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Danish Trends in Major Amputation After Vascular Reconstruction in Patients With Peripheral Arterial Disease 2002—2014

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WHAT THIS PAPER ADDS

This population based cohort study provides data on the risk of PAD associated major amputation after revascularisation of the lower limb. Although more revascularisations are performed yearly, levels of major amputation after vascular reconstruction remain high. The risk of amputation is highly associated with the severity of PAD with ulcers/gangrene being the strongest predictor. Geographic variation in risk of amputation after revascularisation is found, but cannot be fully explained by geographic differences in the intensity of vascular treatment.

Objective: Contemporary information on major amputations after revascularisation in Denmark is sparse. This population based national study aimed to determine outcomes following revascularisation for PAD and to identify predictors of major amputation after revascularisation, including geographical variation.

Methods: Data on patients with PAD undergoing revascularisation (endovascular, open, and hybrid procedures) from 2002 to 2014 were obtained from the Danish Vascular Registry and linked with information from population based healthcare and administrative databases. Cox proportional hazards regression was used to assess the relationship between major amputation and the various associated factors.

Results: In all 25,982 first time vascular reconstructions for PAD were performed between 2002 and 2014 and major amputations were performed in 2883 (11.1%) of the patients. The total number of revascularisations increased up to 2010 and thereafter numbers decreased slightly. A trend towards endovascular revascularisation as first time revascularisation was seen (36.6% in 2002 vs. 59.0% in 2014, $p < .001$). Median time from first revascularisation to major amputation was 4.66 months (range 0.03—146.88 months), and 63.1% of major amputations were performed within one year following revascularisation. No change in the number of amputations performed within one year after revascularisation was found during the study ($p = .251$). The strongest predictor for major amputations was ulcers/gangrene (HR 8.06, CI 7.11—9.13, $p < .001$) at the time of revascularisation. Geographic variation for intensity of revascularisation was observed and geographic differences in amputation free survival for patients with intermittent claudication and ulcers/gangrene were found.

Conclusion: Although more patients with PAD undergo revascularisation, one in 10 still ends up with a major amputation of the lower limb. The risk of amputation was highly associated with the severity of the vascular disease at the time of revascularisation, with ulcers/gangrene as the strongest predictor. Geographic differences in vascular treatment intensity were found, but these failed to explain the differences in risk of major amputation after revascularisation across catchment areas.

Keywords: Peripheral arterial disease, Amputation, Revascularisation, Treatment intensity
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INTRODUCTION

Symptomatic peripheral arterial disease (PAD) is a cause of significant morbidity, mortality, and decreased quality of life. During the last decades an increase in revascularisation performed for PAD has been reported.[1] Although the aim of revascularisation is to preserve the limb, and to reduce the risk of major amputation, the incidence of PAD related major amputations has shown vast variability.[2]

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The majority of major amputations are performed in patients with critical limb ischaemia (CLI), but some might be performed in patients with intermittent claudication (IC). Factors found to influence the fate of the limb are comorbidity,[3,4] socioeconomic factors,[5,6] and surgical volume in vascular centres.[7]

However, contemporary information on major amputations after revascularisation, for both IC and CLI, is sparse. The Danish Vascular Registry is a national clinical registry containing information on all vascular procedures including all revascularisations: bypass surgery, endovascular interventions, endarterectomy, and hybrid procedures. By cross linkage of information from the Danish Vascular Registry with information from national Danish Registries, the aim was to explore trends in revascularisation and outcomes following revascularisation for PAD. Furthermore, attempts were made to identify predictors of major amputation after revascularisation and to explore whether there were geographical differences in amputation free survival.

METHODS

The Danish population (approximately 5.7 million) is provided with a tax supported healthcare system and each citizen receives a unique civil registration number, which enables individual linkage between population based administrative and healthcare registries.[8] Study information was obtained from the Danish Vascular Registry, the Civil Registration System, the Danish National Patient Registry, the Danish National Prescription Registry, the Integrated Database for Labor Marked Research Agency, and Statistic Denmark.

The project was approved by the Danish Data Protection Agency (2008-58-0035). According to Danish legislation, analysis was done on anonymised data, and, therefore, no patient informed consent or approval by the local ethics committee was required.

Study population

Patients $\geq$50 years of age with a PAD diagnosis undergoing lower limb revascularisation by open surgery, endovascular reconstruction, or both from 2002 to 2014 were identified in the Danish Vascular Registry. The patients underwent revascularisation for IC (Rutherford 1—3), ischaemic rest pain (Rutherford 4), ulceration or gangrene (Rutherford 5—6), or acute limb ischaemia (ALI) (defined as a sudden decrease in limb perfusion causing a potential threat to limb viability).[9] If the patient had more than one revascularisation during the study period, the first vascular reconstruction was used as the index procedure. Patients with first time lower limb revascularisation prior to 2002 were excluded.

