*	*Trend*	*p*
Hospital admissions by peripheral arterial disease						
Total number, n	51329	11607	15345	24377	--	--
Cases per year, mean±SD	3208.0±783.3	2321.0±280.9	3069.0±161.7	4063.0±273.0	↑↑	<0.01
Total Revascularization procedures						
Total revascularization procedures, n	25252	4841	7231	13180	↑↑	--
Cases per year, mean±SD	1578.3±573.0	968.2±235.5	1446.2±110.0	2196.7±287.1	↑↑	<0.01
Revascularization procedures						
Endovascular, mean±SD	709.0±488.7	212.6±136.4	565.4±108.8	1243.3±287.4	↑↑	<0.01
Open surgery, mean±SD	869.0±103.2	755.6±108.7	880.8±27.3	953.3±19.2	↑↑	<0.01
Endovascular procedures						
Men, mean±SD	499.0±308.6	168.4±111.7	426.4±73.7	834.2±148.6	↑↑	<0.01
Women, mean±SD	178.0±229.8	44.2±25.0	139.0±37.4	409.2±78.3	↑↑	<0.01
Open Surgery						
Men, mean±SD	712.0±91.9	610.0±82.9	714.0±35.1	795.0±12.4	↑↑	<0.01
Women, mean±SD	156.0±25.0	146.0±28.1	166.0±32.9	156.0±12.5	↑↓	<0.01
Amputations						
Total, mean±SD	2165.0±396.6	1673.0±157.1	2164.0±99.7	2575.0±30.8	--	--
Major, mean±SD	1413.0±192.6	1168.4±87.4	1469.6±87.4	1569.5±81.4	↑↑	<0.01
Minor, mean±SD	752.0±227.1	504.6±89.0	694.6±32.8	1005.0±78.8	↑↑	<0.01

Table 2 **Patients characteristics and comorbidities of patients submitted to endovascular or open interventions.**

	Endovascular (n total=11350) n (%)	Open (n total=13902) n (%)	p
Male	8807 (77.6)	12019 (86.5)	**<0.01**
Age	67.0 ± 11.7	66.0 ± 11.1	**<0.01**
Charlson Index	1.5 ± 1.6	1.3 ± 1.4	**<0.01**
Hospitalization days	15.0 ± 19.7	21.3 ± 36.6	**<0.01**
Myocardial Infarction	988 (8.7)	1226 (8.8)	0.77
Congestive Heart Failure	801 (7.1)	844 (6.19)	**<0.01**
Cerebrovascular disease	791 (7.0)	954 (6.9)	0.76
Dementia	26 (0.2)	40 (0.3)	0.43
Chronic pulmonary disease	830 (7.3)	1300 (9.4)	**<0.01**
Peptic ulcer disease	105 (0.9)	151 (1.1)	0.23
Liver disease	170 (1.5)	181(1.3)	0.21
Diabetes with chronic complication	1718 (15.1)	1528 (11.0)	**<0.01**
Renal disease	1579 (13.9)	1167 (8.4)	**<0.01**
Any malignancy, including lymphoma and leukemia, except malignant neoplasm of skin	139 (1.2)	186 (1.3)	0.46
Metastatic solid tumor	18 (0.16)	24 (0.2)	0.91
AIDS/HIV	27 (0.2)	26 (0.2)	0.46

last time periods (p<0.01) (Table 1). In the remained 13902 hospital admissions along the fifteen analyzed years, open surgery procedures were realized. There was an increase of 1.3 times in the number of open procedures between 2000-2004 and 2010-2015, and the difference between these time periods was statistically significant (p<0.01).

In a subgroup analysis by gender, women were more frequently treated with endovascular procedures (53.3%). Of 2848 admissions in which women received endovascular intervention, there was a progressive increase of these procedures of 9.3 times over the three time periods (p<0.01) (Figure 3). Male patients, on the other hand, mainly underwent open approaches (87.2%), and the mean incidence increased 1.3 times since 2000-2004 (p<0.01). For female patients, although there was an increase in open procedures in 2000-2004, a subsequent decrease in the use of these techniques was observed between 2005-2009 and 2010-2015 (Figure 3).

