UTILIZATION AND OUTCOMES OF INTERVENTIONAL PROCEDURES FOR PERIPHERAL OCCLUSIVE ARTERIAL DISEASE IN ONTARIO: A POPULATION-BASED STUDY

by

Mohammed Al-Omran

A thesis submitted in conformity with the requirements for the degree of Master's of Science
Graduate Department of Health Administration
University of Toronto

© Copyright by Mohammed Al-Omran 2001
The author has granted a non-exclusive licence allowing the National Library of Canada to reproduce, loan, distribute or sell copies of this thesis in microform, paper or electronic formats.

The author retains ownership of the copyright in this thesis. Neither the thesis nor substantial extracts from it may be printed or otherwise reproduced without the author's permission.

L’auteur a accordé une licence non exclusive permettant à la Bibliothèque nationale du Canada de reproduire, prêter, distribuer ou vendre des copies de cette thèse sous la forme de microfiche/film, de reproduction sur papier ou sur format électronique.

L’auteur conserve la propriété du droit d’auteur qui protège cette thèse. Ni la thèse ni des extraits substantiels de celle-ci ne doivent être imprimés ou autrement reproduits sans son autorisation.

0-612-63066-8
ABSTRACT

Master's of Science, Department of Health Administration, University Of Toronto, 2001
Mohammed Al-Omran

This thesis describes the utilization and outcomes of interventional procedures for peripheral occlusive arterial disease in Ontario for fiscal years 1991 to 1998, using Ontario's administrative databases. The age and sex adjusted rate of arterial bypass surgery (ABS) fell significantly (p=0.0002), whereas the rate of angioplasty increased significantly (p=0.0005). However, the combined rate for revascularization procedures (ABS and angioplasty) was stable over the same time. The 5-year cumulative survival and major amputation-free survival rates for patients who underwent ABS were 61.5% and 83.4%, respectively and for patients who underwent angioplasty were 69% and 92.2%, respectively. These trends suggest a 'substitution effect' of angioplasty for bypass surgery, which in turn may reflect a change in the practice pattern of vascular surgeons in Ontario. Long-term survival and amputation-free survival rates may be used as a measure of the population-based effectiveness of revascularization procedures.
ACKNOWLEDGEMENT

I would like to thank the following people for their advice and input for this thesis. This study would not be possible without the support and guidance of my thesis supervisor, Dr Jack Tu. My thesis committee members, Drs. Daryl Kucey and K.Wayne Johnston, greatly improved this work through their insightful comments, clinical expertise, and helpful suggestions. Dr. Muhammad Mamdani provided important advice and assistance with programming. The ICES staff provided invaluable advice, friendship and technical assistance.

I dedicate this thesis to my parents, with thanks for their love and support during my many years of schooling.
# TABLE OF CONTENTS

Abstract.......................................................................................................................... ii
Acknowledgement .......................................................................................................... iii
Table of Contents ........................................................................................................... iv
List of Tables ................................................................................................................... vi
List of Figures .................................................................................................................. vii
List of Appendices .......................................................................................................... ix

Introduction .................................................................................................................... 1
  1.1 Rationale ................................................................................................................ 1
  1.2 Study Objectives ................................................................................................... 4

Background ...................................................................................................................... 6
  2.1 Pathophysiology ................................................................................................... 6
  2.2 Risk Factors ........................................................................................................... 8
  2.3 Coexisting Vascular Disease ............................................................................... 9
  2.4 Clinical Presentation ............................................................................................ 10
    2.4.1 Intermittent Claudication (IC) .................................................................... 10
    2.4.2 Critical Limb Ischemia (CLI) ................................................................. 11
    2.4.3 Acute Limb Ischemia (ALI) ................................................................... 12
  2.5 Interventionsal Management of POAD ............................................................... 13
    2.5.1 Revascularization procedures ................................................................... 13
      2.5.1.1 Indications for intervention ............................................................ 13
      2.5.1.2 Interventional procedures .............................................................. 13
      2.5.1.3 Aortoiliac Occlusive Disease ......................................................... 14
      2.5.1.4 Infragenual Occlusive Disease ....................................................... 16
    2.5.2 Amputation .................................................................................................. 17
      2.5.2.1 Types of amputation ..................................................................... 17
      2.5.2.2 Amputation level .......................................................................... 18

Methods .......................................................................................................................... 20
  3.1 Overview ................................................................................................................. 20
    3.1.1 Study Design ............................................................................................... 20
    3.1.2 Exposure ....................................................................................................... 20
    3.1.3 Population .................................................................................................... 20
    3.1.4 Outcomes ..................................................................................................... 21
    3.1.5 Unit of analysis ............................................................................................ 21
  3.2 Data Source ............................................................................................................. 21
    3.2.1 Canadian Institute for Health Information (CIHI) Database ................... 21
    3.2.2 Ontario Health Insurance Plan (OHIP) Database .................................. 22
    3.2.3 Registered Persons Data Base (RPDB) .................................................... 23
  3.3 Identification of cases ............................................................................................. 24
    3.3.1 Arterial bypass surgery procedures ......................................................... 24
    3.3.2 Amputation procedures ............................................................................. 24
    3.3.3 Percutaneous transluminal angioplasty procedures ................................ 25
    3.3.4 Outcomes of revascularization procedures ........................................... 26
  3.4 Data validation ......................................................................................................... 27
List of Tables

Table 1: Canadian Classification of Diagnostic, Therapeutic and Surgical Procedures (CCP) codes used to identify patients undergoing lower limb arterial reconstruction, or amputation ........................................... 31

Table 2: International Classification of Disease, ninth revision (ICD-9) codes used to exclude patients undergoing amputation for an indication other than peripheral occlusive arterial disease ........................................... 31

Table 3: Characteristics of patients who underwent revascularization procedures of the lower extremity secondary to peripheral occlusive disease, in Ontario, for fiscal years 1991 to 1998 ........................................... 40

Table 4: Characteristics of patients who underwent amputation of the lower extremity secondary to peripheral occlusive disease, in Ontario, for fiscal years 1991 to 1998 ........................................... 40

Table 5: Validation of the arterial bypass surgery and amputation procedures codes ........................................... 41

Table 6: Prevalence of risk factors as abstracted from the matched patients' charts ........................................... 41

Table 7: Agreement between matched patients' charts and corresponding CIHI records for several co-morbidities ........................................... 42

Table 8: Average age-adjusted rates and rate ratios of interventional procedures for peripheral occlusive arterial disease in Ontario, for fiscal years 1991 to 1998 ........................................... 43

Table 9: Linear trends estimates for changes in the rates of peripheral occlusive arterial disease interventional procedures, in Ontario, for fiscal years 1991 to 1998, as determined using least square linear regression ........................................... 44

Table 10: Linear trends estimates for changes in the age-specific rates of peripheral occlusive arterial disease interventional procedures, in Ontario, for fiscal years 1991 to 1998, as determined using least square linear regression ........................................... 45

Table 11: Risk factors for death post revascularization procedures for peripheral occlusive arterial disease, as determined using a Cox proportional hazard model ........................................... 47

Table 12: Risk factors associated with amputation post revascularization procedures for peripheral occlusive arterial disease, as determined using a Cox proportional hazard model ........................................... 48

Table 13: Risk factors associated with major amputation post revascularization procedures for peripheral occlusive arterial disease, as determined using a Cox proportional hazard model ........................................... 49

Table 14: Risk factors associated with minor amputation post revascularization procedures for peripheral occlusive arterial disease, as determined using a Cox proportional hazard model ........................................... 50

Table 15: Peripheral occlusive arterial disease interventional procedure trends comparison with previously published population-based studies ........................................... 84
List of Figures

Figure 1: Flow chart to identify eligible records for analysis from the Canadian Institute for Health Information for amputation procedures in Ontario, from April 1, 1991 to March 31, 1999..........................51

Figure 2: Flow chart to identify eligible records for analysis from the Canadian Institute for Health Information for arterial bypass surgery (ABS) procedures in Ontario, from April 1, 1991 to March 31, 1999...........................................................................52

Figure 3: Flow chart to identify eligible records for analysis from the Ontario Health Insurance Plan database for percutaneous transluminal angioplasty (PTA) procedures in Ontario, from April 1, 1992 to March 31, 1999..........................................................53

Figure 4: Trends in bypass surgery and angioplasty combined rates (per 100,000 adults aged 45 years and older) in Ontario, for fiscal years 1992-1998, by year and sex..........................54

Figure 5: Trends in arteria bypass surgery rates (per 100,000 adults aged 45 years and older) in Ontario, for fiscal years 1991-1998, by year and sex..................................................54

Figure 6: Trends in aorto-iliac-femoral bypass surgery rates (per 100,000 adults aged 45 years and older) in Ontario, for fiscal years 1991-1998, by year and sex ......................................................55

Figure 7: Trends in other peripheral bypass surgery rates (per 100,000 adults aged 45 years and older) in Ontario, for fiscal years 1991-1998, by year and sex ......................................................55

Figure 8: Trends in percutaneous transluminal angioplasty rates (per 100,000 adults aged 45 years and older) in Ontario, for fiscal years 1992-1998, by year and sex ......................................................56

Figure 9: Trends in amputation rates (per 100,000 adults aged 45 years and older) in Ontario, for fiscal years 1991-1998, by year and sex..................................................57

Figure 10: Trends in Major amputation rates (per 100,000 adults aged 45 years and older) in Ontario, for fiscal years 1991-1998, by year and sex..................................................57

Figure 11: Trends in Minor amputation rates (per 100,000 adults aged 45 years and older) in Ontario, for fiscal years 1991-1998, by year and sex......................................................58

Figure 12: Trends in below-knee amputation rates (per 100,000 adults aged 45 years and older) in Ontario, for fiscal years 1991-1998, by year and sex......................................................59

Figure 13: Trends in above-knee amputation rates (per 100,000 adults aged 45 years and older) in Ontario, for fiscal years 1991-1998, by year and sex......................................................59

Figure 14: Average annual rate of arterial bypass surgery and angioplasty combined (per 100,00 aged 45 years and older) in Ontario, for fiscal years 1991-1998, by age group and sex..........................60

Figure 15: Average annual rate of arterial bypass surgery (per 100.00 aged 45 years and older) in Ontario, for fiscal years 1991-1998, by age group and sex..................................................60

Figure 16: Average annual rate of aorto-iliac-femoral bypass surgery (per 100.00 aged 45 years and older) in Ontario, for fiscal years 1991-1998, by age group and sex..........................61

Figure 17: Average annual rate of other peripheral bypass surgery (per 100.00 aged 45 years and older) in Ontario, for fiscal years 1991-1998, by age group and sex.................................61
Figure 18: Average annual rate of percutaneous transluminal angioplasty (per 100.00 aged 45 years and older) in Ontario, for fiscal years 1992-1998, by age group and sex ................................................................. 62

Figure 19: Average annual rate of amputation (per 100.00 aged 45 years and older) in Ontario, for fiscal years 1991-1998, by age group and sex ............................................................... 63

Figure 20: Average annual rate of major amputation (per 100.00 aged 45 years and older) in Ontario, for fiscal years 1991-1998, by age group and sex ............................................................... 63

Figure 21: Average annual rate of below-knee amputation (per 100.00 aged 45 years and older) in Ontario, for fiscal years 1991-1998, by age group and sex ............................................................... 64

Figure 22: Average annual rate of above-knee amputation (per 100.00 aged 45 years and older) in Ontario, for fiscal years 1991-1998, by age group and sex ............................................................... 64

Figure 23: Average annual rate of minor amputation (per 100.00 aged 45 years and older) in Ontario, for fiscal years 1991-1998, by age group and sex ............................................................... 65

Figure 24: Kaplan-Meier survival curves post bypass surgery ............................... 66

Figure 25: Kaplan-Meier survival curve post percutaneous transluminal angioplasty .... 66

Figure 26: Kaplan-Meier amputation-free survival curves post bypass surgery ............................... 67

Figure 27: Kaplan-Meier amputation-free survival curve post angioplasty ............................... 67

Figure 28: Kaplan-Meier major amputation-free survival curves post bypass surgery ............................... 68

Figure 29: Kaplan-Meier major amputation-free survival curve post angioplasty ............................... 68

Figure 30: Kaplan-Meier minor amputation-free survival curves post bypass surgery ............................... 69

Figure 31: Kaplan-Meier minor amputation-free survival curve post angioplasty ............................... 69
List of Appendices

Appendix 1: Validation form ..............................105

Appendix 2: Ethical approval for chart review from Sunnybrook Hospital .................106
CHAPTER 1

INTRODUCTION

The purpose of this chapter is to:

1. Provide the rationale for the study;
2. Introduce the study objectives.

1.1 Rationale

Peripheral occlusive arterial disease (POAD) is an arteriosclerotic occlusive disease of the aortoiliac and/or femoropopliteal arterial system. Clinical manifestations of this condition typically begin with intermittent claudication and may progress to disabling pain at rest, infectious complications, and ultimately gangrene and limb loss. The risk factors for POAD are the same as those for atherosclerosis in general and include male sex, advanced age, cigarette smoking, hypertension, diabetes, and hyperlipidaemia.

The prevalence of intermittent claudication (IC) varies from 0.4 to 14.4%. This wide variation in prevalence can be explained by; age, sex, and geographical location of the population studied and by the diagnostic technique used to identify patients with IC.

Treatment of POAD depends on the stage of the disease. It includes risk factors modification, exercise programs, good foot care, antibiotic use, and surgical intervention. Interventions are directed toward the relief of symptoms, improvement in quality of life, and limb salvage.
The evaluation of therapeutic effectiveness of POAD interventional procedures requires the use of outcome measures that assess factors affecting patients directly (e.g. quality of life, survival, amputation-free survival and pain relief) and clinical measures (e.g. laboratory test scores).\textsuperscript{15}

Despite a significant growth in specialized vascular manpower and facilities, it has been proven difficult to measure the population-based therapeutic effectiveness of surgery for POAD.\textsuperscript{16}

Since limb salvage is considered one of the primary goals of the interventional management of POAD especially in patients with critical limb ischemia,\textsuperscript{17,18} tentative conclusions might be drawn by examining the outcome of surgery for POAD as measured by the rate of lower-extremity amputation.\textsuperscript{19}

In order to identify the population-based therapeutic effectiveness of surgery for POAD, the association between the revascularization procedures and amputation rates has been examined in many studies.\textsuperscript{16,20-24} The assumption in these studies is that if revascularization procedures avoid the need for amputation in some patients, then a negative correlation should exist between rates of amputation and revascularization procedures.\textsuperscript{24}

Several population-based studies have reported decreased rates of amputation in association with an increase in the use of revascularization procedures.\textsuperscript{22-24} On the other hand, some studies showed no change in lower-extremity amputation rate.\textsuperscript{16,20,21}

The limitations of these studies make drawing conclusions as to effectiveness of surgery in preventing amputation extremely difficult. These limitations include:
1) Estimates of the procedure rates were at the population level rather than at the patient level, and therefore might reflect the incidence of multiple procedures for the same patient.