The registry contains information about indication for surgery, date and type of surgery, patient characteristics, and smoking habits.[10]

Outcome variable: major amputation

Data were obtained from the Danish National Patient Registry, which contains information on all in- and outpatient discharges from hospitals since 1977 and includes information on date of surgery, discharge diagnoses, and procedure codes at an individual level. Diagnostic coding is recorded using the International Classification of Diseases (8th revision until 1993, and 10th revision subsequently)[11] and since 1996 surgical procedures are coded according to the Scandinavian classifications of surgical and other procedures (NOMESCO).[12]

Information on major amputations was obtained for the years 2002—2014. A major amputation was defined as an amputation above the ankle, corresponding to NOMESCO procedure codes KNFQ09, KNFQ19, KNFQ99, KNGQ09, KNGQ19, and KNGQ99. Only major amputations performed at or after the index revascularisation date were included. If a patient had had more than one major amputation the earliest was used as the index amputation. Follow up time was the time from date of index revascularisation to date of first amputation or death, or until December 31, 2014, if patients did not undergo amputation or died in the study period. Since all procedures/events within the Danish healthcare system are recorded continuously and without exception into the national registries, no patients were lost to follow up. The Danish Patient Registry is continuously validated.[8]

Covariables

Data on covariables were acquired from the Danish Vascular Registry (age, sex, and smoking habits), the Danish National Patient Registry (comorbidity), the Integrated Database for Labor Market Research (socioeconomic variables), and the Danish National Prescription Registry (prescribed medication).

A comorbidity variable for cardiovascular disease (CVD) was defined to include coronary arterial disease (I20—25), stroke and transient ischaemic attack (I63—I67 and G45). Data were extracted from the Danish Patient Registry using the corresponding diagnoses. Both diabetes and hypertension are underreported, and for that reason diabetes and hypertension were defined according to prescribed medication using information from the Danish National Prescription Registry. A patient was given the diagnosis diabetes and/or hypertension if they had received antidiabetic or antihypertensive medication respectively in the year prior to revascularisation.

Prescriptions filled by the patients for antiplatelet drugs (including low dose aspirin, dipyridamole, and clopidogrel) and lipid lowering drugs, at the time of revascularisation, were obtained from the latter register.

Revascularisation procedures were divided into endovascular procedures and open surgery. Patients having a hybrid procedure involving both an endovascular procedure and open surgery were assigned to the open surgery group. The level of revascularisation procedure was divided into aorto-iliac procedures and infrainguinal procedures (including procedures on the groin arteries).

Patients were classified according to marital status (married/unmarried) and educational level (primary or lower secondary school, upper secondary and vocational education, higher education, or missing data). A patient was unmarried if they were divorced, widowed, or never married. Married patients included those living with a partner.

Treatment intensity

In Denmark seven vascular centres provide all relevant arterial reconstructions and each cover a unique catchment area, covering the surrounding municipalities, with population sizes ranging from 190,000 to 590,000 people ≥50 years of age.

Annual revascularisation rates for each vascular catchment area were calculated using the number of revascularisations as numerator and number of inhabitants ≥50 years of age from the corresponding catchment area as denominator. Rates are presented per 100,000 inhabitants ≥50 years of age. Revascularisation rates for each vascular catchment area were further stratified for indication (IC, rest pain, ulcers/gangrene, and ALI) separately, using same procedures as described above.

Statistics

Descriptive statistics were derived according to data type. Continuous variables are reported as means, and categorical variables are displayed as frequencies. Cuzick's test for trend was used to explore trend in revascularisation procedures, and indication performed across year of revascularisation. For this analysis, rest pain and ulcers/gangrene were combined into CLI.

Both univariable and multivariable Cox proportional hazards regression were used to assess the relationship between major amputation and the various associated factors, under the assumption of proportional hazards. Potential predictors for amputation were registered at time of first revascularisation. All independent variables, regardless of their statistical significance in the univariable analysis were introduced in the models. When modelling the Cox proportional hazard analysis assessing geographic variation, the variables were entered in a three step manner: 1, crude; 2, controlled for calendar year (index revascularisation year), risk factors, and socioeconomic variables; and 3, treatment intensity. The variables were entered in this way to ascertain the relative effect of patient related risk factors and treatment intensity. The assumption of proportional hazards was checked using conventional diagnostic plots. Amputation free survival was defined as avoidance of major amputation and was evaluated using Kaplan—Meier methods. Statistical analyses were performed using STATA/IC 14 (StataCorp LP, College Station, TX, USA).

RESULTS

Between 2002 and -2014, 25,982 patients had a first time revascularisation for PAD with a median follow up of 3.3 years (range 0 – 13.0 years). In all, 38,469 revascularisations were performed in these patients and 7922 (30.5%; 95% CI 30.0—31.0%) patients had more than one procedure during the study period (mean 1.5 procedures, SD 0.92, range 1—12). The national treatment intensity was 187 per 100,000 inhabitants ≥50 years of age.

Trend in revascularisation

An increase in the total number of first time procedures was seen up to 2010 and thereafter numbers decreased slightly (Fig. 1A). A significant trend towards endovascular revascularisation as first time revascularisation was observed, with 640 (36.6%) procedures in 2002 versus 1126 (59.0%) in 2014 ($p < .001$). IC was the most frequent indication for first time revascularisation (45.5%), and most often an endovascular procedure was performed (64.3%). A trend towards more endovascular procedures performed in patients with IC was seen (361 [51.2%] in 2002 vs. 565 [71.3%] in 2014, $p < .001$). A significant overall increase in IC as indication was observed during the study period ($p < .001$), although a peak was seen in 2009. In contrast, ALI as the indication became less frequent (187 [10.7%] in 2002 vs. 106 [5.6%] in 2014, $p < .001$). CLI was the indication in 46.3% of all first time revascularisations, and increased from 819 (46.8%) in 2002 to 990 (51.6%) in 2014 ($p = .005$) (Fig. 1B). Infrainguinal revascularisations counted for 60.5%, although the number of this type of procedure decreased during the period (Fig. 1C). Most infrainguinal revascularisations were open procedures, but infrainguinal endovascular procedures increased significantly (147 [12.2%] in 2002 vs. 343 [31.2%] in 2014, $p < .001$) (Fig. 1C). CLI as an indication for infrainguinal endovascular procedures increased from 73 (49.7%) in 2002 to 270 (78.7%) in 2014 ($p < .001$).