Compared to patients submitted to open surgery, endovascular patients were older (67.0 ± 11.7 vs 66.0 ± 11.1, p<0.01), present a higher charlon index (1.5 ± 1.6 vs 1.3 ± 1.4, p<0.01), higher incidence of congestive heart failure (7.1% vs 6.1%), diabetes with chronic complication (15.1% vs 11.0%) and renal disease (13.9% vs 8.4%). On the other hand, compared to patients submitted to endovascular surgery, patients submitted to open surgery were more frequently male (86.5% vs 77.6%), had higher hospital stay (21.3 ± 36.6 vs 15.0 ± 19.7, p<0.01) and chronic pulmonary disease incidence (9.4% vs 7.3%, p<0.01).

The mean age of patients undergoing endovascular procedures was 67.0±11.7 years, and 77.6% were male. Patients treated with endovascular procedures had a mean hopitalization time of 15.0±19.7 days.

Patients who underwent open surgery were mainly male (86.5%) and the mean age was 66.0 ± 11.0 years. The mean hospitalization time was 21.25 ± 36.62 days.

Amputation

A total of 34633 amputations, 22607 major (65.3%) and 12026 minor (34.7%) amputations, were performed during fifteen years of follow-up (Table 2).

The mean number of lower limb amputations increased by 1.5 times between 2000-2004 and 2010-2015. This increase was driven by an almost stabilization in the mean rate of major lower limb amputations (1.3 times increase) and by a 2.0 times increase in the mean incidence of minor lower limb amputations (Figure 4/2B).

In-hospital mortality

A total of 4706 patients died during hospital admission between 2000 and 2015. The proportion of patients who died in the hospital decreased over the 15-year period. The mean mortality rate was 10.6% in the period of 2000-2004, 9.8% in 2005-2009 and 8.2% between 2010-2015, resulting in an overall decrease of 23.1% over the 15 years (p<0.01) (Figure 5).

DISCUSSION

Hospital admissions due to peripheral arterial disease increased in Portugal between 2000 and 2015. The overall revascularization procedures had been increasing from 2000 to 2015, particularly since 2008, coinciding with the rise in endovascular developments. Additionally, there was an overall increase in amputations that corresponded to a stabilization of the major amputations and an increase in the minor amputations over the 15-year period.

Contrary to large studies showing decreasing trends in PAD incidence across European Union along the last years, our study found an increase in hospital admissions for peripheral arterial disease in Portugal.[9, 10] Consequently, throughout the 15 years of evaluation, there was a gradual increase in admissions for revascularization procedures, particularly after 2008. This increase was primarily driven by the adoption of endovascular interventions, which saw widespread global development and usage during that time[11, 12]. This might be associated with several causes: first, an improvement in

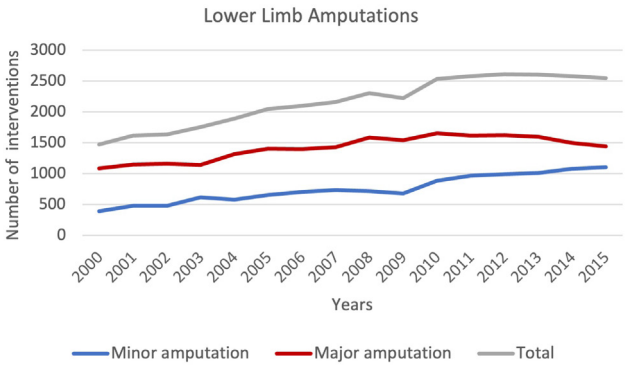

Figure 4 *Trend in amputations realized in Portuguese hospitals from 2000 to 2015, by amputation type and year.*

Figure 5 *Trend in in-hospital mortality rate (%) in patients admitted by peripheral arterial disease, by year.*

Table S1 **ICD-9-CM procedure codes suitable for peripheral arterial disease treatment (revascularization and amputation procedures).**