2) Failure to examine rates of primary and secondary amputation separately. Primary amputation is defined as amputation of the ischemic lower extremity without an antecedent attempt at revascularization. Secondary amputation is defined as amputation for the ischemic lower extremity with a previous attempt for revascularization. Arterial bypass surgery may prevent or delay secondary amputation but has no role for primary amputation. Therefore, if the overall reduction in the amputation rate is as a result of reduction in the primary amputation rather than reduction in the secondary amputation, attribution of increased use of bypass surgery, as a cause of this reduction is not true. Furthermore, if there is overall reduction in amputation rate but the rate of secondary amputation is increasing, this will give a further false impression of the effect of bypass surgery.

3) The amputation rate is not an appropriate outcome measure for most cases of angioplasty. This is because; most angioplasty procedures are performed for life-style limiting claudication, unlike bypass operations that are performed in most cases for ischemic rest pain or to prevent tissue loss.

4) The incidence of the underlying POAD is not known.

Determination of amputation rate in patients surviving post revascularization procedures (amputation-free survival rate) may overcome some of these limitations in order to assess how well bypass procedures prevent or delay amputation.
Another outcome that can be used to evaluate revascularization procedures on a population-based level is the long-term survival rate post surgery.

In Canada, limited population-based data are available on the utilization of arterial bypass surgery (ABS), percutaneous transluminal angioplasty (PTA), and amputation for POAD. Furthermore, population-based outcomes as measured by survival and amputation-free survival rates following revascularization procedures are not known.

Conducting such a study in Ontario could act as an impetus for establishing a broader picture on the utilization of POAD interventional procedures, and could determine how well bypass surgery prevents or delays amputation. Such information may help in decision making for the provision of vascular services. In addition, it may serve as a basis for formulating or reformulating hypotheses that are tested in an analytic design at the patient level to examine the effect of vascular services on patient care.

1.2 Study Objectives

This thesis evaluates the epidemiology and outcomes of POAD interventional procedures in Ontario. The study objectives were:

1) To determine age and sex variation in the utilization of interventional procedures for POAD in Ontario over the past decade.

The specific questions to be answered were:

a. Did utilization rates of interventional procedures for POAD differ by age group in Ontario over the past decade?
b. Did utilization rates of interventional procedures for POAD differ by sex in Ontario over the past decade?

2) To determine time trends in rates of interventional procedures for POAD in Ontario over the past decade.

The specific question to be answered was:

Have the rates of interventional procedures for POAD changed over the past decade in Ontario?

3) To measure the outcomes of revascularization procedures (arterial bypass surgery and percutaneous transluminal angioplasty) for POAD at the patient level and to determine the factors affecting these outcomes.

The specific questions to be answered were:

a. What are the 5-year survival rates in patients who underwent revascularization procedures for POAD?

b. What are the 5-year amputation rates in patients surviving post revascularization procedures for POAD (5-year amputation-free survival rates)?

c. Do age, sex and co-morbidities affect the outcomes in patients who undergo revascularization procedures for POAD?
CHAPTER 2
BACKGROUND

The objectives of this chapter are to:

1. Review the pathophysiology of POAD;
2. Review the risk factors for POAD;
3. Summarize coexisting vascular disease with POAD;
4. Describe the clinical presentation of POAD;
5. Summarize the interventional management of POAD.

2.1 Pathophysiology

Atherosclerosis is a degenerative systemic arterial disease, which begins early in life.\textsuperscript{25,26} It is characterized by thickening and hardening of medium-size and larger arteries with narrowing of the arterial lumen by atherosclerotic plaques.\textsuperscript{27} The basic lesion is a raised focal plaque, which develops within the intimal layer of the arterial wall.\textsuperscript{28-31} Plaque disruption results in alteration of endothelial integrity that lead to thrombus formation.\textsuperscript{32}

Once the thrombus formed, further clot deposition occurs and leads to narrowing of the arteries.\textsuperscript{33}

It is generally accepted that the atherosclerotic plaque is the precursor of occlusive lesions leading to the expression of clinical symptoms in POAD.\textsuperscript{32,34} Plaques are distributed in a segmental pattern throughout the body. Lesions are commonly found in the terminal aorta, the aortic bifurcation, the common iliac bifurcation, the common femoral, and the popliteal and proximal portions of the tibial arteries.\textsuperscript{35}
As stenosis develops slowly over a period of time in the larger arteries, blood flow is diverted through the smaller arterial branches (collateral circulation) proximal to the stenotic areas. The ability to develop collateral circulation even with total occlusion of a major artery can keep the patient from becoming symptomatic at rest. This compensating mechanism however, is not often able to meet the increased metabolic demand imposed by exercise and ischemic pain may occur.

As a stenosis extends more proximally involving longer segments and vessels become occluded, perfusion is further compromised and pain occurs at rest. The leg may feel cold, pulses may become weak or absent and the skin is often pale. Superficial skin ulcers may occur either spontaneously or following trauma. Ultimately, gangrene may develop.

The lack of a developed collateral circulation is what makes an acute lesion more dangerous than a slow progression of chronic disease that leads to an occlusion. Collateral development is often an adequate compensatory mechanism when stenoses occur in the large more proximal arteries. However, there are relatively few collateral vessels in the lower leg and stenotic and occlusive disease in the distal popliteal and proximal tibial arteries can cause severe rest pain and ischemia.
2.2 Risk Factors

The risk factors for developing POAD are similar to those for other atherosclerotic lesion and include:

1) **Age:** The prevalence of POAD increases with age in both sexes.\(^1\)-\(^3\),\(^12\),\(^37\)-\(^41\) In addition, there is a general pattern of a gradual increase in prevalence up to the age of 70 years.\(^2\),\(^3\),\(^41\)-\(^43\) While only 1 to 2% of people younger than 70 years of age suffer from intermittent claudication, this figure rises to 10% in those older than age 70.\(^44\) Age also has been associated with an increase risk of local disease progression.\(^15\),\(^45\)

2) **Sex:** The prevalence of POAD in men is greater than that for women at all age groups. The overall male/female prevalence ratio is 1.2 to 2.\(^1\),\(^2\),\(^6\),\(^15\),\(^46\) In addition, male gender has been associated with an increase risk of local disease progression.\(^15\),\(^47\)

3) **Smoking:** Most of the epidemiological studies of POAD have confirmed that cigarette smoking is a strong risk factor for the development of POAD.\(^2\),\(^3\),\(^5\)-\(^9\),\(^12\),\(^37\),\(^48\),\(^49\) The relative risk for developing POAD in smokers ranging from 1.7\(^2\) to as high as 7.5\(^3\) In addition, the diagnosis of POAD is made up to a decade earlier in smokers than in nonsmokers.\(^50\),\(^51\) Furthermore, the evidence suggests that smoking may in fact be a more important risk factor for the development and progression of POAD than it is for coronary artery disease.\(^7\)-\(^9\)

4) **Diabetes mellitus:** Many studies have shown an association between diabetes and the development of POAD.\(^5\)-\(^9\),\(^48\),\(^52\),\(^53\) Overall, intermittent claudication seems to be about twice as common among diabetic patients as among non-diabetic patients.\(^15\) POAD in patients with diabetes is more aggressive, with early large vessels involvement coupled with microangiopathy. In patients with POAD and diabetes, the progression of the local
disease and the risk of major amputation are much higher when compared with non-diabetic patients.40,54,55

5) Hypertension: In most studies, systolic blood pressure is positively correlated with the development of POAD.5-8,12,37,48,49 The relative risk for developing POAD in hypertensive individuals is 2.5 in men and 3.9 in women.6 However, some studies failed to show this association.2,40,56 The role of hypertension in the progression of the local disease is not clear. Although Jelnes et al 55 noted that the risk of deterioration was related to hypertension, Dormandy and Murray 57 found that hypertension did not influence the local progression of POAD.

6) Hyperlipidemia: There is conflicting evidence regarding the relationship between hyperlipidemia and POAD. Although some studies have showed strong association between cholesterol level and POAD,6,10 others have failed to confirm this association.3,49,58 However there is evidence that treatment of hyperlipidemia reduces both the progression and incidence of POAD.59,60

7) Other risk factors: A number of other potential risk factors have been investigated. Serum fibrinogen,3,61,62 hematocrit,6,61,62 and blood viscosity61,62 are consistently higher in POAD patients.

2.3 Coexisting Vascular Disease

POAD, coronary artery disease (CAD) and cerebrovascular disease (CVD) are all manifestations of atherosclerosis and often co-exist in the same patients.

In patients with POAD, the prevalence of CAD varies between 35 to 60%, when CAD was diagnosed by history, clinical examination and electrocardiography.3,5,11,57,63
By duplex examination, carotid disease has been found in 26 to 50% of patients with POAD. In addition, the prevalence of abdominal aortic aneurysms in POAD was found to be twice that of the general population.

2.4 Clinical Presentation

2.4.1 Intermittent Claudication (IC)

Symptoms: IC is one of the most characteristic symptoms of POAD. Patients complain of profound fatigue, aching, or crampy pain in the leg after exertion that is relieved by rest. The two key features of claudication are its consistent reproducible occurrence at a constant distance and its prompt relief by rest (within minutes). The symptoms appear distal to the site of vascular occlusion. In iliac occlusion, the discomfort is in the thigh or buttock, while in superficial femoral artery occlusion, the symptoms are found in the calf.

Prevalence: The prevalence of intermittent claudication ranging from 0.4 to 14.4%. The wide range in prevalence can be explained by; age, sex, and geographical location of the population studied and by the diagnostic technique used to identify patients with IC.

Treatment: Most claudication can be managed without surgery. In most patients, a routine exercise program and cessation of smoking will result in noticeable improvement in walking distance. Other atherosclerotic risk factors should also be controlled.

Intervention by percutaneous transluminal angioplasty (PTA) and stenting or surgery is only indicated in selected patients with IC in whom exercise treatment has failed. In most IC patients, who require intervention, the disease is focal and treatment with PTA will be sufficient to improve the flow. However, if the disease is diffuse, surgical intervention is required (see below).
Prognosis: The prognosis of patients with IC is considered to be favorable.\(^7^0\) It is a stable disease in 70 to 80\% of the patients\(^5^5,7^0-7^2\) and it is generally clinically accepted that only about 25\% of caludicants will deteriorate.\(^1^5,2^6\) About 1 to 10\% of patients with IC may require reconstructive surgery to improve their circulatory flow.\(^2^6\) Amputation may be required in 1 to 2\% of all patients.\(^1^5\) The long-term survival rates of these patients are 75\%, 50\%, and 30\% at 5, 10, and 15 years, respectively,\(^1^5\) and the most common cause of death in these patients is CAD.\(^1^5\)

2.4.2 Critical Limb Ischemia (CLI)

CLI is the term used to delineate those patients whose arterial disease resulted in a breakdown of the skin (ulcer or gangrene) or pain in the foot at rest.\(^1^5\)

Symptoms: The history is dominated by pain; in most cases, the pain is severe, intolerable, occurs at night, and it only responds to strong analgesics or opiates. The pain is localized in the distal part of the foot or in the vicinity of an ischemic ulcer or gangrenous toe. Elevating the foot exacerbates the pain and keeping the foot in a dependent position may relieve it. Severe ischemia is often associated with atrophy of calf muscles and loss of hair growth over the dorsum of the toes and foot. Arterial ulcers usually involve the tips of the toes, the heel of the foot, or wherever local pressure has caused further decrease of perfusion. Gangrene usually affects the digits; in severe cases, it may involve the distal parts of the forefoot. The arterial pulse is usually absent or diminished.

Prevalence: There is little direct information on the incidence and prevalence of CLI. The incidence of CLI has been estimated to be 30 to 50 per 100,000 per year.\(^1^5\)
**Treatment:** All patients with ulcers, gangrene, or pain in the foot attributable to POAD should be considered an urgent case. The basic treatment should include; pain control, foot care, topical therapy for ulcer and gangrene, the use of systemic antibiotics in patients with cellulites, and risk factors and coexisting diseases control. Most of the patients with CLI require revascularization to avoid major amputation. Patients with focal disease and restorable run-off will generally benefit from PTA. However most patients with CLI have diffuse disease and poor run-off where surgical intervention is required (see below).

**Prognosis:** The prognosis of patients with CLI is considered to be bad. The primary amputation rate ranging from 10% to approximately 40%. The 5-year survival rate ranging from 38 to 48% in patients treated operatively, and from 12 to 68% in patients requiring re-operative surgery. De Wess and Rob found that virtually all (95%) patients who presented with ischemic gangrene and 80% of those presenting with rest pain were dead within 10 years.

**2.4.3 Acute Limb Ischemia (ALI)**

ALI is any sudden decrease or worsening in the limb perfusion causing a potential threat to extremity viability. ALI is caused by sudden obstruction of the arterial system by an embolus, thrombosis, or combination of the two.

**Symptoms:** Sudden onset of diffuse and poorly localized leg pain. The pain is usually associated with diminished or absent pulses, pale and cold leg, numbness or parasthesia, and loss of motor function.
**Treatment:** The treatment of ALI is an emergency situation. All patients should be started on heparin infusion. If the limb is threatened, thrombectomy should be performed with or without thrombolytic therapy. A bypass procedure should be performed if the treatment is not successful. In case of irreversible leg ischemia, amputation should be done.

**Prognosis:** The mortality rate of ALI is 10 to 20%. The long-term morbidity include limb loss and renal failure from myoglobinuria. The limb salvage rate after treatment is 81% at one year.

---

2.5 Interventional Management of POAD

2.5.1 Revascularization procedures

2.5.1.1 Indications for intervention include:

1) Severe claudication not responding to conservative management including exercise programs.

2) Rest pain.

3) Tissue loss.

4) ALI with reversible ischemia not responding to thrombectomy.

2.5.1.2 Interventional procedures

Many classification systems have been developed to address the best interventional procedures for patients with POAD. Generally, PTA with or without stenting is
preferred for patients with focal disease and restorable run-off, and surgery is preferred for patients with diffuse disease and poor run-off. Most of the patients with IC have focal disease and can benefit from PTA; conversely, most CLI patients have diffuse disease that requires surgical intervention.

2.5.1.3 Aortoiliac Occlusive Disease

PTA is generally applied to more focal disease of the distal abdominal aorta, common iliac arteries, and external iliac arteries. For diffuse, extensive, complex, multilevel, multifocal, or totally occluded atherosclerotic segments of the infrarenal abdominal aorta and iliac arteries, the procedure of choice is surgery.

A) Surgical procedures

1) Aortobifemoral bypass (ABF): It is the most commonly performed procedure. The distal anastomosis is usually performed on the common femoral artery and proximal anastomosis is performed on the infrarenal aorta near the renal arteries. The procedure is associated with 1 to 5% operative mortality. The cumulative survival rates are 68 to 80% and 38 to 52% at 5 and 10 years, respectively. The cumulative limb salvage rates are 76 to 95% and 82 to 91% at 5 and 10 years, respectively. The cumulative graft patency rates are 80 to 94% and 62 to 83% at 5 and 10 years respectively.

2) Unilateral aorto or iliac to femoral bypass: When a single iliac is involved in the ischemic process, it may be desirable to conduct a unilateral procedure. The procedure is associated with a 0 to 5% operative mortality. The cumulative graft patency rate is 83 to 92% at 3 years. The cumulative survival rates are 78
to 90% and 55% at 3 and 5 years, respectively. The cumulative limb salvage rate is 77 to 88% at 3 years.