Patient characteristics

More men (54.5%) than women (45.5%) were revascularised ($p < .001$), and no change in the male/female ratio was seen during the study period ($p = .408$). The mean age at the time of revascularisation was 70.2 years (SD 9.84) (68.6 years for men vs. 72.2 years for women, $p < .001$). The distribution between age groups and baseline patient characteristics are shown in Table 1.

In all, 16,012 (61.6%) used a statin at the time of revascularisation and 17,450 (67.2%) took a platelet inhibitor, but despite that, only 13,133 (50.5%) were taking both (increasing from 14.6% in 2002 to 59.1% in 2014, $p < .001$). For both single and combined use of statins and platelet inhibitors, significantly fewer patients, who afterwards underwent amputation, were using secondary medical prevention at the time of first time revascularisation ($p < .001$ for both single and combine use). An increase in comorbidity was seen. Diabetes rose from 19.5% in 2002 to 22.9% in 2014 ($p < .001$), and CVD rose from 37.8% in 2002 to 42.4% in 2014 ($p < .001$).

Major amputations

In all, 2883 (11.1% (95% CI 10.7—11.5%)) patients had major amputation following revascularisation and of these 1820 (63.1%; 95% CI 61.4—64.9%) were carried out within one year of revascularisation. The median time from first revascularisation procedure to major amputation was 4.66 months (range 0.03—146.9). Cuzick's test for trend showed no change in the proportion of amputations performed within one year of revascularisation during the study ($p = .251$). This was also true analysing IC, CLI and ALI individually ($p = .0785$, $p = .120$, and $p = .183$, respectively). Most major amputations followed open

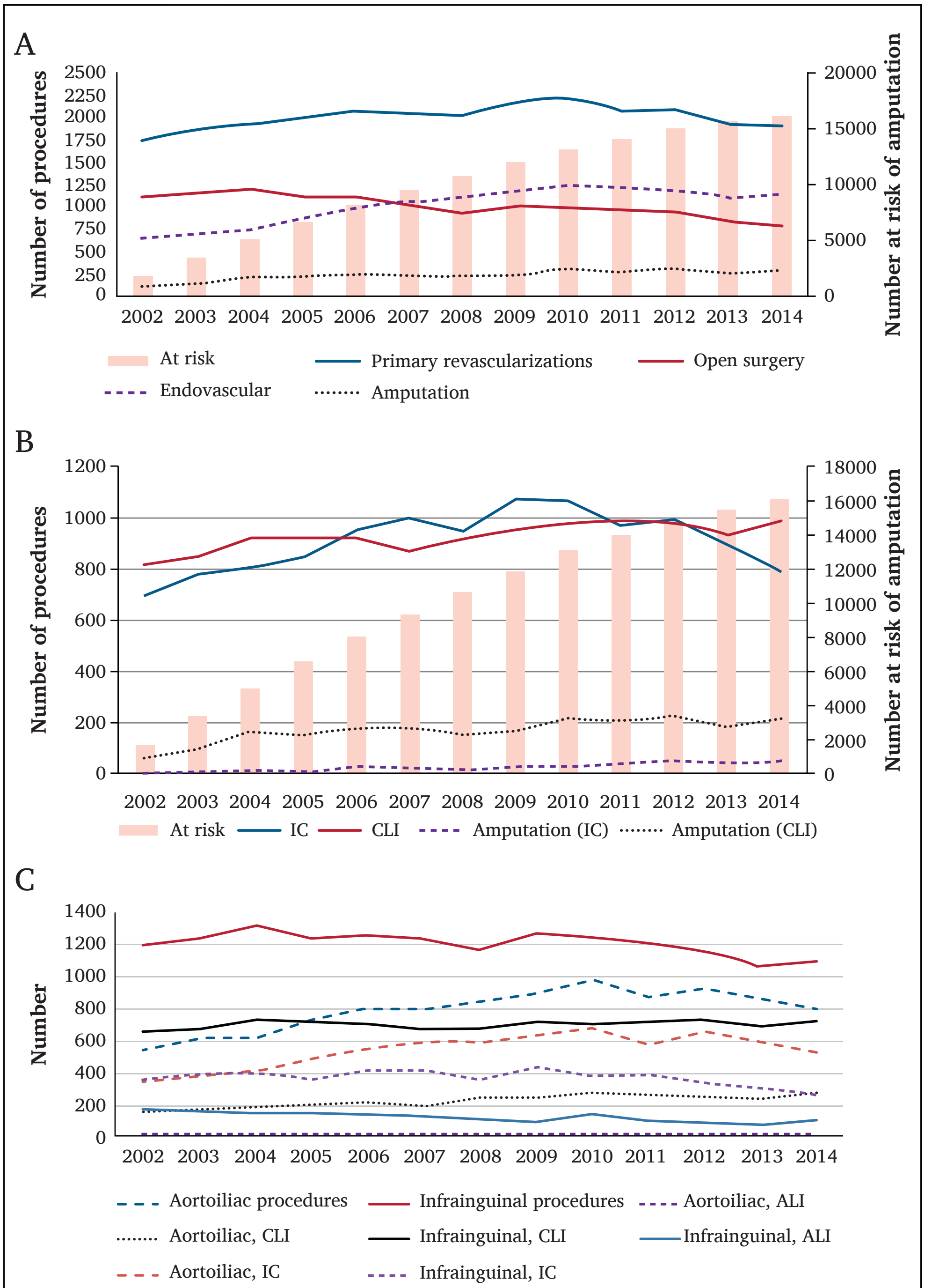

Figure 1. Total numbers of patients with primary revascularisation per year, and (A) yearly number of endovascular procedures, open revascularisations, post-interventional major amputations, and numbers at risk of amputation; (B) yearly number of patients presenting with CLI (critical limb ischaemia), IC (intermittent claudication), numbers of post-interventional major amputations for each group and numbers at risk of amputation; (C) yearly numbers of aorto-iliac and infrainguinal procedures.