	Code	Description
Revascularization procedures		
Endovascular procedures	**39.50**	Angioplasty or atherectomy of other non-coronary vessel(s)
	39.90	Insertion of non-drug-eluting peripheral vessel stent(s)
	00.55	Insertion of drug-eluting peripheral vessel stent(s)
Open procedures	**38.1**	Endarterectomy
	39.2	Other shunt or vascular bypass
	39.29	Other (peripheral) vascular shunt or bypass
Amputation procedures		
Minor amputations	**84.10**	Lower limb amputation, not otherwise specified
	84.11	Amputation of toe
	84.12	Amputation through foot
	84.13	Disarticulation of ankle
Major amputations	**84.14**	Amputation of ankle through malleoli of tibia and fibula
	84.15	Other amputation below the knee
	84.16	Disarticulation of knee
	84.17	Amputation above knee
	84.18	Disarticulation of hip

the access to the healthcare services for PAD patients that contributes to the increase in hospital admissions and revascularizations; second, an increase in mean lifetime along last decades lead us to treat more patients at increasing ages and with higher comorbidity[13, 14], also patients that wouldn't be candidates for treatment in the recent past[15]; third, recurrent readmission for redo revascularizations were necessary because of revascularization failure. Endovascular techniques offer a less invasive approach, making them suitable for high-risk patients deemed unfit for surgical bypass. Patients with renal disease and diabetes mellitus, often associated with predominantly below-the-knee arterial disease, were commonly treated using endovascular techniques[16], as observed in our study. Hospitalization time was significantly lower in cases involving endovascular procedures, as expected based on previous studies[17, 18].

Regarding amputations, firstly it is important to consider the level of amputation. Major amputations are often a result of failed conservative or surgical treatment failure, while minor amputations are often used as an adjunct to revascularization, aiming to prevent the need for more proximal amputations[19]. The increase in minor amputations might be attributed to the higher use of minimally invasive endovascular procedures to preserve limbs in high-risk patients, who might otherwise be candidates for conservative treatment or to primary major amputation. Between 2000 and 2015, we observed a slight increase in the incidence of major lower limb amputation rates in the first 8 years, followed by a stabilization. We cannot exclude that we might be having a stable number of amputations, despite a higher number of patients treated (note that we quantified burden of procedures and not number of treated patients), which is favorable. It is also important to note that in-hospital mortality declined, which indicates a success of the therapy escalation.

The substantial medical costs associated with revascularization procedures, particularly in the endovascular era, can be a financial burden (>$15,000 per patient) relative to open interventions[20]. Additionally, endovascular interventions often have lower long patency rates, leading to frequent necessary recurrent interventions, further increasing the economic burden of this treatment[21]. Therefore, an economic and clinical analysis is urgently necessary to determine the cost-effectiveness of newer therapeutic strategies in lower limb revascularizations.

The rate of mortality decreased along the 15-year period, which could be attributed to the adoption of less invasive techniques for the treatment of peripheral arterial disease[22].

Limitations

The first limitation is that the analysis was based on hospital admissions, rather than individual patients. According with this, we could not differentiate the patients that were only submitted to endovascular or open repair, to the ones that were submitted to sequential revascularization procedures in the same hospital admission. For the same reason, hybrid revascularization procedures had to be excluded from this analysis. Also, patient's consecutive admissions for recurrent endovascular or open surgery in

different admissions could not be specifically counted. Thus, the increase in total revascularization admission rates (mainly endovascular) could be explained by recurrent interventions after index procedures or because more technical skills have been developed in Portuguese centers, which allows to treat patients that would be candidates to primary amputation in the past. Therefore, these issues would be important to consider in future studies.

Furthermore, we could not relate each episode of endovascular or open revascularization with minor and/or major amputations. These could bias and limit the validity of the results, particularly when estimating incidence or prevalence rates in the target population, but also limits the individualization of outcome each admission episode along the time. To date, this remains a major limitation of hospital episode statistics (HES) such as the nationwide DRG statistics, and it should be taken in consideration when interpreting the findings.

Secondly, since this is an observational study, numerous confounding factors that were not discussed could have influenced the observed results.

Both limitations should be considered while interpreting the findings of this study, and further research with more comprehensive data and control for potential confounding factors may provide more robust insights into the trends and outcomes of peripheral arterial disease, revascularization, and amputations in the studied population.

CONCLUSION

In Portugal, both hospital admissions due to peripheral arterial disease and revascularization procedures have shown a continuous increase in recent years, with endovascular procedures being the most performed. Furthermore, there has been an increase in the rates of minor limb amputations, while the incidence of major amputations has remained relatively stable. Despite the advancements in endovascular techniques and the higher costs associated with endovascular revascularization procedures, the persistence of major amputations are still a matter of concern, justifying a throughout evaluation of cost-efficacy and planning for vascular interventions.

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