3) Extra-anatomic bypass:

a) Femoral-femoral bypass: It may be used for patients with unilateral iliac disease if the remaining artery does not have a significant disease. The procedure is associated with a 0 to 6% operative mortality. The cumulative graft patency rate is 57 to 92% at 5 years. The cumulative survival rate is 70 to 80% at 6 years. The limb salvage rates are 85% and 83% at 3 and 6 years, respectively.

b) Axillofemoral bypass: This procedure used for high-risk patients who require vascularization but cannot tolerate ABF. The procedure is associated with 3 to 11% operative mortality. The cumulative graft patency rate is 59 to 76% at 5 years. The cumulative limb salvage rate is 75 to 89% at 5 years. The cumulative survival rates are 39 to 45% and 23% at 5 and 10 years, respectively.

B) PTA and Stenting procedures

These procedures are predominantly performed for claudication; 77 to 82% of iliac PTA and 78 to 86% of iliac stenting are performed for patients with IC. PTA and stent placement have the advantages of lower morbidity and mortality risk compared with open surgical revascularization. However, PTA and stents offer a lower durability of the results as compared with surgery. The 30-day mortality rate averaged 0.8% for PTA and 1% for stent procedures. The mean systemic complication rate is 1.3%; the local
complications rate, 9.6%; and the mean rate of major complications necessitating treatment is 4.3% for PTA and 5.2% for stents.\textsuperscript{115} Four-year primary patency rates are 65% for stenoses versus 54% for occlusions after PTA to treat claudication and are 53% for stenoses versus 44% for occlusions after PTA to treat critical ischemia.\textsuperscript{115} Four-year primary patency rates are 77% for stenoses versus 61% for occlusions after stent placement to treat claudication and 67% for stenoses versus 53% for occlusions after stent placement to treat critical ischemia.\textsuperscript{115}

2.5.1.4 Infrainguinal Occlusive Disease

This includes occlusive disease of the common femoral, superficial, deep femoral, popliteal, and tibial arteries.

\textbf{A) Surgical procedures}

The overall perioperative mortality rate for all patients undergoing infrainguinal arterial reconstruction ranges from 2 to 6%,\textsuperscript{116} and the 5-year cumulative survival rate ranges from 38 to 59%.\textsuperscript{117,116,118} The long-term graft patency and limb salvage rates depend on the graft material used, type of POAD, and the presence of co-morbidities.

1) Femoropopliteal bypass: This procedure is required in patients with occlusive disease in the femoral vessels. The 5-year graft patency rate is 33 to 88%.\textsuperscript{119} The cumulative limb salvage rate at 5 years is 60 to 98%.\textsuperscript{117,120-126}

2) Femorotibial bypass: This procedure is required in patients with occlusive disease in the popliteal and tibial vessels. The 5-year primary patency rate of vein bypass is 56 to 69%, with 5-year limb salvage rates of 47 to 92%.\textsuperscript{120,127-132}
B) PTA and Stenting procedures

The efficacy of these procedures depends on the anatomic selection of the lesions and the patient selection.\textsuperscript{15} Patients with focal disease and restorable run-off will generally benefit; conversely, patients with diffuse disease and poor run-off will not.\textsuperscript{15} For femoropopliteal PTA, 50 to 70\% of anatomically selected patients will show clinical benefit at 2 years. Tibial PTA has generally been reserved for limb salvage patients, and with appropriate patients selection, 2-year limb salvage rates of 80\% can be expected.\textsuperscript{15}

2.5.2 Amputation

2.5.2.1 Types of amputation

I) Primary amputation:

Primary amputation is defined as amputation of the ischemic lower extremity without antecedent attempt at revascularization.\textsuperscript{15}

Indications for primary amputation include\textsuperscript{15}:

1) Unreconstructible arterial occlusive disease.

2) POAD patient with terminal illness or very limited life expectancy because of comorbid conditions.

3) Necrosis of significant areas with persistent infection that may lead to systemic sepsis.

4) A patient who has no potential for ambulation even after successful revascularization as in patients with fixed, unremediable flexion contracture of the leg.
5) ALI with prolonged irreversible ischemia, or if the severely ischemic limb could jeopardize the patient’s life.

II) Secondary amputation:
Secondary amputation is defined as amputation for the ischemic lower extremity with a previous attempt for revascularization.

Indications for secondary amputation include:\textsuperscript{15}:

1) Unreconstructible arterial occlusive disease after revascularization has been attempted and vascular intervention is no longer possible.

2) Persistent infection despite aggressive vascular reconstruction.

3) Limb continues to deteriorate despite the presence of a patent graft.

2.5.2.2 Amputation level
The primary goal of amputation is to obtain primary healing of the lower extremity at the most distal level possible.

I) Minor amputation:
It includes toe and forefoot amputations. It is a simple procedure to preserve the limb function. However, Distal ischemia is a frequent cause of non-healing metatarsal amputations requiring re-treatment by major amputation especially in patients with diabetes.\textsuperscript{133} In a study of 1043 patients who had foot amputation, nearly 40% required a more proximal foot amputation to treat a non-healing distal amputation.\textsuperscript{134} Similarly, in a study of 90 diabetic patients who had a great toe amputation, 17% subsequently had a below knee amputation.\textsuperscript{135}

II) Major amputation:
It includes ankle, below-knee, and above-knee amputation. Operative mortality ranges from 4 to 30%. Morbidity ranges from 20 to 37%. Approximately 15% of the patients who had major amputation require contralateral major amputation in two years.
CHAPTER 3

METHODS

The objectives of this chapter are to:

1. Provide an overview of the study methodology;
2. Describe the databases used;
3. Describe the algorithms used to identify the cases;
4. Describe the method used for data validation;
5. Outline the statistical methods used for data analysis.

3.1 Overview

3.1.1 Study Design

A retrospective population-based cohort study utilizing Ontario's administrative databases was conducted for the fiscal years 1991 to 1998 (April 1 of the indicated year to March 31 of the following year).

3.1.2 Exposure

POAD interventional procedures. These include lower extremity arterial bypass surgery (ABS), percutaneous transluminal angioplasty (PTA), and amputation (major and minor).

3.1.3 Population

Only women and men aged 45 years and older in Ontario comprised the study population, since fewer than 3% of patients undergoing these procedures are under the age of 45 years.  

141
3.1.4 Outcomes

The main outcomes of interest are:

1) Utilization rates of POAD interventional procedures by age and sex.

2) Temporal trends in the rates of interventional procedures for POAD.

3) At the patient level, long-term survival and amputation-free survival following revascularization procedures and factors predicting these.

3.1.5 Unit of analysis

For the rates calculation, the interventional procedures at a population-level were used as the unit of analysis. For the survival analysis, the patient was used as the unit of analysis.

3.2 Data Source

The study was conducted at the Institute for Clinical Evaluative Science in Ontario (ICES). The ICES has many administrative databases for the health care system in Ontario. Of these databases the following were used;

3.2.1 Canadian Institute for Health Information (CIHI) Database

Cases of arterial bypass surgery and amputation were obtained from the Canadian Institute for Health Information (CIHI) hospital discharge abstract database. This database records discharges from any Ontario acute care hospital including day surgeries. All of this information is abstracted from patient charts, coded and inputted locally into hospital databases by trained personnel, then included in summaries sent to various central CIHI databases. The diagnosis codes are based on the International Classification of Disease, Ninth Revision (ICD-9) and the treatment codes are based on the Canadian Classification of Diagnostic, Therapeutic and Surgical Procedures (CCP). The main
data elements include four types of information. The first type is demographic-information on age, sex, and area of residence. The second type focuses on disease, both the primary diagnosis (most responsible diagnosis) and the secondary diagnosis and complications (up to 16 diagnosis). The third type of data specifies the procedures provided by the physician (up to 10 procedures). The fourth type of data specifies hospital services provided—information on admission category, length of stay and special care unit stay. Studies have shown that less than three percent of the records from Ontario are missing demographic data. A study of Ontario data on most responsible diagnosis and principal procedures revealed an 81 per cent level of agreement for the most responsible diagnosis and 88 per cent for the primary procedures between the database and patients charts. Problems are evident, however when the information is reabstracted for secondary diagnosis and procedures. The agreement level in the Ontario study dropped to 37 per cent and 53 per cent respectively.

3.2.2 Ontario Health Insurance Plan (OHIP) Database

Since not all PTA procedures were done as in-patient procedures, CIHI cannot provide full information about PTA. Therefore, the OHIP database was used to determine PTA procedures. This database records claims paid for health care providers by the Ontario Ministry of Health (MOH). These OHIP claims are prepared by the service providers and submitted to the district MOH office. From there, they are sent to the central office in Kingston for electronic processing. The diagnosis and the procedure codes are based on the MOH fee service and diagnosis codes. The main data elements include three types of information. The first type is patient and physician identifier. The second type is the
code for service provided, date of service, and associated diagnosis. The third type of
data is the fee paid. The OHIP data lacks the demographic information on the patients
and has poor recording for comorbidities. Furthermore, physicians may or may not record
the diagnosis on the claims statement because in most cases the diagnosis is not required
for payment.\textsuperscript{144} The level of agreement between OHIP claims and hospital records is
procedure-specific. Iron et al\textsuperscript{147} found high levels of agreement between hospital records
and OHIP claims for hysterectomy (94\%) and cholecystectomy (93\%), while for
mastectomy it was 80\%.

3.2.3 Registered Persons Data Base (RPDB)

This database records personal information that describes people who are, or were,
entitled to medical services under OHIP. All of this information is inputted by the MOH.
The main data elements include name, birth date, gender, address, and death indicator.

Each patient in these databases (CIHI, OHIP, RPDB) has the same unique encrypted
identifier called the ICES key number (IKN). By the IKN these databases can be linked.

The fact that the administrative databases were not originally intended to be used for
a research purpose has caused debate on the issue of patient privacy and consent. At
ICES, where the study was conducted, the problem of patient confidentiality is assisted
by having strict policies, which deny access to any person-identifiable data, and limit
access to anonymous data. In addition, all staff working with the databases are required to
sign a pledge of confidentiality.
3.3 Identification of cases

3.3.1 Arterial bypass surgery procedures

Using the CIHI database, discharge abstracts for all patients 45 years of age and older who were discharged between April 1, 1991 and March 31, 1999 with a procedure code (CCP codes 51.25 and 51.29) for lower-extremity arterial bypass surgery were obtained (Table 1). Records with CCP code 51.25 were considered as aorto-ilio-femoral bypass cases (AIF), while records with CCP code 51.29 were considered as other peripheral bypass (OPB). To ensure that only procedures for POAD were included, records with a primary diagnosis code indicating abdominal aortic aneurysm (ICD-9 Codes 441.3-441.7), iliac artery aneurysm (ICD-9 Codes 442.0 and 442.2) or lower extremity artery aneurysm (ICD-9 Code 442.3) were excluded. Duplicate records, which are defined as a record with similar IKN, admission date, procedure and diagnosis codes, were excluded. Records with missing IKN also were excluded.

In order to identify the characteristics of the patients undergoing these procedures, the data was sorted by IKN, to transform the data to the patient level. The comorbidities of the patients including; diabetes mellitus (ICD-9 code 250), hypertension (ICD-9 code 401-405) and coronary artery disease (ICD-9 code 410-414) were identified from the records for each patient.

3.3.2 Amputation procedures

Using the CIHI database, discharge abstracts for all patients 45 years of age and older who were discharged between April 1, 1991 and March 31, 1999 with a procedure code (CCP codes 96.11-96.15) for lower-extremity amputation were obtained (Table 1).
Records with toe (CCP code 96.11) or through-foot (CCP code 96.12) amputations were defined as minor amputation, while records with ankle (CCP code 96.13), below-knee (CCP code 96.14) or above-knee (CCP code 96.15) amputations were defined as major amputation. To ensure that only amputations for POAD were included, records with a primary diagnosis code indicating trauma, congenital anomalies, or tumors (Table 2) were excluded. Duplicate records and abstracts with missing IKN were excluded.

In order to identify the characteristics of the patients undergoing these procedures, the data was sorted by the IKN, to transform the data to the patient level. The co-morbidities of the patients including; diabetes mellitus (ICD-9 code 250), hypertension (ICD-9 code 401-405) and coronary artery disease (ICD-9 code 410-414) were identified from the records for each patient.

### 3.3.3 Percutaneous transluminal angioplasty procedures

Since the OHIP claim records at ICES for the fiscal year 1991 are not complete, the decision was made to include only the records for the fiscal years 1992 to 1998.

Claims for all patients between April 1, 1992 and March 31, 1999 with a service code for lower-extremity PTA (J025) were obtained from OHIP database. Service code J025 is not specific for lower-extremity angioplasty, but it was also used for renal angioplasty till 1994 and is still in use for upper extremity and carotid PTA. However, in more than 85% of the cases this code is used for POAD (personal communication with Dr.Stuart Bell, Radiology department at Sunnybrook Hospital).

Although not all physicians record the diagnosis in OHIP claims, records with diagnosis codes indicating renal vascular anomalies (code 593.8), hypertensive renal disease (code
403), renal failure (codes 584, 584), transient ischemic attack (code 435), or chronic arteriosclerotic cerebrovascular disease (code 437) were excluded in an effort to decrease the number of renal and carotid angioplasty cases. To obtain the demographic features of the patients who underwent PTA, the claim records were linked to the RPDB by the IKN. Any record for patients under the age of 45 years was excluded. Duplicate records, which are defined as a record with similar IKN, service date, procedure and diagnosis codes, were excluded. Records with missing IKN also were excluded.

In order to identify the characteristics of the patients who underwent these procedures, the data was sorted by the IKN, to transform the data to the patient level.

3.3.4 Outcomes of revascularization procedures

The follow-up period was defined as the time from the admission date for ABS and the service date for PTA until readmission for amputation (major or minor), death, or March 31, 1999.

After identifying the patients who underwent ABS or PTA as previously described, these patients were followed up in the CIHI database from the date of surgery (admission date for ABS, either AIF or OPB) or from the PTA service date until the date of amputation (admission date for amputation) by the IKN. In addition, these patients were followed up from the date of procedure until the date of death by linking the patients' records to the RPDB using the IKN.
3.4 Data validation

To validate the coding for POAD surgical procedures, 300 CIHI discharge abstract records with ABS or amputation codes and a hospital code indicating the Sunnybrook hospital were randomly selected over the study period. These records were compared with the corresponding patients’ charts from the Sunnybrook hospital to assess the level of agreement for procedure coding. In addition, matched charts were used to determine the prevalence of diabetes, hypertension, coronary artery disease, hyperlipidemia, and smoking in these patients (Appendix 1). Ethical approval to review the patient charts was obtained from the Sunnybrook and Women's College Research Ethics Board (Appendix 2).