revascularisations or hybrid procedures (63.6%). The median time from open revascularisation to amputation was 4.25 months (range 0.03—146.9 months) versus 5.52 months (range 0.03—142.8 months), for endovascular revascularisation ($p = .005$). Patients having an endovascular procedure had significantly better amputation free survival than the open group (HR 0.55, CI 0.51—0.59, $p < .001$). This was still true after adjustment for age, sex, smoking, type of revascularisation, indication, comorbidity, combined use of statin and platelet inhibitors, marital status, educational level, and calendar year (HR 0.81, CI 0.75—0.88, $p < .001$) (Table 2). From 2009 more above than

Table 1. Patient characteristics

	Total, n (%)	Revascularisation without subsequent amputation, n (%)	Revascularisation and amputation, n (%)
N	25,982	23,099 (88.9)	2883 (11.1)
Age, years			
50–59	4037 (15.5)	3705 (16.0)	332 (11.5)
60–69	8534 (32.9)	7786 (33.7)	748 (26.0)
70–79	8549 (32.9)	7542 (32.7)	1007 (34.9)
80–89	4293 (16.5)	3592 (15.6)	701 (24.3)
≥ 90	569 (2.2)	474 (2.1)	95 (3.3)
Sex			
Male	14,146 (54.5)	12,470 (54.0)	1676 (58.1)
Type of revascularisation			
Open surgery	13,017 (50.1)	11,183 (48.4)	1834 (63.6)
Endovascular	12,965 (49.9)	11,916 (51.6)	1049 (36.4)
Level of revascularisation			
Aorto-iliac	10,259 (39.5)	9651 (41.8)	608 (21.1)
Infrainguinal	15,723 (60.5)	13,448 (58.2)	2275 (78.9)
Indication			
Intermittent claudication	11,813 (45.5)	11,452 (49.6)	361 (12.5)
Rest pain	4912 (18.9)	4338 (18.8)	574 (19.9)
Ulcers or gangrene	7127 (27.4)	5498 (23.8)	1629 (56.5)
Acute ischaemia	1777 (6.8)	1492 (6.5)	285 (9.9)
Arteriosclerosis not specified	353 (1.4)	319 (1.4)	34 (1.2)
Comorbidity			
Hypertension	19,040 (73.3)	16,792 (72.7)	2248 (78.0)
CVD	10,785 (41.5)	9440 (40.9)	1345 (46.7)
Diabetes	5279 (20.3)	4466 (19.3)	813 (28.2)
Smoking			
Non-smoker	13,310 (51.2)	11,851 (51.3)	1459 (50.6)
Smoker	11,790 (45.4)	10,504 (45.5)	1286 (44.6)
Unknown	882 (3.4)	744 (3.2)	138 (4.8)
Secondary medical treatment			
Statins	16,012 (61.6)	14,700 (63.6)	1312 (45.5)
Platelet inhibitors	17,450 (67.2)	15,781 (68.3)	1669 (57.9)
Statins and platelet inhibitors	13,133 (50.5)	12,121 (52.5)	1012 (35.1)
Amputation level			
Above knee			1530 (53.1)
Below knee			1353 (46.9)
Socioeconomics			
Marital status			
Married	13,231 (50.9)	11,965 (51.8)	1266 (43.9)
Not married	12,751 (49.1)	11,134 (48.2)	1617 (56.1)
Education level			
No information	1944 (7.5)	1641 (7.1)	303 (10.5)
Primary and lower secondary school	12,459 (48.0)	11,003 (47.6)	1456 (50.5)
Upper secondary school and vocational education	8941 (34.4)	8067 (34.9)	874 (30.3)
Higher education	2638 (10.2)	2388 (10.3)	250 (8.7)

Data are presented as absolute numbers (percentages).

below knee amputations was performed ($p < .001$). Most major amputations (58.1%) were performed in men and they were significantly younger than women (70.7 vs. 75.4 years, $p < .001$). Ulcers/gangrene was the most frequent indication for revascularisation preceding amputation (56.5%). Median amputation free survival according to indication for revascularisation is shown in Fig. 2.

Mortality rates

Thirty day and one year mortality rates after revascularisation are presented in Table 3. A decrease in 30 day mortality after revascularisation was found over time (3.4% in 2002 vs. 2.6% in 2014, $p = .013$), while no change in one year mortality was seen (13.2% in 2002 vs. 12.2% revascularised in 2013)

Variables affecting major amputation

Univariable analysis showed significance of all predictor variables, except smoking and calendar year. Table 2 shows the results of the multivariable cox regression analysis showing that only smoking was not predictive of major amputation after adjusting for other covariables. Higher education and medical treatment with statins and/or

Table 2. Results of multivariable Cox regression analysis for amputation free survival in 25,982 patients with first time revascularisation

Variable	HR	CI 95%	*p*
Age	1.02	1.01–1.02	<0.001
Sex (male)	1.33	1.22–1.44	<0.001
Smoking	1.05	0.97–1.14	0.210
Type of procedure			
Open surgery	Ref.		
Endovascular	0.81	0.75–0.88	<0.001
Indication			
Intermittent claudication	Ref.		
Rest pain	3.81	3.32–4.37	<0.001
Ulcers or gangrene	8.06	7.11–9.13	<0.001
Acute ischaemia	5.44	4.60–6.44	<0.001
Comorbidity			
Hypertension	1.23	1.12–1.36	<0.001
CVD	1.25	1.15–1.36	<0.001
Diabetes	1.16	1.06–1.28	0.001
Secondary medical treatment			
Statins and platelet inhibitors	0.67	0.61–0.73	<0.001
Socioeconomics			
Marital status			
Married	Ref.		
Not married	1.21	1.12–1.31	<0.001
Education level			
Primary and lower secondary school	Ref.		
Upper secondary school and vocational education	0.96	0.88–1.05	0.332
Higher education	0.85	0.74–0.98	0.026
No information	0.90	0.78–1.04	0.143
Year			
Per one year increase	1.01	1.00–1.02	0.062

Adjusted for age, sex, smoking, type of revascularisation, indication, comorbidity, combined use of statin and platelet inhibitors, marital status, educational level, and calendar year of revascularisation. CVD = cardiovascular disease; HR = hazard ratio; CI = confidence interval.

platelet inhibitors at the time of revascularisation both had a protective effect on risk of amputation, while CLI and ALI were the strongest predictors of major amputations.

Variation according to vascular catchment areas

Variation was seen between vascular catchment areas, both in total treatment intensity (from 270 to 141 per 100,000), and regarding indications (Fig. 3). Significant differences in the risk of major amputation after revascularisation existed between the vascular catchment areas, as shown in Tables 4 and 5. When adjusted for age, sex, smoking, comorbidity, medical therapy, demographics, type of revascularisation, and calendar year three catchment areas had a significantly lower risk of amputation than the rest, while two had significantly higher risk (Table 4). This was still true after further adjustment for vascular treatment intensity.

Living in the catchment area with highest treatment intensity was associated with a significantly lower amputation risk after revascularisation than the rest of the catchment areas (HR 0.63, $p = .003$), but living in the catchment area with the next highest treatment intensity was associated with a 51% higher risk of amputation (HR 1.51, $p = .004$) after revascularisation for IC. An association between risk of amputation after revascularisation and catchment area was also seen in patients with ulcers/gangrene, while no association was found for rest pain or ALI (Table 4). These associations did not change when further adjusted for vascular treatment intensity (Table 5).

DISCUSSION

In this large national registry based study, trends in first time revascularisation procedures and the association between peripheral revascularisation and subsequent major amputation were explored. It was found that although the numbers of first time revascularisation procedures increased during the study period, the numbers of open procedures decreased. Despite this yearly increase, no change in amputations performed within one year of revascularisation was seen. The strongest independent predictors of major amputation were ulcers/gangrene, ALI, and rest pain, while diabetes was only associated with a 16% increased risk, and current smoking didn't influence limb survival. The importance of secondary medical prevention was emphasised by an independent relative risk reduction for major amputation of 33% using statins and low dose aspirin, which are in accordance with international guidelines for the treatment of PAD.[9]

Finally, geographical differences in risk of major amputation following revascularisation were also found.

One of the key strengths of the study is the combination of national governmental and clinical registries. Mandatory contributions from all seven Danish vascular centres results in high reliability and validity for the Danish Vascular Registry[10] and thus excludes selection bias.

One of the study's strength as well as a limitation is the use of registry data. The procedure coding on major amputations and vascular reconstruction are highly reliable. However, a methodological limit with respect to the National Danish Patients Registry is the lack of a reliable coding for laterality, but the number of subsequent contralateral major amputations is expected to be small.

Trend in revascularisation

A significant increase in revascularisation procedures performed yearly was found because of a major increase in endovascular procedures, rising from 51.2% in 2002 to 71.3% in 2014. These findings support the trend towards increasing treatment of PAD by endovascular revascularisation reported by others.[1,13] Several reasons for this rise in revascularisation, and in particular endovascular procedures, might exist. Firstly, a decrease in the threshold for intervention, in patients with IC and in patients with CLI, is likely to represent a major contribution to the increase in revascularisation procedures. Secondly, a rise in awareness of PAD might have contributed to the increase in revascularisation numbers.

It has been argued that an endovascular first approach leads to better limb survival[14] and it has been argued that it