3.5 Statistical analysis

3.5.1 Rates calculation

The age of the patients at the time of procedure were divided into five age groups (45-54, 55-64, 65-74, 75-84, > 85 years). The age-specific rates for women, men, and both were calculated for each interventional procedure by using the Ontario age and sex stratified population for the relevant year as the denominator. Overall rates for each procedure were calculated using Ontario population aged 45 years and over for the relevant year as the denominator. Rates were directly standardized to 1991 Ontario population aged 45 years and over by sex and the five age groups (45-54, 55-64, 65-74, 75-84, ≥ 85 years).

Ontario population estimates for each year were obtained from Statistics Canada.\textsuperscript{148} Confidence intervals for the rate ratios were calculated according to the methods
recommended by Rosner. Changes in the rates of procedures over the study period were assessed by least square linear regression with year as the independent variable and the adjusted rate as the dependent variable. Results of the regression analysis are presented as linear trend estimates with corresponding standard errors. The linear trend estimate indicates the size and direction of the average rate of change per year in the underlying incidence.

3.5.2 Data validation

The percentage of matched CIHI records with patients' charts were calculated for both ABS and amputation records. Using patients' charts as the gold standard, sensitivity, specificity, positive and negative predictive values and overall accuracy were calculated to describe the validity and accuracy for co-morbidities recording in the matched CIHI records. Sensitivity refers to the proportion of the patients' charts with the co-morbid diagnoses that have a positive CIHI recording for the diagnoses, whereas specificity refers to the proportion of the charts without the co-morbid diagnoses that have a negative CIHI recording for the diagnoses. Accuracy and validity refer to how closely a CIHI record of having/not having a co-morbidity condition corresponds with the presence/absence of such a condition.

3.5.3 Survival analysis

3.5.3.1 Survival rates post revascularization procedures

The Kaplan-Meier method (product-limit method) was used to estimate the cumulative survival rates post arterial bypass surgery and percutaneous transluminal angioplasty.
Survival time was defined as the time in years from the procedure date until death occurred. If a patient had more than one procedure, the follow-up was started from the first procedure. Data on patients who did not die before the end of study (March 31, 1999) was considered censored data.

Patients who underwent ABS were subdivided into AIF and OPB groups. Survival rates were calculated for these groups in a similar way and compared using the log-rank test.

### 3.5.3.2 Amputation-free survival rates post revascularization procedures

The Kaplan-Meier method (product-limit method)\(^ {150}\) was used to estimate the cumulative amputation-free survival rates post both arterial bypass surgery and percutaneous transluminal angioplasty.

Amputation-free survival time was defined as the time in years from the procedure date until amputation occurred. If a patient had more than one procedure, the follow-up was started from the first procedure. Also if a patient had more than one amputation after the procedure, the first one was counted as the event. Data on patients who did not experience the event before the end of study (March 31, 1999) and data on patients who died before an amputation occurred were considered censored data. Similarly, major amputation and minor amputation-free survival rates were calculated for each procedure.

Patients who underwent ABS were subdivided into AIF and OPB groups. Any, major and minor amputation-free survival rates were calculated for these groups in similar way and compared using the log-rank test.
A Cox-proportional hazard model was used to determine the effect of age at the time of the procedure, sex and co-morbidities (diabetes mellitus, hypertension, CAD) on the survival rates and any, major, or minor amputation-free survival rates post ABS, AIF, and OPB. Since the OHIP database lacks information on co-morbidities, the Cox-proportional model was only fitted for age and sex post PTA. Age was entered into the model as a continuous variable. Other variables were entered in the model as dichotomous variables: sex (male, female), comorbidity variables (present or absent). All variables were entered into the model simultaneously without the use of stepwise or conditional procedures.

Demographic differences between patients undergoing different procedures were assessed by means of chi-square test for categorical variables and t-test for continuous variables. All P-values reported were two tailed, and were considered significant at the 0.05 level.

Statistical analyses were performed using Statistical Applications Software of the SAS Institute, version 8 (Carey, North Carolina).
Table 1: Canadian Classification of Diagnostic, Therapeutic and Surgical Procedures (CCP) codes used to identify patients undergoing lower limb arterial reconstruction, or amputation

<table>
<thead>
<tr>
<th>CCP code</th>
<th>Operation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>51.25</td>
<td>Aorto-iliac-femoral bypass</td>
<td>aortofemoral, aortoiliac, aortopopliteal, iliofemoral</td>
</tr>
<tr>
<td>51.29</td>
<td>Other (peripheral) shunt or bypass</td>
<td>femoropopliteal, femoroperoneal, femrotibial, femoral-femoral, axillary-femoral</td>
</tr>
<tr>
<td>96.11</td>
<td>Amputation and disarticulation of toes</td>
<td>Partial or complete toe amputation</td>
</tr>
<tr>
<td>96.12</td>
<td>Amputation and disarticulation of foot</td>
<td>Amputation below ankle, transmetatarsal amputation</td>
</tr>
<tr>
<td>96.13</td>
<td>Amputation and disarticulation of ankle</td>
<td>Amputation of ankle through malleoli of tibia and fibula</td>
</tr>
<tr>
<td>96.14</td>
<td>Amputation of lower leg</td>
<td>Below knee amputation</td>
</tr>
<tr>
<td>96.15</td>
<td>Amputation of thigh</td>
<td>Above knee amputation</td>
</tr>
</tbody>
</table>

Table 2: International Classification of Disease, ninth revision (ICD-9) codes used to exclude patients undergoing amputation for an indication other than peripheral occlusive arterial disease

<table>
<thead>
<tr>
<th>ICD-9 code</th>
<th>Disease classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>170</td>
<td>Malignant bone tumor</td>
</tr>
<tr>
<td>171</td>
<td>Malignant connective tissue tumor</td>
</tr>
<tr>
<td>213</td>
<td>Benign neoplasm of bone</td>
</tr>
<tr>
<td>730</td>
<td>Osteomyelitis</td>
</tr>
<tr>
<td>740-759</td>
<td>Congenital abnormalities</td>
</tr>
<tr>
<td>800-900</td>
<td>Trauma</td>
</tr>
<tr>
<td>901-904</td>
<td>Arterial injury</td>
</tr>
<tr>
<td>940-950</td>
<td>Burns</td>
</tr>
</tbody>
</table>
CHAPTER 4

RESULTS

The objectives of this chapter are to:

1. Present the baseline characteristics of the patients and the procedures;
2. Present the results of the data validation studied;
3. Present the incidence and temporal trends of the procedures;
4. Present age and gender distributions of the procedures;
5. Present the outcomes of POAD revascularization procedures and factors associated with these outcomes.

4.1 Baseline characteristics

4.1.1 Eligible records for analysis

Figures 1.2 and 3 summarize the number of eligible records for amputation, ABS, and PTA that we identified from CIHI and OHIP databases, which were used for the analysis.

4.1.2 Characteristics of procedures and patients

4.1.2.1 Revascularization procedures

33,171 revascularization procedures were performed in Ontario for fiscal years 1992 to 1998. 8.8% of the patients had both bypass surgery and angioplasty. The patients' characteristics are shown in table 3.
4.1.2.1.1 Arterial bypass surgery

19,332 ABS procedures were performed in Ontario during the study period with AIF and OPB procedures representing 22.7% and 77.3% of the ABS procedures, respectively. The operation: patient ratio for ABS, AIF, and OPB procedures were 1.22:1, 1.08:1, and 1.24:1, respectively. The patients’ characteristics are shown in table 3.

4.1.2.1.2 Percutaneous transluminal angioplasty

16,334 PTA procedures were performed in Ontario for fiscal years 1992 to 1998. The procedure: patient ratio was 1.42:1. Since the OHIP database does not record the comorbidities of the patients, only age and sex of the patients are presented in table 3.

4.1.2.2 Amputation

17,534 amputations were performed in Ontario during the study period with major and minor amputations representing 62% and 38% of the amputation cases, respectively. The operation: patient ratio for any amputation, major amputation, and minor amputation were 1.35:1, 1.20:1 and 1.20:1, receptively. BKA, AKA and ankle amputation representing 54.6%, 48% and 1.4% of the major amputation cases, respectively. The procedure was performed bilaterally on 9.2% of the BKA patients and on 8% of the AKA patients. The characteristics of the patients identified as having undergone amputation are shown in table 4.

Although patients who underwent PTA were slightly younger than those who underwent ABS, the patients who underwent amputation were older than those treated with either angioplasty or bypass surgery (p< 0.0001). Diabetes was more common in patients who
underwent amputation when compared to patients who underwent bypass surgery (p<0.0001).

4.2 Data validation

300 CIHI records randomly selected over the study period, with ABS or amputation procedure codes and were compared to the corresponding patients' charts from Sunnybrook Hospital. 93% of the CIHI records matched with the patients' charts. (Table 5).

The prevalence of POAD risk factors was abstracted from the matched charts and is shown in table 6. In general there was under reporting of co-morbidities in the matched CIHI records. Although, the accuracy of recording diabetes was reasonably good (89%) in the matched CIHI records for amputation, the overall accuracy of recording other co-morbidities was low (Table 7). The high accuracy for reporting lipid disorder most likely relates to the low prevalence in the patients' charts.

4.3 Temporal trends in rates of interventional procedures

4.3.1 Revascularization procedures

Table 8 presents the average annual age and sex adjusted rates and male to female age-adjusted rate ratios for revascularization procedures over the study period.

Figure 4 shows the rates of revascularization procedures (the combination of bypass surgery and angioplasty) for fiscal years 1992 to 1998, adjusted for age and sex.

The age and sex adjusted rate for the revascularization procedures was stable over the study period (Table 9). Although younger age groups showed declining rates of
revascularization procedures, the older age groups showed an increasing trend (Table 10-a).

4.3.1.1 Arterial bypass surgery

Figures 5 to 7 present the rates of ABS, AIF, and OPB for the fiscal years 1991 to 1998, adjusted for age and sex. The age and sex adjusted rate of ABS has fallen significantly over the study period. This trend was influenced by the significant declines in the age-adjusted rates for both genders (Table 9). Although all age groups showed declining rates of ABS, the 85 years and older age group showed an increasing trend of borderline significance (p=0.06) (Table 10-b).

When ABS procedures were subdivided to AIF and OPB procedures, a similar pattern was observed for AIF (Tables 9 and 10-c). The OPB age and sex adjusted rate has fallen significantly. This trend was influenced by a significant decline in the male age-adjusted rate but not female (Table 9). All age groups showed declining rates except the 85 years and older age group which showed an increasing trend of borderline significant (Table 10-d).

4.3.1.2 Percutaneous Transluminal Angioplasty

Figure 8 shows the rates of PTA for the fiscal years 1992 to 1998, adjusted for age and sex. The age and sex adjusted rate of PTA has increased significantly over the study period. This increase in the rate reflected significant increases observed in both sexes (Table 9). All age groups have shown significant increases in the age-specific rates over the study period (Table 10-e).
4.3.2 Amputation

Table 8 presents the average annual age and sex adjusted rates and male to female age-adjusted rate ratios for amputation procedures over the study period. Rates of amputation, major amputation, minor amputation, BKA, and AKA for fiscal years 1991 to 1998 are shown in figures 9 to 13.

The age and sex adjusted rate of major amputation has fallen slightly over the study period. The age-adjusted rates for women and men fell slightly, but it failed to reach significance for men (Table 9). Although all age groups showed slight, but not significant reduction in the rate of major amputation, the 85 years and older age group showed a reduction by an average of 4.68 procedures per 100,000 per year ($R^2= 0.52, p=0.06$) (Table 10-g). Similar patterns of AKA rates were observed (Tables 9 and 10-h). There was no significant linear trend for BKA (Tables 9 and 10-i). On the other hand, the age and sex adjusted rate of minor amputation has fallen slightly, but it failed to reach significance (Tables 9 and 10-j). The average age and sex adjusted rate ratio of above- to below-knee amputation was 1:1.24 (ranging from 1:1.1 to 1:1.4).

4.4 Age and gender differences

4.4.1 Revascularization procedures

The overall age-specific rate of ABS followed a similar pattern for males and females, but males had higher rates at all age groups (Figure 14). The rate was peaked in males and females at 2 age groups (the 75-84 years, and the 85 years and older age groups).
4.4.1.1 Arterial bypass surgery

The overall age-specific rate of ABS followed a similar pattern for males and females, but males had higher rates at all age groups (Figure 15). The rate was highest in males and females aged 75-84 years. Similar patterns were observed for the age-specific rates when procedures were subdivided to AIF and OPB groups. For the AIF group, the rate was highest in males and female aged 65-74 years (Figure 16). For the OPB group, the rate was highest in males and females aged 75-84 years (Figure 17).

4.4.1.2 Percutaneous transluminal angioplasty

The age-specific incidence of PTA followed a similar pattern for males and females, but males had higher rates at all age groups (Figure 18). The rate was highest in males and females aged 65-74 years.

4.4.2 Amputation

The age-specific rate of amputation followed a similar pattern for males and females, but males had higher rates at all age groups. The rate of amputation increased with age advancement and was highest in males and females aged 85 years and older (Figure 19). For major amputation (including BKA and AKA), the age-specific rates were higher in males at all age groups and the rate was highest in the 85 years and older age group (Figures 20-22). However, for minor amputation, the rate was highest for patients aged 75-84 years (Figure 23).
4.5 Survival post revascularization procedures

Mean follow-up for the patients who underwent ABS was $3.1 \pm 2.4$ years. 5,074 patients died during follow-up. The five-year survival rate for these patients was $61.5\% \pm 0.38\%$ (Figure 24). When survival rates were compared between the patients who underwent AIF and those who underwent OPB procedures, the 5-year survival rates were $74.7\% \pm 0.8\%$ versus $56.8\% \pm 0.6\%$, respectively ($p<0.0001$ by log rank test) (Figure 24).

Increased risk of death post ABS was associated with increased age, male sex, CAD and diabetes. On the other hand, hypertension was associated with decreased risk (Table 11).

For patients who underwent PTA, the mean follow-up was $3.1 \pm 2$ years. 2,556 patients died during follow-up. The 5-year survival rate was $68.9\% \pm 0.6\%$ (Figure 25). Risk of death post PTA was higher in males and older patients (Table 11).

4.6 Amputation-free survival post revascularization procedures

4.6.1 Amputation-free survival

Freedom from any amputation in the surviving patients post ABS at 5 years was $77.2\% \pm 0.4\%$ (Figure 26). It was significantly better at 5 years for patients who underwent AIF ($91.5\% \pm 0.5\%$) than those who underwent OPB ($72.7\% \pm 0.5\%$; $p<0.0001$) (Figure 26).

Increased risk of amputation post ABS was associated with increased age, male sex, and diabetes. On the other hand, hypertension was associated with decreased risk (Table 12).

The 5-year amputation-free survival for patients who underwent PTA was $90.0\% \pm 0.4\%$ (Figure 27). Risk of amputation post PTA was higher in males and older patients (Table 12).
4.6.2 Major amputation-free survival

Major amputation-free survival post ABS was 83.4% ± 0.37% at 5 years (Figure 28).

The 5-year major amputation-free survival for patients who underwent AIF was 94.0% ± 0.5%, as compared to 79.4% ± 0.5% for those who underwent OPB (p<0.0001) (Figure 28).

Male sex, increased age, diabetes, and CAD were associated with increased risk of major amputation post ABS, whereas hypertension was linked to decreased risk (Table 13). The 5-year major amputation-free survival for patients who underwent PTA was 92.2% ± 0.34% (Figure 29). Increased risk of major amputation post PTA was associated with increased age and male sex (Table 13).

4.6.3 Minor amputation-free survival

Minor amputation-free survival post ABS was 89.8% ± 0.3% at 5 years (Figure 30).

It was significantly better at 5 years for patient who underwent AIF (96.3% ± 0.3%) than those who underwent OPB (87.4% ± 0.35%; p<0.0001) (Figure 30).

Male sex, increased age, and diabetes were associated with increased risk of minor amputation post ABS, whereas hypertension was linked to decreased risk (Table 14). Minor amputation-free survival post PTA was 96.2% ± 0.23% at 5 years (Figure 31). Risk of minor amputation post PTA was higher in males and in older patients (Table 14).
Table 3: Characteristics of patients who underwent revascularization procedures of the lower extremity secondary to peripheral occlusive disease, in Ontario, for fiscal years 1991 to 1998.

<table>
<thead>
<tr>
<th></th>
<th>ABS</th>
<th>AIF</th>
<th>OPB</th>
<th>PTA</th>
<th>ABS &amp; PTA* (combined)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of procedures</td>
<td>19,332</td>
<td>4,380</td>
<td>14,952</td>
<td>16,344</td>
<td>33,171</td>
</tr>
<tr>
<td>Number of patients</td>
<td>15,824</td>
<td>4,053</td>
<td>12,072</td>
<td>11,548</td>
<td>25,192</td>
</tr>
<tr>
<td>Age mean (+/- SD)</td>
<td>66.3(11.9)</td>
<td>61.8(10.3)</td>
<td>67.7(11.9)</td>
<td>65.6(10.1)</td>
<td>65.9(11.3)</td>
</tr>
<tr>
<td>Sex (% F/M)</td>
<td>37.6/62.4</td>
<td>42/58</td>
<td>36.1/63.9</td>
<td>40.2/59.8</td>
<td>38.9/61.1</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>4447(28.1)</td>
<td>665(16.4)</td>
<td>3851(31.9)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>3497(22.1)</td>
<td>969(23.9)</td>
<td>2607(21.6)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>CAD* (%)</td>
<td>3766(23.8)</td>
<td>960(23.9)</td>
<td>2885(23.9)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Lipid disorder (%)</td>
<td>316(2)</td>
<td>117(2.9)</td>
<td>193(1.6)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

* For fiscal years 1992 to 1998

± Coronary artery disease

ABS: Arterial bypass surgery, AIF: Aorto-iliac-femoral bypass surgery, OPB: Other peripheral bypass surgery, PTA: Percutaneous transluminal angioplasty

Table 4: Characteristics of patients who underwent amputation of the lower extremity secondary to peripheral occlusive disease, in Ontario, for fiscal years 1991 to 1998.

<table>
<thead>
<tr>
<th>Amputation</th>
<th>Major amputation</th>
<th>Minor amputation</th>
<th>Above knee amputation</th>
<th>Below knee amputation</th>
<th>Ankle amputation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of procedures</td>
<td>17534</td>
<td>10844</td>
<td>6690</td>
<td>4771</td>
<td>5921</td>
</tr>
<tr>
<td>Number of patients</td>
<td>12968</td>
<td>9034</td>
<td>5580</td>
<td>4408</td>
<td>5423</td>
</tr>
<tr>
<td>Age mean (+/- SD)</td>
<td>71(11.1)</td>
<td>72.1(10.9)</td>
<td>68.8(10.9)</td>
<td>73.9(10.7)</td>
<td>70.4(10.7)</td>
</tr>
<tr>
<td>Sex (% F/M)</td>
<td>38.9/61.1</td>
<td>38.4/61.6</td>
<td>37.6/62.4</td>
<td>42.2/57.8</td>
<td>35.2/64.8</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>7302(56.3)</td>
<td>4953(54.8)</td>
<td>3655(65.5)</td>
<td>1932(43.8)</td>
<td>3465(63.9)</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>2328(17.9)</td>
<td>1779(19.7)</td>
<td>993(17.8)</td>
<td>853(19.4)</td>
<td>1169(21.6)</td>
</tr>
<tr>
<td>CAD (%)</td>
<td>3095(23.9)</td>
<td>2515(27.8)</td>
<td>1152(20.7)</td>
<td>1303(29.6)</td>
<td>1509(27.8)</td>
</tr>
<tr>
<td>Lipid disorder (%)</td>
<td>107(0.83)</td>
<td>79(0.87)</td>
<td>57(1)</td>
<td>34(0.8)</td>
<td>59(1.1)</td>
</tr>
</tbody>
</table>
Table 5: Validation of the arterial bypass surgery and amputation procedures codes

<table>
<thead>
<tr>
<th></th>
<th>Arterial bypass surgery</th>
<th>Amputation</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of the Canadian Institute for Health Information (CIHI) records obtained</td>
<td>150</td>
<td>150</td>
<td>300</td>
</tr>
<tr>
<td>Number of CIHI records matched with patients charts</td>
<td>137</td>
<td>142</td>
<td>279</td>
</tr>
<tr>
<td>% matched</td>
<td>91.3</td>
<td>94.7</td>
<td>93.0</td>
</tr>
</tbody>
</table>

Table 6: Prevalence of risk factors as abstracted from the matched patients’ charts

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Arterial bypass surgery</th>
<th>Amputation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes Mellitus (%)</td>
<td>60 (43.8)</td>
<td>90 (63.4)</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>73 (53.3)</td>
<td>57 (40.1)</td>
</tr>
<tr>
<td>Coronary artery disease (%)</td>
<td>59 (43.1)</td>
<td>56 (39.4)</td>
</tr>
<tr>
<td>Hyperlipidaemia (%)</td>
<td>15 (11.0)</td>
<td>10 (7.0)</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>71 (51.8)</td>
<td>60 (42.3)</td>
</tr>
<tr>
<td>Total</td>
<td>137</td>
<td>142</td>
</tr>
</tbody>
</table>
Table 7: Agreement between matched patients' charts and corresponding CIHI records for several co-morbidities.

a) Arterial bypass surgery charts

<table>
<thead>
<tr>
<th>Co-morbidities</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive Predictive Value (%)</th>
<th>Negative Predictive Value (%)</th>
<th>Overall Accuracy (% agreement)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>56.6</td>
<td>82.1</td>
<td>70.8</td>
<td>71.1</td>
<td>71.0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>52.1</td>
<td>89.1</td>
<td>84.4</td>
<td>62.0</td>
<td>69.3</td>
</tr>
<tr>
<td>CAD</td>
<td>42.4</td>
<td>94.9</td>
<td>86.2</td>
<td>68.5</td>
<td>72.3</td>
</tr>
<tr>
<td>Lipid disorders</td>
<td>20.0</td>
<td>100</td>
<td>100</td>
<td>91.2</td>
<td>91.2</td>
</tr>
</tbody>
</table>

b) Amputation charts

<table>
<thead>
<tr>
<th>Co-morbidities</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive Predictive Value (%)</th>
<th>Negative Predictive Value (%)</th>
<th>Overall Accuracy (% agreement)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>86.7</td>
<td>94.2</td>
<td>96.3</td>
<td>80.3</td>
<td>89.4</td>
</tr>
<tr>
<td>Hypertension</td>
<td>50.8</td>
<td>91.8</td>
<td>80.6</td>
<td>73.6</td>
<td>75.4</td>
</tr>
<tr>
<td>CAD</td>
<td>28.6</td>
<td>94.2</td>
<td>76.2</td>
<td>66.9</td>
<td>68.3</td>
</tr>
<tr>
<td>Lipid disorders</td>
<td>20.0</td>
<td>100</td>
<td>100</td>
<td>94.3</td>
<td>94.4</td>
</tr>
</tbody>
</table>

Sensitivity = TP X 100% / (TP+FN), Specificity = TN X 100% / (TN+FP)  
Positive Predictive Value = TP X 100% / (TP+FP), Negative Predictive Value = TN X 100% / (TN+FN)  
Overall Accuracy = (TP+TN) X 100% / (TP+TN+FP+FN)  
TP= true positive results, TN= true negative results, FP= false positive results, FN= false negative results
Table 8: Average age-adjusted rates and rate ratios of interventional procedures for peripheral occlusive arterial disease in Ontario, for fiscal years 1991 to 1998 (rates per 100,000 aged 45 years and older)

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Age and sex adjusted rate</th>
<th>Age-adjusted rate for men</th>
<th>Age-adjusted rate for women</th>
<th>Rates Ratio (men vs women)</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABS</td>
<td>68.8</td>
<td>92.50</td>
<td>47.90</td>
<td>1.93</td>
<td>1.79-2.11</td>
</tr>
<tr>
<td>AIF</td>
<td>15.7</td>
<td>19.70</td>
<td>12.10</td>
<td>1.63</td>
<td>1.38-1.95</td>
</tr>
<tr>
<td>OPB</td>
<td>53.1</td>
<td>72.80</td>
<td>35.80</td>
<td>2.03</td>
<td>1.86-2.25</td>
</tr>
<tr>
<td>PTA*</td>
<td>65.2</td>
<td>83.40</td>
<td>49.10</td>
<td>1.70</td>
<td>1.58-1.86</td>
</tr>
<tr>
<td>ABS &amp; PTA* (combined)</td>
<td>132.8</td>
<td>174.3</td>
<td>96.2</td>
<td>1.81</td>
<td>1.68-1.98</td>
</tr>
<tr>
<td>Amputation</td>
<td>62.00</td>
<td>83.00</td>
<td>43.50</td>
<td>1.91</td>
<td>1.77-2.10</td>
</tr>
<tr>
<td>Major amputation</td>
<td>38.30</td>
<td>50.60</td>
<td>27.50</td>
<td>1.84</td>
<td>1.66-2.07</td>
</tr>
<tr>
<td>Minor Amputation</td>
<td>23.70</td>
<td>32.50</td>
<td>16.00</td>
<td>2.03</td>
<td>1.78-2.37</td>
</tr>
<tr>
<td>AKA</td>
<td>16.90</td>
<td>20.70</td>
<td>13.40</td>
<td>1.54</td>
<td>1.32-1.83</td>
</tr>
<tr>
<td>BKA</td>
<td>20.90</td>
<td>29.00</td>
<td>13.80</td>
<td>2.10</td>
<td>1.83-2.47</td>
</tr>
</tbody>
</table>

* For fiscal years 1992 to 1998
ABS: Arterial bypass surgery, AIF: Aorto-iliac-femoral bypass, OPB: Other peripheral bypass
PTA: Percutaneous transluminal angioplasty, AKA: Above-knee amputation, BKA: Below-knee amputation
Table 9: Linear trends estimates for changes in the rates of peripheral occlusive arterial disease interventional procedures, in Ontario, for fiscal years 1991 to 1998, as determined using least square linear regression.

a) Age and sex adjusted rates (per 100,000 population aged 45 years and older)

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Linear trend Estimate*</th>
<th>Standard Error</th>
<th>p value</th>
<th>R-square</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial bypass surgery</td>
<td>-2.35</td>
<td>0.30</td>
<td>0.0002</td>
<td>0.91</td>
</tr>
<tr>
<td>Aorto-iliac femoral bypass</td>
<td>-1.10</td>
<td>0.15</td>
<td>0.0003</td>
<td>0.91</td>
</tr>
<tr>
<td>Other peripheral bypass</td>
<td>-1.25</td>
<td>0.20</td>
<td>0.0007</td>
<td>0.87</td>
</tr>
<tr>
<td>Percutaneous transluminal angioplasty</td>
<td>2.84</td>
<td>0.35</td>
<td>0.0005</td>
<td>0.93</td>
</tr>
<tr>
<td>Bypass surgery and angioplasty (combined)</td>
<td>0.52</td>
<td>0.45</td>
<td>0.30</td>
<td>0.21</td>
</tr>
<tr>
<td>Amputation</td>
<td>-0.91</td>
<td>0.28</td>
<td>0.02</td>
<td>0.63</td>
</tr>
<tr>
<td>Major amputation</td>
<td>-0.45</td>
<td>0.18</td>
<td>0.05</td>
<td>0.52</td>
</tr>
<tr>
<td>Minor amputation</td>
<td>-0.46</td>
<td>0.20</td>
<td>0.06</td>
<td>0.47</td>
</tr>
<tr>
<td>Above-knee amputation</td>
<td>-0.39</td>
<td>0.15</td>
<td>0.04</td>
<td>0.52</td>
</tr>
<tr>
<td>Below-knee amputation</td>
<td>0.005</td>
<td>0.17</td>
<td>0.98</td>
<td>0.000</td>
</tr>
</tbody>
</table>

b) Age adjusted rates for women (per 100,000 women aged 45 years and older)

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Linear trend Estimate*</th>
<th>Standard Error</th>
<th>p value</th>
<th>R-square</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial bypass surgery</td>
<td>-1.33</td>
<td>0.32</td>
<td>0.006</td>
<td>0.74</td>
</tr>
<tr>
<td>Aorto-iliac femoral bypass</td>
<td>-0.94</td>
<td>0.13</td>
<td>0.0003</td>
<td>0.90</td>
</tr>
<tr>
<td>Other peripheral bypass</td>
<td>-0.39</td>
<td>0.24</td>
<td>0.16</td>
<td>0.30</td>
</tr>
<tr>
<td>Percutaneous transluminal angioplasty</td>
<td>2.19</td>
<td>0.34</td>
<td>0.001</td>
<td>0.89</td>
</tr>
<tr>
<td>Bypass surgery and angioplasty (combined)</td>
<td>0.98</td>
<td>0.26</td>
<td>0.01</td>
<td>0.74</td>
</tr>
<tr>
<td>Amputation</td>
<td>-1.14</td>
<td>0.35</td>
<td>0.02</td>
<td>0.64</td>
</tr>
<tr>
<td>Major amputation</td>
<td>-0.34</td>
<td>0.20</td>
<td>0.14</td>
<td>0.32</td>
</tr>
<tr>
<td>Minor amputation</td>
<td>-0.80</td>
<td>0.23</td>
<td>0.02</td>
<td>0.66</td>
</tr>
<tr>
<td>Above-knee amputation</td>
<td>-0.22</td>
<td>0.20</td>
<td>0.32</td>
<td>0.16</td>
</tr>
<tr>
<td>Below-knee amputation</td>
<td>-0.09</td>
<td>0.20</td>
<td>0.64</td>
<td>0.04</td>
</tr>
</tbody>
</table>

c) Age adjusted rates for men (per 100,000 men aged 45 years and older)