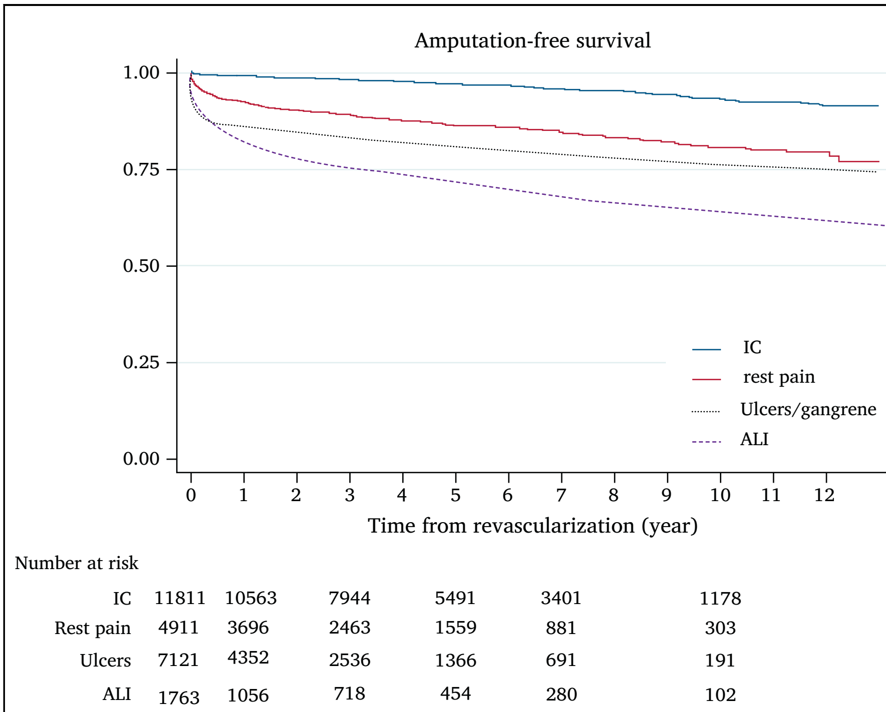

Figure 2. Amputation free survival for each indication. ALI = acute limb ischaemia; IC = intermittent claudication.

might not.[15] In the Cox regression analysis here it was found that having an open procedure first predicted a poorer outcome than endovascular procedure first (HR 0.55, $p < .001$), also after adjusting for indication and other factors (HR 0.81, $p < .001$). This could advocate for a better limb survival when having an endovascular procedure first, although one should be careful with this conclusion. Firstly, most endovascular procedures were performed in patients with IC, who have a lower risk of major amputation following revascularisation. Secondly, an endovascular first approach has not been formally adopted in Denmark. Thirdly, there is no information about the magnitude of the vascular disease, meaning that the choice of revascularisation modality highly depends on length, number, and location of stenoses/occlusions in the vessels. A short occlusion in a larger vessel is more likely to be treated endovascularly while more extended multiple occlusions are more likely to be treated by bypass surgery and this could lead to a treatment selection bias which could not be adjusted for.

Trend in major amputation

During the follow up period, 11.1% of patients had a major amputation, with 63% performed within the first year following revascularisation. These findings are lower than reported by others[16,17] with similar study populations. In all, 7.0% of patients had an amputation within the first year. This is in accordance with Gutacker et al.,[18] but in the literature the range of one year amputation free survival is wide mainly due to differences in study populations.[18–20]

It has previously been reported that age, sex, smoking, comorbidity (hypertension, CVD, and diabetes), and indication for revascularisation are predictors of major

Table 3. **Mortality rates after revascularisations in patients without subsequent amputation and patients with amputation, respectively**

	Mortality rate at 30 days, % (95% CI)			Mortality rate at 1 year, % (95% CI)		
	Revascularisation without subsequent amputation	With subsequent amputation	*p*	Revascularisation without subsequent amputation	With subsequent amputation	*p*
Total	3.0 (2.8–3.2)	4.6 (3.8–5.4)	<0.001	11.0 (10.6–11.4)	20.3 (19.1–21.4)	<0.001
IC	0.5 (0.3–0.6)	1.1 (0.4–1.8)	0.075	3.5 (3.1–3.8)	8.0 (6.1–10.0)	<0.001
CLI	4.3 (3.9–4.7)	4.0 (3.2–4.8)	0.493	17.2 (16.4–18.0)	20.8 (19.2–22.4)	<0.001
Rest pain	3.0 (2.5–3.6)	4.7 (3.3–6.2)	0.035	12.1 (11.1–13.1)	19.0 (16.2–21.7)	<0.001
Ulcers/gangrene	5.3 (4.6–5.7)	3.7 (2.7–4.8)	0.010	21.2 (20.2–22.3)	21.4 (19.4–23.4)	0.879
ALI	14.3 (12.6–16.1)	14.0 (10.0–18.1)	0.892	28.4 (26.0–30.7)	32.6 (27.4–37.9)	0.145

ALI = acute limb ischaemia; CLI = critical limb ischaemia; IC = intermittent claudication; CI = confidence interval.

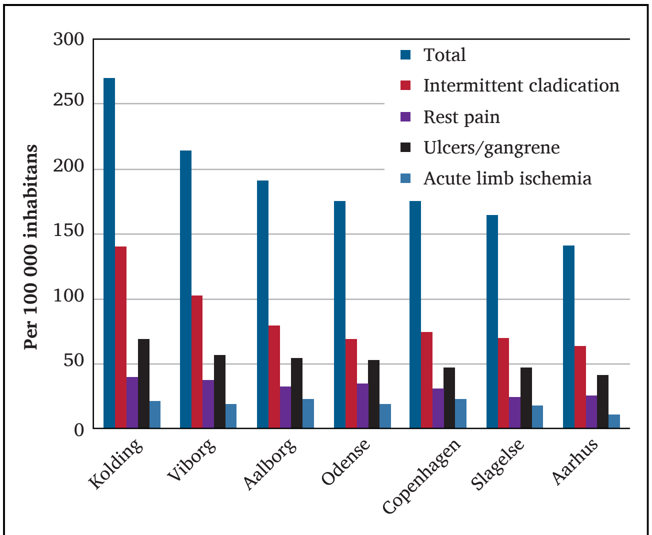

Figure 3. Average treatment intensity by catchment area in 2002–2014, by indication.

amputation in revascularised patients.[14,16,19] The data confirm this, although smoking didn't predict amputation in this cohort.

The severity of PAD has been strongly associated with the risk of major amputation, ulcers and gangrene being the strongest predictors,[14,19] which agrees with these results.