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Linear trend Estimate*</th>
<th>Standard Error</th>
<th>p value</th>
<th>R-square</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial bypass surgery</td>
<td>-3.50</td>
<td>0.50</td>
<td>0.0004</td>
<td>0.89</td>
</tr>
<tr>
<td>Aorto-iliac femoral bypass</td>
<td>-1.28</td>
<td>0.18</td>
<td>0.0004</td>
<td>0.89</td>
</tr>
<tr>
<td>Other peripheral bypass</td>
<td>-2.23</td>
<td>0.37</td>
<td>0.001</td>
<td>0.86</td>
</tr>
<tr>
<td>Percutaneous transluminal angioplasty</td>
<td>3.60</td>
<td>0.54</td>
<td>0.001</td>
<td>0.90</td>
</tr>
<tr>
<td>Bypass surgery and angioplasty (combined)</td>
<td>-0.01</td>
<td>0.78</td>
<td>0.99</td>
<td>0.00</td>
</tr>
<tr>
<td>Amputation</td>
<td>-0.65</td>
<td>0.47</td>
<td>0.21</td>
<td>0.25</td>
</tr>
<tr>
<td>Major amputation</td>
<td>-0.58</td>
<td>0.24</td>
<td>0.05</td>
<td>0.49</td>
</tr>
<tr>
<td>Minor amputation</td>
<td>-0.07</td>
<td>0.34</td>
<td>0.84</td>
<td>0.01</td>
</tr>
<tr>
<td>Above-knee amputation</td>
<td>-0.59</td>
<td>0.25</td>
<td>0.05</td>
<td>0.48</td>
</tr>
<tr>
<td>Below-knee amputation</td>
<td>0.12</td>
<td>0.22</td>
<td>0.61</td>
<td>0.05</td>
</tr>
</tbody>
</table>

* Change in the rate per 100,000 per year
± For fiscal years 1992 to 1998
Table 10: Linear trends estimates for changes in the age-specific rates of peripheral occlusive arterial disease interventional procedures, in Ontario, for fiscal years 1991 to 1998, as determined using least square linear regression.

a) Arterial bypass surgery and angioplasty age-specific rates (per 100,000)

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Linear trend Estimate*</th>
<th>Standard Error</th>
<th>p value</th>
<th>R-square</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-54</td>
<td>-0.41</td>
<td>0.55</td>
<td>0.49</td>
<td>0.10</td>
</tr>
<tr>
<td>55-64</td>
<td>-1.60</td>
<td>0.93</td>
<td>0.15</td>
<td>0.37</td>
</tr>
<tr>
<td>65-74</td>
<td>1.86</td>
<td>1.16</td>
<td>0.15</td>
<td>0.36</td>
</tr>
<tr>
<td>75-84</td>
<td>4.82</td>
<td>1.85</td>
<td>0.05</td>
<td>0.58</td>
</tr>
<tr>
<td>&gt;=85</td>
<td>5.66</td>
<td>2.27</td>
<td>0.055</td>
<td>0.50</td>
</tr>
</tbody>
</table>

b) Arterial bypass surgery age-specific rates (per 100,000)

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Linear trend Estimate*</th>
<th>Standard Error</th>
<th>p value</th>
<th>R-square</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-54</td>
<td>-1.37</td>
<td>0.24</td>
<td>0.001</td>
<td>0.84</td>
</tr>
<tr>
<td>55-64</td>
<td>-3.34</td>
<td>0.30</td>
<td>0.0001</td>
<td>0.95</td>
</tr>
<tr>
<td>65-74</td>
<td>-3.10</td>
<td>0.90</td>
<td>0.014</td>
<td>0.66</td>
</tr>
<tr>
<td>75-84</td>
<td>-2.31</td>
<td>1.15</td>
<td>0.09</td>
<td>0.40</td>
</tr>
<tr>
<td>&gt;=85</td>
<td>2.10</td>
<td>0.89</td>
<td>0.06</td>
<td>0.48</td>
</tr>
</tbody>
</table>

c) Aorto-iliac femoral bypass age-specific rates (per 100,000)

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Linear trend Estimate*</th>
<th>Standard Error</th>
<th>p value</th>
<th>R-square</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-54</td>
<td>-0.73</td>
<td>0.14</td>
<td>0.002</td>
<td>0.81</td>
</tr>
<tr>
<td>55-64</td>
<td>-1.82</td>
<td>0.20</td>
<td>0.0002</td>
<td>0.91</td>
</tr>
<tr>
<td>65-74</td>
<td>-1.42</td>
<td>0.44</td>
<td>0.02</td>
<td>0.64</td>
</tr>
<tr>
<td>75-84</td>
<td>-0.56</td>
<td>0.32</td>
<td>0.13</td>
<td>0.34</td>
</tr>
<tr>
<td>&gt;=85</td>
<td>0.10</td>
<td>0.36</td>
<td>0.83</td>
<td>0.01</td>
</tr>
</tbody>
</table>

d) Other peripheral bypass age-specific rates (per 100,000)

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Linear trend Estimate*</th>
<th>Standard Error</th>
<th>p value</th>
<th>R-square</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-54</td>
<td>-0.64</td>
<td>0.16</td>
<td>0.007</td>
<td>0.73</td>
</tr>
<tr>
<td>55-64</td>
<td>-1.72</td>
<td>0.32</td>
<td>0.002</td>
<td>0.82</td>
</tr>
<tr>
<td>65-74</td>
<td>-1.68</td>
<td>0.62</td>
<td>0.034</td>
<td>0.55</td>
</tr>
<tr>
<td>75-84</td>
<td>-1.75</td>
<td>1.13</td>
<td>0.17</td>
<td>0.29</td>
</tr>
<tr>
<td>&gt;=85</td>
<td>2.01</td>
<td>0.90</td>
<td>0.07</td>
<td>0.45</td>
</tr>
</tbody>
</table>

e) Percutaneous transluminal angioplasty age-specific rates (per 100,000)

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Linear trend Estimate*</th>
<th>Standard Error</th>
<th>p value</th>
<th>R-square</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-54</td>
<td>0.70</td>
<td>0.29</td>
<td>0.06</td>
<td>0.55</td>
</tr>
<tr>
<td>55-64</td>
<td>1.94</td>
<td>0.63</td>
<td>0.03</td>
<td>0.65</td>
</tr>
<tr>
<td>65-74</td>
<td>5.39</td>
<td>0.78</td>
<td>0.001</td>
<td>0.90</td>
</tr>
<tr>
<td>75-84</td>
<td>6.72</td>
<td>0.92</td>
<td>0.001</td>
<td>0.91</td>
</tr>
<tr>
<td>&gt;=85</td>
<td>3.01</td>
<td>1.33</td>
<td>0.07</td>
<td>0.51</td>
</tr>
</tbody>
</table>
f) Amputation age-specific rates (per 100,000)

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Linear trend Estimate</th>
<th>Standard Error</th>
<th>p value</th>
<th>R-square</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-54</td>
<td>-0.29</td>
<td>0.20</td>
<td>0.19</td>
<td>0.26</td>
</tr>
<tr>
<td>55-64</td>
<td>-0.42</td>
<td>0.22</td>
<td>0.11</td>
<td>0.38</td>
</tr>
<tr>
<td>65-74</td>
<td>-0.55</td>
<td>0.72</td>
<td>0.48</td>
<td>0.10</td>
</tr>
<tr>
<td>75-84</td>
<td>-2.55</td>
<td>1.07</td>
<td>0.06</td>
<td>0.49</td>
</tr>
<tr>
<td>&gt;=85</td>
<td>-6.78</td>
<td>2.68</td>
<td>0.04</td>
<td>0.52</td>
</tr>
</tbody>
</table>

g) Major amputation age-specific rates (per 100,000)

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Linear trend Estimate</th>
<th>Standard Error</th>
<th>p value</th>
<th>R-square</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-54</td>
<td>-0.10</td>
<td>0.11</td>
<td>0.39</td>
<td>0.26</td>
</tr>
<tr>
<td>55-64</td>
<td>-0.05</td>
<td>0.28</td>
<td>0.28</td>
<td>0.38</td>
</tr>
<tr>
<td>65-74</td>
<td>-0.25</td>
<td>0.44</td>
<td>0.59</td>
<td>0.10</td>
</tr>
<tr>
<td>75-84</td>
<td>-1.45</td>
<td>0.89</td>
<td>0.15</td>
<td>0.49</td>
</tr>
<tr>
<td>&gt;=85</td>
<td>-4.68</td>
<td>2.03</td>
<td>0.06</td>
<td>0.52</td>
</tr>
</tbody>
</table>

h) Above-knee amputation age-specific rates (per 100,000)

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Linear trend Estimate</th>
<th>Standard Error</th>
<th>p value</th>
<th>R-square</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-54</td>
<td>-0.05</td>
<td>0.05</td>
<td>0.41</td>
<td>0.11</td>
</tr>
<tr>
<td>55-64</td>
<td>-0.17</td>
<td>0.15</td>
<td>0.30</td>
<td>0.18</td>
</tr>
<tr>
<td>65-74</td>
<td>-0.43</td>
<td>0.35</td>
<td>0.26</td>
<td>0.20</td>
</tr>
<tr>
<td>75-84</td>
<td>-1.20</td>
<td>0.61</td>
<td>0.10</td>
<td>0.39</td>
</tr>
<tr>
<td>&gt;=85</td>
<td>-2.66</td>
<td>1.51</td>
<td>0.13</td>
<td>0.34</td>
</tr>
</tbody>
</table>

i) Below-knee amputation age-specific rates (per 100,000)

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Linear trend Estimate</th>
<th>Standard Error</th>
<th>p value</th>
<th>R-square</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-54</td>
<td>-0.01</td>
<td>0.07</td>
<td>0.86</td>
<td>0.01</td>
</tr>
<tr>
<td>55-64</td>
<td>0.16</td>
<td>0.19</td>
<td>0.42</td>
<td>0.11</td>
</tr>
<tr>
<td>65-74</td>
<td>0.24</td>
<td>0.52</td>
<td>0.66</td>
<td>0.03</td>
</tr>
<tr>
<td>75-84</td>
<td>-0.12</td>
<td>0.40</td>
<td>0.78</td>
<td>0.01</td>
</tr>
<tr>
<td>&gt;=85</td>
<td>-1.68</td>
<td>0.90</td>
<td>0.11</td>
<td>0.37</td>
</tr>
</tbody>
</table>

j) Minor amputation age-specific rates (per 100,000)

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Linear trend Estimate</th>
<th>Standard Error</th>
<th>p value</th>
<th>R-square</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-54</td>
<td>-0.19</td>
<td>0.12</td>
<td>0.17</td>
<td>0.29</td>
</tr>
<tr>
<td>55-64</td>
<td>-0.38</td>
<td>0.29</td>
<td>0.24</td>
<td>0.22</td>
</tr>
<tr>
<td>65-74</td>
<td>-0.30</td>
<td>0.48</td>
<td>0.55</td>
<td>0.06</td>
</tr>
<tr>
<td>75-84</td>
<td>-1.10</td>
<td>0.66</td>
<td>0.15</td>
<td>0.32</td>
</tr>
<tr>
<td>&gt;=85</td>
<td>-2.1</td>
<td>1.16</td>
<td>0.12</td>
<td>0.36</td>
</tr>
</tbody>
</table>

* Change in the rate per 100,000 per year
± For fiscal years 1992 to 1998
Table 11: Risk factors for death post revascularization procedures for peripheral occlusive arterial disease, as determined using a Cox proportional hazard model

a) Post arterial bypass surgery

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Risk Ratio</th>
<th>95% Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per each year of age)</td>
<td>1.054</td>
<td>1.051-1.057</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>male sex</td>
<td>1.26</td>
<td>1.19-1.33</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.91</td>
<td>0.85-0.97</td>
<td>0.0038</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1.48</td>
<td>1.40-1.57</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.68</td>
<td>1.59-1.78</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

b) Post aorto-iliac-femoral bypass surgery

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Risk Ratio</th>
<th>95% Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per each year of age)</td>
<td>1.066</td>
<td>1.059-1.074</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>male sex</td>
<td>1.21</td>
<td>1.06-1.39</td>
<td>0.0052</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.92</td>
<td>0.79-1.08</td>
<td>0.3006</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1.52</td>
<td>1.32-1.74</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.56</td>
<td>1.33-1.83</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

c) Post other peripheral bypass surgery

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Risk Ratio</th>
<th>95% Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per each year of age)</td>
<td>1.048</td>
<td>1.045-1.051</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>male sex</td>
<td>1.24</td>
<td>1.17-1.33</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.91</td>
<td>0.84-0.98</td>
<td>0.011</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1.50</td>
<td>1.41-1.61</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.63</td>
<td>1.53-1.73</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

d) Post percutaneous transluminal angioplasty

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Risk Ratio</th>
<th>95% Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per each year of age)</td>
<td>1.057</td>
<td>1.052-1.061</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>male sex</td>
<td>1.25</td>
<td>1.16-1.36</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>
Table 12: Risk factors associated with amputation post revascularization procedures for peripheral occlusive arterial disease, as determined using a Cox proportional hazard model

a) Post arterial bypass surgery

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Risk Ratio</th>
<th>95% Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per each year of age)</td>
<td>1.033</td>
<td>1.029-1.037</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>male sex</td>
<td>1.28</td>
<td>1.19-1.38</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.82</td>
<td>0.75-0.89</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1.08</td>
<td>0.99-1.17</td>
<td>0.08</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3.20</td>
<td>2.98-3.45</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

b) Post aorto-iliac-femoral bypass surgery

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Risk Ratio</th>
<th>95% Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per each year of age)</td>
<td>1.028</td>
<td>1.015-1.040</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>male sex</td>
<td>1.47</td>
<td>1.15-1.88</td>
<td>0.002</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.82</td>
<td>0.62-1.08</td>
<td>0.1540</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>0.98</td>
<td>0.75-1.28</td>
<td>0.8853</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.81</td>
<td>2.18-3.60</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

c) Post other peripheral bypass surgery

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Risk Ratio</th>
<th>95% Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per each year of age)</td>
<td>1.025</td>
<td>1.021-1.029</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>male sex</td>
<td>1.22</td>
<td>1.12-1.32</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.84</td>
<td>0.77-0.92</td>
<td>0.0003</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1.12</td>
<td>1.03-1.22</td>
<td>0.0083</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.91</td>
<td>2.69-3.14</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

d) Post percutaneous transluminal angioplasty

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Risk Ratio</th>
<th>95% Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per each year of age)</td>
<td>1.032</td>
<td>1.024-1.039</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>male sex</td>
<td>1.41</td>
<td>1.22-1.63</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>
Table 13: Risk factors associated with major amputation post revascularization procedures for peripheral occlusive arterial disease, as determined using a Cox proportional hazard model

a) Post arterial bypass surgery

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Risk Ratio</th>
<th>95% Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per each year of age)</td>
<td>1.030</td>
<td>1.026-1.035</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>male sex</td>
<td>1.22</td>
<td>1.12-1.34</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.84</td>
<td>0.75-0.93</td>
<td>0.0007</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1.14</td>
<td>1.04-1.26</td>
<td>0.0208</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.50</td>
<td>2.28-2.73</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

b) Post aorto-iliac-femoral bypass surgery

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Risk Ratio</th>
<th>95% Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per each year of age)</td>
<td>1.024</td>
<td>1.009-1.040</td>
<td>0.0017</td>
</tr>
<tr>
<td>male sex</td>
<td>1.65</td>
<td>1.21-2.24</td>
<td>0.0014</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.90</td>
<td>0.64-1.26</td>
<td>0.5373</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>0.99</td>
<td>0.72-1.39</td>
<td>0.9813</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.46</td>
<td>1.80-3.36</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