Despite an increase in revascularisation rate, the results still show a poor outcome for patients with CLI. This might be explained by the fact that although vascular procedures have indeed increased markedly, the largest increase was seen in patients with IC, which is not likely to affect the amputation rate. The reason for the shift in amputation level towards more above knee amputations is uncertain. An explanation could be that patients are getting older and are more fragile when major amputation becomes a necessity, and surgeons choose to go above knee to ensure wound healing and avoid re-amputations.

Trend in geographical variation

Regional differences in amputation rates have been ascribed, at least in part, to socioeconomic differences in the populations,[6,21] and the intensity of revascularisation.[22]

Table 4. Cox proportional hazard ratio for amputation free survival for each catchment area compared to the rest of the country

Catchment area	Total (N = 25,629)		Intermittent claudication (N = 11,813)		Rest pain (N = 4912)		Ulcers/gangrene (N = 7127)		Acute ischaemia (N = 1777)	
	HR[b]	CI 95%	HR[a]	CI 95%	HR[a]	CI 95%	HR[a]	CI 95%	HR[a]	CI 95%
Kolding	0.79*	0.71–0.88	0.63*	0.46–0.85	0.80	0.62–1.04	0.82*	0.71–0.95	0.86	0.59–1.23
Viborg	1.22*	1.09–1.37	1.51*	1.15–1.99	1.27	0.99–1.65	1.13	0.96–1.33	1.13	0.75–1.73
Aalborg	1.12	1.00–1.25	1.12	0.81–1.55	1.15	0.90–1.48	1.15	1.00–0.55	0.83	0.54–1.26
Odense	0.84*	0.73–0.97	0.57*	0.36–0.93	0.83	0.61–1.12	0.90	0.74–1.09	0.86	0.58–1.35
Copenhagen	0.89*	0.82–0.98	1.07	0.83–1.38	0.93	0.76–1.13	0.80*	0.71–0.90	1.12	0.86–1.45
Slagelse	1.00	0.95–1.16	0.93	0.68–1.28	0.99	0.78–1.25	1.02	0.89–1.17	1.04	0.75–1.45
Aarhus	1.37*	1.22–1.53	1.24	0.92–1.68	1.19	0.92–1.53	1.52*	1.31–1.75	1.11	0.67–1.85

HR = hazard ratio; CI = Confidence interval. **p*-value <.05. Kolding (n = 4676 patients); Viborg (n = 2744 patients); Aalborg (n = 2964 patients); Odense (n = 2357 patients); Copenhagen (n = 6359 patients); Slagelse (n = 3780 patients); Aarhus (n = 2749 patients).
[a] Adjusted for age, sex, smoking, type of revascularization, comorbidity, combined use of statin and platelet inhibitors, marital status, educational level, and calendar-year.
[b] Adjusted for a and indication. Catchment areas are listed according to vascular treatment intensity.

Table 5. The impact of annual municipal treatment intensity on amputation free survival for each catchment area compared to the rest of the country

Catchment area	Total (N = 25,629)		Intermittent claudication (N = 11,813)		Rest pain (N = 4912)		Ulcers/gangrene (N = 7127)		Acute ischaemia (N = 1777)	
	HR[d]	CI 95%	HR[c]	CI 95%	HR[c]	CI 95%	HR[c]	CI 95%	HR[c]	CI 95%
Kolding	0.80*	0.71–0.89	0.66*	0.47–0.93	0.79	0.61–1.02	0.81*	0.70–0.94	0.86	0.59–1.23
Viborg	1.23*	1.09–1.38	1.60*	1.21–2.12	1.27	0.98–1.64	1.13	0.96–1.33	1.15	0.76–1.74
Aalborg	1.12	1.00–1.25	1.09	0.79–1.51	1.15	0.90–1.49	1.15	1.00–1.34	0.83	0.54–1.26
Odense	0.84*	0.73–0.97	0.56*	0.35–0.90	0.83	0.61–1.11	0.90	0.74–1.09	0.89	0.58–1.36
Copenhagen	0.89*	0.81–0.97	1.06	0.82–1.38	0.92	0.76–1.13	0.80*	0.71–0.90	1.11	0.85–1.46
Slagelse	1.00	0.89–1.11	0.88	0.64–1.21	1.00	0.78–1.26	1.02	0.88–1.17	1.05	0.75–1.46
Aarhus	1.15*	1.03–1.29	1.18	0.87–1.60	1.22	0.94–1.57	1.56*	1.34–1.81	1.14	0.67–1.92

HR = hazard ratio; CI = Confidence interval. **p*-value <.05. Kolding (n = 4676 patients); Viborg (n = 2744 patients); Aalborg (n = 2964 patients); Odense (n = 2357 patients); Copenhagen (n = 6359 patients); Slagelse (n = 3780 patients); Aarhus (n = 2749 patients).
[c] Adjusted for age, sex, smoking, type of revascularization, comorbidity, combined use of statin and platelet inhibitors, marital status, educational level, calendar-year, and vascular treatment intensity.
[d] Adjusted for c and indication. Catchment areas are listed as in Table 4. **p*-value <.05.

Significant variation in post-interventional amputations was seen across catchment areas. After adjustment for socioeconomic factors, comorbidity, and secondary medical treatment three catchment areas had better amputation free survival than the others, suggesting that the variation cannot be solely explained by differences in catchment area populations.

Another explanation for the geographic difference in post-interventional amputation could be differences in vascular treatment intensity. Although, it was found that patients living in the catchment area with the highest treatment intensity had lower risk of major amputation after revascularisation, patients living in the catchment area with the next highest treatment intensity had a significantly higher risk of amputation, while no significant differences was found for patients living in lower intensity areas.

However, difference in treatment strategies cannot fully explain the differences between catchment areas, as adjustment for local treatment intensity left two catchment areas still associated with a better outcome, and one catchment area with a poorer outcome. Differences in the risk of having a major amputation after revascularisation for ulcers/gangrene was also seen between catchment areas with similar treatment intensities. These findings might represent dissimilarities in awareness of ulcers/gangrene in patients with PAD, the severity of ulcers/gangrene at the time of revascularisation, pre- and post-operative wound care, or even difference in surgical willingness for revascularisation in this group of patients. This is an assumption and cannot be answered by the data.

CONCLUSION

A significant increase was seen in first time revascularisations during the study period, especially because of a rise in the number of endovascular procedures performed. Despite this increase, no differences in major amputations in the year following revascularisation was seen. Geographic differences in vascular treatment intensity were found, but these failed to explain the differences in risk of major amputation after revascularisation across catchment areas.

CONFLICTS OF INTEREST

None.

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COUP D'OEIL

Traumatic Deviation of the Popliteal Artery

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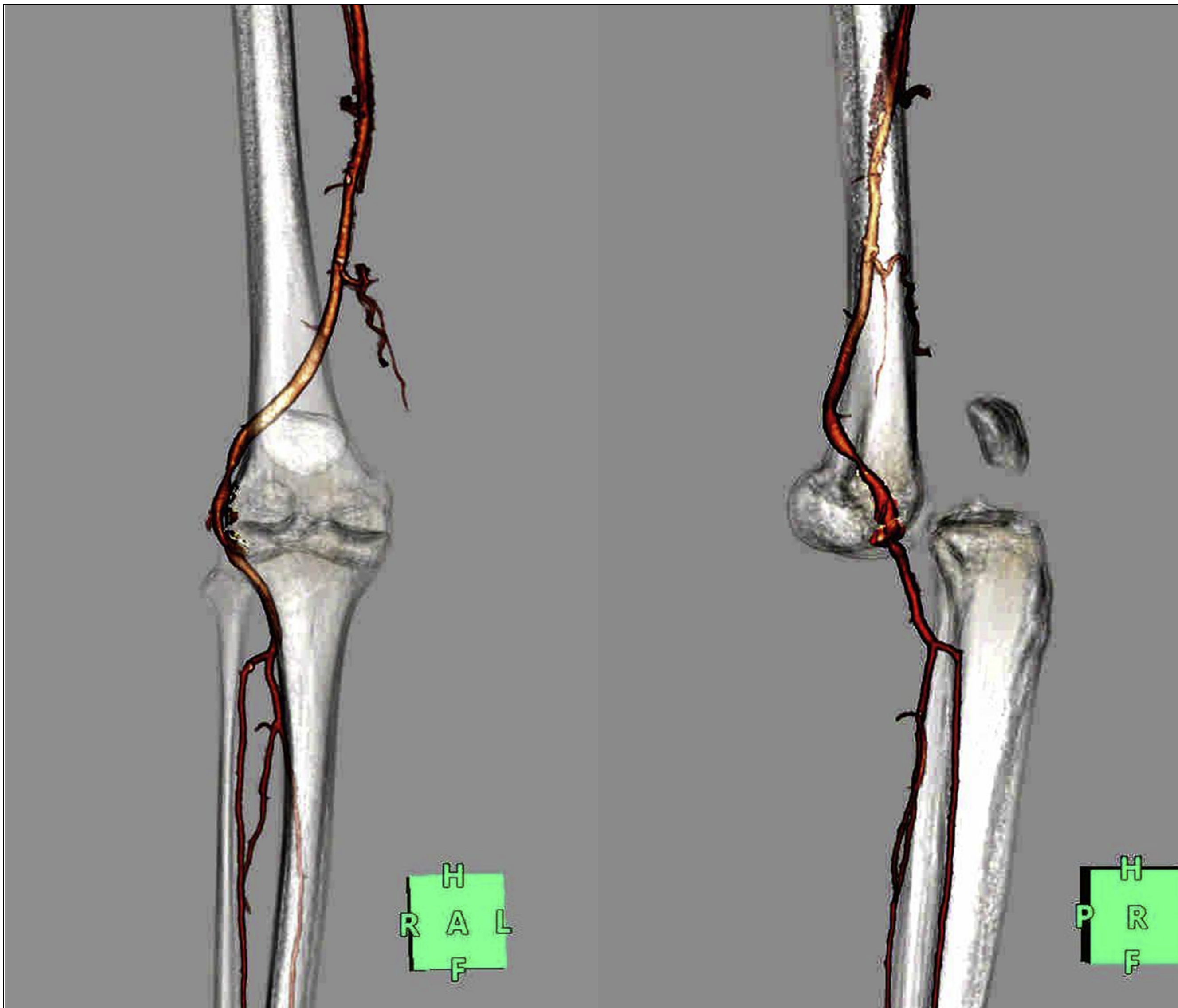

A 51 year old man was admitted with traumatic knee dislocation with clinical signs of acute limb ischaemia. A computed tomography scan confirmed the knee dislocation and also major axial deviation of the right popliteal artery outside the knee joint. After reduction of the dislocation under general anaesthesia, a check digital subtraction angiogram was performed. It demonstrated correct realignment of the right popliteal artery with a short stenosis subsequently treated by transluminal balloon angioplasty. The patient recovered well on both vascular and orthopaedic fronts.

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