c) Post other peripheral bypass surgery

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Risk Ratio</th>
<th>95% Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per each year of age)</td>
<td>1.021</td>
<td>1.017-1.026</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>male sex</td>
<td>1.14</td>
<td>1.03-1.25</td>
<td>0.0082</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.86</td>
<td>0.76-0.96</td>
<td>0.0071</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1.20</td>
<td>1.08-1.33</td>
<td>0.0005</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.23</td>
<td>2.03-2.44</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

d) Post percutaneous transluminal angioplasty

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Risk Ratio</th>
<th>95% Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per each year of age)</td>
<td>1.035</td>
<td>1.027-1.044</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>male sex</td>
<td>1.44</td>
<td>1.22-1.70</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>
Table 14: Risk factors associated with minor amputation post revascularization procedures for peripheral occlusive arterial disease, as determined using a Cox proportional hazard model

a) Post arterial bypass surgery

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Risk Ratio</th>
<th>95% Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per each year of age)</td>
<td>1.028</td>
<td>1.028-1.034</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>male sex</td>
<td>1.37</td>
<td>1.22-1.54</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.79</td>
<td>0.70-0.90</td>
<td>0.0004</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>0.98</td>
<td>0.87-1.11</td>
<td>0.7437</td>
</tr>
<tr>
<td>Diabetes</td>
<td>4.93</td>
<td>4.42-5.51</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

b) Post aorto-iliac-femoral bypass surgery

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Risk Ratio</th>
<th>95% Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per each year of age)</td>
<td>1.04</td>
<td>1.019-1.056</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>male sex</td>
<td>1.37</td>
<td>0.96-1.95</td>
<td>0.0856</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.72</td>
<td>0.48-1.09</td>
<td>0.1222</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>0.93</td>
<td>0.63-1.38</td>
<td>0.7324</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3.69</td>
<td>2.60-5.24</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

c) Post other peripheral bypass surgery

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Risk Ratio</th>
<th>95% Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per each year of age)</td>
<td>1.021</td>
<td>1.016-1.027</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>male sex</td>
<td>1.33</td>
<td>1.18-1.50</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.82</td>
<td>0.72-0.94</td>
<td>0.0048</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1.01</td>
<td>0.89-1.14</td>
<td>0.9283</td>
</tr>
<tr>
<td>Diabetes</td>
<td>4.56</td>
<td>4.06-5.12</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

c) Post percutaneous transluminal angioplasty

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Risk Ratio</th>
<th>95% Confidence Interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per each year of age)</td>
<td>1.026</td>
<td>1.014-1.037</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>male sex</td>
<td>1.61</td>
<td>1.27-2.03</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>
Figure 1: Flow chart to identify eligible records for analysis from the Canadian Institute for Health Information for amputation procedures in Ontario, from April 1, 1991 to March 31, 1999.

21,173 records with amputation procedure codes

Excluded

3,319 records with indications other than POAD

17,854 records with amputation procedures coded most likely for POAD

138 duplicate records

Excluded

393 records with missing ICES key number

870 records for patients age <45 years

16,453 remaining records for analysis
Figure 2: Flow chart to identify eligible records for analysis from the Canadian Institute for Health Information for arterial bypass surgery (ABS) procedures in Ontario, from April 1, 1991 to March 31, 1999.

24,800 records with ABS procedure codes

Excluded

4,599 records with indications other than POAD

20,201 records with ABS procedures coded most likely for POAD

57 duplicate records

Excluded

457 records with missing ICES key number

818 records for patients age <45 years

18,869 remaining records for analysis
Figure 3: Flow chart to identify eligible records for analysis from the Ontario Health Insurance Plan database for percutaneous transluminal angioplasty (PTA) procedures in Ontario, from April, 1992 to March 31, 1999.

17,879 records with PTA procedure codes

- Excluded

73 records with indications other than POAD

17,806 records with PTA procedures coded most likely for POAD

- Excluded

1462 records for patients age <45 years

16,344 remaining records for analysis

0 duplicate records

0 records with missing ICES key number

* A diagnosis was not reported in 12,702 (71%) of these records.
Figure 4: Trends in bypass surgery and angioplasty combined rates (per 100,000 adults aged 45 and older) in Ontario, for fiscal years 1992-1998, by year and sex

Year

Age and sex adjusted rate
Age-adjusted rate in female
Age-adjusted rate in male

Figure 5: Trends in arterial bypass surgery rates (per 100,000 adults aged 45 and older) in Ontario, for fiscal years 1991-1998, by year and sex

Year

Age and sex adjusted rate
Age adjusted rate in female
Age adjusted rate in male
Figure 6: Trends in aorto-iliac-femoral bypass surgery rates (per 100,000 adults aged 45 and older) in Ontario, for fiscal years 1991-1998, by year and sex

Figure 7: Trends in other peripheral bypass surgery rates (per 100,000 adults aged 45 and older) in Ontario, for fiscal years 1991-1998, by year and sex
Figure 8: Trends in percutaneous transluminal angioplasty rates (per 100,000 adults aged 45 and older) in Ontario, for fiscal years 1992-1998, by year and sex.
Figure 9: Trends in amputation rates (per 100,000 adults aged 45 and older) in Ontario, for fiscal years 1991-1998, by year and sex.

Figure 10: Trends in major amputation rates (per 100,000 adults aged 45 and older) in Ontario, for fiscal years 1991-1998, by year and sex.
Figure 11: Trends in minor amputation rates (per 100,000 adults aged 45 and older) in Ontario, for fiscal years 1991-1998, by year and sex.
Figure 12: Trends in below-knee amputation rates (per 100,000 adults aged 45 and older) in Ontario, for fiscal years 1991-1998, by year and sex

Figure 13: Trends in above-knee amputation rates (per 100,000 adults aged 45 and older) in Ontario, for fiscal years 1991-1998, by year and sex
Figure 14: Average annual rate of arterial bypass surgery and angioplasty combined (per 100,000 adults aged 45 years and older) in Ontario, for fiscal years 1992-1998, by age group and sex.

Figure 15: Average annual rate of arterial bypass surgery (per 100,000 adults aged 45 years and older) in Ontario, for fiscal years 1991-1998, by age group and sex.
Figure 16: Average annual rate of aorto-iliac-femoral bypass surgery (per 100,000 adults aged 45 years and older) in Ontario, for fiscal years 1991-1998, by age group and sex

Figure 17: Average annual rate of other peripheral bypass surgery (per 100,000 adults aged 45 years and older) in Ontario, for fiscal years 1991-1998, by age group and sex
Figure 18: Average annual rate of percutaneous transluminal angioplasty (per 100,000 adults aged 45 years and older) in Ontario, for fiscal years 1992-1998, by age group and sex.
Figure 19: Average annual rate of amputation (per 100,000 adults aged 45 years and older) in Ontario, for fiscal years 1991-1998, by age group and sex.

Figure 20: Average annual rate of major amputation (per 100,000 adults aged 45 years and older) in Ontario, for fiscal years 1991-1998, by age group and sex.
Figure 21: Average annual rate of below-knee amputation (per 100,000 adults aged 45 years and older) in Ontario, for fiscal years 1991-1996, by age group and sex.

Figure 22: Average annual rate of above-knee amputation (per 100,000 adults aged 45 years and older) in Ontario, for fiscal years 1991-1998, by age group and sex.
Figure 23: Average annual rate of minor amputation (per 100,000 adults aged 45 years and older) in Ontario, for fiscal years 1991-1998, by age group and sex.
Figure 24: Kaplan-Meier survival curves post bypass surgery

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIF</td>
<td>4,053</td>
<td>3,333</td>
<td>2,802</td>
<td>2,263</td>
<td>1,784</td>
<td>1,315</td>
<td>829</td>
<td>410</td>
<td></td>
</tr>
<tr>
<td>ABS</td>
<td>15,824</td>
<td>12,192</td>
<td>9,749</td>
<td>7,515</td>
<td>5,660</td>
<td>3,952</td>
<td>2,453</td>
<td>1,148</td>
<td></td>
</tr>
<tr>
<td>OPB</td>
<td>12,072</td>
<td>9,068</td>
<td>7,121</td>
<td>5,381</td>
<td>3,979</td>
<td>2,711</td>
<td>1,670</td>
<td>756</td>
<td></td>
</tr>
</tbody>
</table>

AIF = Aorto-iliac femoral bypass, ABS = Aorterial bypass surgery, OPB = Other peripheral bypass

Figure 25: Kaplan-Meier survival curve post percutaneous transluminal angioplasty (number of patients=11,546)
Figure 26: Kaplan-Meier amputation-free survival curves post bypass surgery

Patients at risk

<table>
<thead>
<tr>
<th></th>
<th>AIF</th>
<th>ABS</th>
<th>OPB</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>4.053</td>
<td>15.024</td>
<td>12.072</td>
</tr>
<tr>
<td>1</td>
<td>3.195</td>
<td>10.764</td>
<td>7.757</td>
</tr>
<tr>
<td>2</td>
<td>2.663</td>
<td>9.508</td>
<td>5.989</td>
</tr>
<tr>
<td>3</td>
<td>2.149</td>
<td>6.545</td>
<td>4.507</td>
</tr>
<tr>
<td>4</td>
<td>1.688</td>
<td>4.899</td>
<td>3.287</td>
</tr>
<tr>
<td>5</td>
<td>1.240</td>
<td>3.413</td>
<td>2.234</td>
</tr>
<tr>
<td>6</td>
<td>0.773</td>
<td>2.116</td>
<td>1.371</td>
</tr>
<tr>
<td>7</td>
<td>0.380</td>
<td>0.975</td>
<td>0.608</td>
</tr>
<tr>
<td>8</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 27: Kaplan-Meier amputation-free survival curve post percutaneous transluminal angioplasty
(number of patients=11,548)

Cumulative amputation-free survival

Number of patients at risk

<table>
<thead>
<tr>
<th></th>
<th>8,459</th>
<th>6,482</th>
<th>4,811</th>
<th>3,319</th>
<th>2,059</th>
<th>1,044</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>6,482</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>4,811</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>3,319</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>2,059</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1,044</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Figure 28: Kaplan-Meier major amputation-free survival curves post bypass surgery

<table>
<thead>
<tr>
<th>Patients at risk</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIF</td>
<td>4,053</td>
<td>3,256</td>
<td>2,721</td>
<td>2,189</td>
<td>1,717</td>
<td>1,259</td>
<td>789</td>
<td>391</td>
<td></td>
</tr>
<tr>
<td>ABS</td>
<td>15,824</td>
<td>11,267</td>
<td>8,885</td>
<td>6,809</td>
<td>5,079</td>
<td>3,534</td>
<td>2,183</td>
<td>1,009</td>
<td></td>
</tr>
<tr>
<td>OPB</td>
<td>12,072</td>
<td>8,200</td>
<td>6,321</td>
<td>4,739</td>
<td>3,458</td>
<td>2,341</td>
<td>1,432</td>
<td>636</td>
<td></td>
</tr>
</tbody>
</table>

Figure 29: Kaplan-Meier major amputation-free survival curve post percutaneous transluminal angioplasty (number of patients=11,548)
CHAPTER 5

DISCUSSION

The objectives of this chapter are to:

1. Discuss the use of interventional procedures;
2. Discuss the outcomes of revascularization procedures;
3. List the major limitations of this study;
4. State the clinical implications of this study;
5. Outline directions for future research.

5.1 Utilization of interventional procedures

Male gender has been associated with higher utilization of interventional procedures for POAD. Similarly, in this study men were found to undergo all types of interventional procedures for POAD more frequently than women. This can be explained by the higher prevalence of POAD in men than in women. The utilization rates of interventional procedures increase with age. The average annual rates showed that the use of angioplasty peaked between the age of 65 to 74 years; arterial bypass surgery peaked at 75 to 84 years of age, and amputation peaked at 85 years of age and older. Similar findings have been shown by Tunis et al. This finding may be explained by the age-related progression of POAD. Younger patients are more likely to have milder forms of POAD that may require only PTA and older patients may have more severe forms of the disease, which require bypass surgery and/or amputation.
The overall rate of arterial bypass surgery for POAD in Ontario decreased during the study period, continuing the trend reported earlier. This pattern could represent a change in either the incidence of POAD or the practice of surgery or perhaps, a combination of both. Although no data are available on the incidence of POAD in Canada, it is unlikely that a reduction in the incidence of POAD can explain the reduction in the ABS rate. This finding may be explained in part by the fact that Ontario's vascular surgeons became more conservative when patients presented with a localized disease and they reserved surgical intervention for patients with more severe forms of the disease. This explanation is supported by the increased rate of angioplasty while the overall rate of revascularization procedures (the combination of bypass surgery and angioplasty) was stable over the same period of time, this finding might indicate a 'substitution effect' of angioplasty for bypass surgery.

The overall major amputation rate fell slightly over the study period. This was most likely driven by the decreased rate in patients aged 85 years and older. This reduction may be explained by the increased rate of arterial bypass surgery in these patients, which may have led to a reduction in the secondary amputation rate.

The below-knee amputation rate did not change over the study period. However, the above-knee amputation rate has fallen slightly.

Although many population-based studies from the United States, Europe and Australia examined the rates of interventional procedures, comparison of our rates with their rates is not possible. This is because they included the population younger than 45 years of age in their analysis and therefore in the denominator for rates calculation. This may be not appropriate since POAD interventional procedures are unlikely to be
performed in persons less than 45 years of age. Furthermore, including the population less than 45 years of age can lead to underestimation of the rates.

Other studies have examined the temporal trends in rates of the POAD interventional procedures (Table 15). Unlike other countries, Ontario's bypass surgery rate continues to fall starting from the 1980s, as has been shown by Simunovic et al, until the late 1990s, as shown by this study. On the other hand, the rate of PTA during the same period is increasing in Ontario as in other countries. The major amputation rate decreased slightly in Ontario, as well as in other studied areas, but in the same period it did not change in Maryland nor in the United Kingdom. Furthermore, the major amputation rate increased in the United States Medicare population. These variations may be explained by: (1) the variations in the surgical practice between countries, (2) the severity of the underlying disease for the patients being treated, (3) the variations in the population studied. For example, in the Dartmouth atlas only the 65 years and older Medicare beneficiaries were studied, (4) most of the studies were conducted in the 1980s, while this study was conducted in the 1990s. Vascular surgeons may have become more familiar with the role of PTA and precise indications of surgery, (5) variations in the incidence and prevalence of POAD between countries, (6) the supply of health care resources, and (7) patient preference.
5.2 Outcomes of revascularization procedures

5.2.1 Survival rates post revascularization procedures

The overall 5-year survival rate for the patients who underwent arterial bypass surgery was 61.5%, as compared to 69% for those who underwent PTA. The higher survival rate in PTA group may be attributed to the higher proportion of patients with intermittent claudication as compared to the surgery group. A study by Dormandy et al.\textsuperscript{45} showed a 70% 5-year survival rate for patients with IC. While other studies have reported a 38% to 48% 5-year survival rate for patients with CLI who were treated operatively.\textsuperscript{44} However, due to the absence of the clinical indications (IC vs CLI) for the intervention in the databases (see below), comparison between the survival rates for these procedures with previously published reports is difficult.

Furthermore, when arterial bypass surgery was subdivided to the two procedures codes, CCP code- 51.25 (AIF) which includes aortofemoral, aortoiliac, aortopopliteal and iliofemoral, and CCP code-51.25 (OPB) which includes distal bypass surgery and extra-anatomic bypass. The 5-year survival rate for patients who underwent AIF was 75%, while it was 57% for those who underwent OPB. Again due to the lack of procedure specificity (see below) comparisons with other reported rates are not straightforward and are difficult. However, we think that most of the procedures under the CCP code-51.25 are aortofemoral surgery and most of the procedures under the CCP code-51.29 are distal bypasses. The 5-year survival rate post AIF fell in the range of the reported 5-year survival rate post-aortobifemoral bypass, ranging from 68% to 80%.\textsuperscript{63,89,91,92} On the other hand, the 5-year survival rate post OPB fell in the range of the reported 5-year survival rate post-infrainguinal arterial reconstruction bypass, ranging from 38% to 59%.\textsuperscript{116-118}
Age, male sex, coronary artery disease, diabetes, and hypertension have all been reported as predictors for increased mortality for patients with POAD. In this study, multivariate models were used to account for these risk factors simultaneously in predicting death post revascularization procedures. Similar findings were found in this study. Age, male sex, diabetes and coronary artery disease were associated with an increased risk of death post revascularization procedures. However, hypertension was associated with decreased risk. It is possible that hypertension showed this effect because it is under-reported in the database.

### 5.2.2 Amputation-free survival rates post revascularization procedures

The 5-year major amputation-free survival rate for the patients who underwent arterial bypass surgery was 83.4%, as compared to 92.2% for those who underwent PTA. Similarly the 5-year minor amputation-free survival was higher for the patients who underwent bypass surgery (90%) than those who underwent PTA (96%). This may be explained by the fact that PTA procedures mostly were done for patients with intermittent claudication, while bypass surgeries mostly were done for patients with critical ischemia. When bypass surgery was subdivided to AIF and OPB groups, the 5-year major and minor amputation-free survival rates for the patients who underwent AIF were 94% and 96%, as compared to 79% and 87% for those who underwent OPB. These findings can be explained by the fact that AIF were done for aortoiliac occlusive disease, while most of the procedures under OPB were done for infrainguinal occlusive disease.

The only population-based study examining amputation-free survival rate post revascularization procedures was by Hallett et al. This group studied the survival-free
estimates for major amputation in 271 non-diabetic patients and 172 diabetic patients who underwent revascularization procedures for POAD. The estimates at 5-year were 95% and 87% for non-diabetic and diabetic, respectively. This study has many limitations including; the small sample size, its small geographical area which may have led to a selection bias for the population studied, and failure to differentiate between the patients who underwent bypass surgery (including aortoiliac and infrainguinal) and those who underwent PTA.

Age, male sex and diabetes are associated with increased risk for the development and local progression of POAD. Although hypertension is associated with increased risk for the development of POAD, its role in the progression of the disease is not well established. Furthermore, age and diabetes are well-documented factors for the increased risk of amputation in the patients with POAD. In this study, the role of these risk factors on amputation rates post revascularization procedures was examined in multivariate statistical models. In all models, age, male sex and diabetes were associated with an increased risk of amputation. In some models CAD was associated with an increased risk of amputation. On the other hand, all models showed that hypertension was associated with decreased risk of amputation. It is possible that hypertension shows this effect because it is under-reported in the database. However, historically, plasma volume expansion has been used for patients with CLI to increase blood pressure, thereby improving distal blood flow. Maintaining an adequate blood pressure is important for limb perfusion and aggressive blood pressure treatment may decrease limb perfusion and thus worsening ischemic pain. Therefore, this association between hypertension and decreased risk of amputation may be true.
5.3 Limitations

This population-based study has several strengths that include: 1) the coverage of the full range of the interventional procedures for POAD in Ontario over the past decade, 2) the Ontario's health care databases used in this study are not affected by the serious selections bias characteristics of the Medicare and Medicaid databases\textsuperscript{163,164} since Canadians access to care is universal and does not change over time\textsuperscript{144}, and 3) the confidentiality of patients are preserved. However, it also has some limitations. In this section, several important limitations of this study will be discussed.

The service codes used in the OHIP database have not kept pace with the developments in medical technologies and interventions, so one is limited to the degree to which certain procedures can be specified. For example, service code J025, which was used to identify cases of PTA, is not specific for lower-extremity angioplasty, but was also used for renal angioplasty until 1994 and is still in use for upper extremity and carotid PTA. Although, an effort was made to decrease the number of renal and carotid angioplasty cases by excluding the records with diagnosis codes indicating diseases other than POAD, only 73 records out of 17,879 were excluded. This is because most physicians do not record the diagnosis on the claims statement since in most cases a diagnosis is not required for payment.\textsuperscript{144} However, an expert opinion was that most of the cases included are for POAD (based on personal communication with Dr. Stuart Bell, Radiology department at Sunnybrook Hospital, where potentially more than 85% of the cases with this code were done for POAD). Another limitation of the OHIP database is the absence of information about the level of PTA, whether aortoiliac or distal PTA. Also, OHIP records do not
provide a clinical indication for the procedure (e.g. whether it was performed for intermittent claudication or critical ischemia. Another limitation is the absence of any co-morbidity recording.

Similarly, the CCP codes 51.25 and 51.29 lack procedure specification since the former is used to code aortofemoral, aortoiliac, aortopopliteal and iliofemoral together, while the latter is used for coding both distal and extra-anatomic bypass surgery for POAD.

Furthermore, the clinical indications for these procedures (IC vs CLI) are not recorded in the CIHI database. These combined, make comparison with other clinical studies difficult, since each procedure has its own indications and natural history.

Other limitations relate to the accuracy of the databases used. Although the percentage of matched CIHI records with patients charts for bypass surgery and amputation procedure codes is high (93%), the validation was only performed in a single teaching hospital in Toronto, which may not represent the whole province. Even though the level of agreement for comorbid conditions recording in the CIHI matched records was higher than what has been reported, it is still low. Given that the comorbidity conditions were underrecorded, this might have affected the multivariate adjustment for survival and amputation-free survival rates. Furthermore, the level of agreement for PTA coding between OHIP database records and the actual physicians claims records was not assessed.

Other limitation relates to the accuracy of recording risk factors in the patients' charts. Although the prevalence of diabetes, hypertension and CAD are consistent with published estimates, the prevalence of smoking and hyperlipidemia are lower than that reported in other studies. This may affect the assumption for
considering the patient's charts as the gold standard for which the database should be compared.

Other limitations relate to the estimation of survival and amputation-free survival rates post revascularization procedures. First, both CIHI and OHIP databases lack specification on which limb the procedure has been done. Therefore, there might be an underestimation of the amputation-free survival rates if the revascularization procedure was done on one limb and the subsequent amputation was done on the other limb at a later date. Second, the information to estimate the survival and amputation-free survival rates was obtained from Ontario databases. Therefore, there is a potential for over estimating the survival and amputation-free survival rates if some of the patients who underwent revascularization procedure had an amputation or died outside Ontario. However, less than 1% of Ontario's population emigrate from Ontario per year and most of these individuals are younger people. Another limitation is related to the definition used for the index procedure. Some of the revascularization procedure cases may be considered as the first procedure for a patient, when it was not. A patient may have had a procedure in Ontario before the start of the study. Furthermore, procedures that were done outside Ontario before the start of the study or during the study period are not captured by CIHI or OHIP. This may result in under-estimating the amputation-free survival rate. Another limitation relates to the risk adjustment for survival and amputation-free survival rates. Smoking is an important risk factor for the development and the progression for POAD. However, CIHI and OHIP do not record smoking status of the patient. Therefore,
the survival rates and amputation-free survival rates were not adjusted for this important risk factor in the multivariate models used.

Another limitation relates to the utilization rates estimate. The rates of procedures were estimated at the population level rather than the patient level, and they therefore may reflect multiple procedures for the same patient. Furthermore, attributing the changes in the rates of interventional procedures over the study period to the surgical practice pattern of vascular surgeons may be biased. This is because the incidence and prevalence of the underlying disease are not known.

Another limitation relates to the amputation rates. Since we cannot obtain a full history on the patients who underwent amputation, whether the amputation was proceeded by another amputation, before the start of the study period. We were unable to differentiate between primary and secondary amputations.
5.4 Clinical Implications

This study provides a comparative global picture of vascular surgery practice in Ontario over the past decade. Utilization of interventional procedures was more common in men and older age groups. The overall trend for bypass surgery decreased while the rate of angioplasty increased over the study period. This may suggest a 'substitution effect' of angioplasty for bypass surgery in patients with limited POAD. However, definite conclusions about the role of angioplasty in the treatment of POAD cannot be drawn from this study, since the clinical indications for these procedures are absent from the databases. Furthermore, we do not know if the patients who underwent angioplasty benefit from the procedure and do not require further intervention especially in the form of bypass surgery. This problem may be solved partially by estimating the bypass surgery free-survival rate post angioplasty and determining the factors affecting the outcome. However, due to the limitations of the databases (e.g., the absence of clinical indication and risk factors in the OHIP database), the role of angioplasty in the treatment of POAD can only be answered by clinical trials.

This study has also documented the relatively low long-term survival rates associated with revascularization procedures at a population level.

Amputation-free survival rate post revascularization can be used to describe the clinical course post-revascularization. In addition, it provides more clinically accepted estimates of the long-term outcome of revascularization procedures at the population-level, since this outcome may be of great interest to patients undergoing revascularization procedures for POAD. Physicians could use the survival and amputation-free survival rates and
factors influencing them to explain to patients the long-term outcomes of revascularization procedures.

5.5 Future Research

The findings of this study provided some initial parameters for investigating the impact of revascularization procedures on amputation rates. This could be achieved by repeating a similarly designed study in Ontario over the next decade and then comparing the outcomes for these two periods of time.

The outcomes of revascularization procedures in the form of survival and amputation-free survival rates may be used by researchers from individual vascular centers to compare their outcomes with the province as a whole.

Giving the limitations of the databases that were used in this study, a province wide vascular registry is needed. In this registry, important limitations of these databases could be eliminated. This could be achieved by including; the indication for the intervention (IC vs CLI), the exact procedure performed (not lumping all procedures under one code), indicating which limb the procedure was performed for, a detailed history of all previous vascular interventions (e.g. amputation), and recording all risk factors including smoking. This registry should be linked with the RPDB database to update the mortality status for all patients.

Further studies are needed to examine the accuracy for recording the POAD interventional procedures in the CIHI database from several hospitals with larger number of records. Furthermore, the level of agreement between the OHIP database and actual physicians' claims needs to be studied.
Finally, the prevalence and incidence of POAD in Ontario should be investigated.

Because without knowing the incidence, we cannot have firm conclusions about the right rate of utilization of interventional procedures.
5.6 Final Conclusions

- Our observed procedure rates are consistent with an age-related progression of
disease and a higher prevalence of disease in men than in women.
- The reduction in the use of bypass surgery and the increased use of angioplasty while
the overall revascularization rate was stable suggest a "substitution effect" of
angioplasty for bypass surgery. This is may reflect a change in the practice pattern of
vascular surgeons in Ontario who became more conservative with patients presented
with a localized disease and reserve the surgical intervention for patients with more
severe forms of the disease
- Our observed long-term survival rates post revascularization procedures are
consistent with the higher mortality rates for patients with POAD.
- Risk of amputation post revascularization increased with age, male sex, and diabetes,
while hypertension was associated with decreased risk.
- Amputation-free survival rates post revascularization for patient with POAD can be
used as a measure of the population-based effectiveness of these procedures.
- Further research is needed to investigate the impact of vascular surgery on amputation
rates and to assess the accuracy of the database in recording POAD interventional
procedures.
Table 15: Peripheral occlusive arterial disease interventional procedure trends comparison with previously published population-based studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Duration</th>
<th>Setting</th>
<th>Arterial bypass surgery</th>
<th>Percutaneous transluminal angioplasty</th>
<th>Major amputation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tunis et al 1991&lt;sup&gt;20&lt;/sup&gt;</td>
<td>1979-89</td>
<td>Maryland, USA</td>
<td>increased (17,633)</td>
<td>increased (2,805)</td>
<td>no change</td>
</tr>
<tr>
<td>Sayers et al 1993&lt;sup&gt;154&lt;/sup&gt;</td>
<td>1974-90</td>
<td>Leicester, UK</td>
<td>increased (1.095)</td>
<td>increased (677)</td>
<td>no change</td>
</tr>
<tr>
<td>Ebskov et al 1994&lt;sup&gt;22&lt;/sup&gt;</td>
<td>1983-90</td>
<td>Denmark</td>
<td>increased</td>
<td>increased</td>
<td>decreased</td>
</tr>
<tr>
<td>Pell et al 1994&lt;sup&gt;24&lt;/sup&gt;</td>
<td>1981-90</td>
<td>Scotland</td>
<td>increased</td>
<td>NA</td>
<td>decreased</td>
</tr>
<tr>
<td>Simunovic et al 1996&lt;sup&gt;141&lt;/sup&gt;</td>
<td>1981-91</td>
<td>Ontario, Canada</td>
<td>decreased (30,751)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Mattes et al 1997&lt;sup&gt;19&lt;/sup&gt;</td>
<td>1980-92</td>
<td>Australia</td>
<td>increased (2,664)</td>
<td>increased (2,184)</td>
<td>decreased</td>
</tr>
<tr>
<td>Hallett et al 1997&lt;sup&gt;23&lt;/sup&gt;</td>
<td>1973-92</td>
<td>Minnesota, USA</td>
<td>increased (733)</td>
<td>increased (59)</td>
<td>decreased</td>
</tr>
<tr>
<td>Feinglass et al 1999&lt;sup&gt;16&lt;/sup&gt;</td>
<td>1979-96</td>
<td>Nation wide, USA</td>
<td>increased</td>
<td>increased</td>
<td>no change&lt;sup&gt;*&lt;/sup&gt;</td>
</tr>
<tr>
<td>The Dartmouth Atlas 2000&lt;sup&gt;155&lt;/sup&gt;</td>
<td>1993-96</td>
<td>Medicare population, USA</td>
<td>increased</td>
<td>increased</td>
<td>increased</td>
</tr>
<tr>
<td>Current study</td>
<td>1991-98</td>
<td>Ontario, Canada</td>
<td>decreased (19,332)</td>
<td>increased (16,344)</td>
<td>decreased slightly (10,844)</td>
</tr>
</tbody>
</table>

NA, data not available

<sup>*</sup> Despite the major amputation rate decreased between 1983/84 and 1991/92, but by 1995/96 the rate of major amputation had increased 10.6% since 1979/80. The overall trend showed no change.

Note: the numbers between parentheses are the numbers of the procedures during the study period if they were mentioned.
REFERENCES


(9) Gordon T, Kannel WB. Predisposition to atherosclerosis in the head, heart, and legs. The Framingham study. JAMA 1972; 221:661-666.


(144) Williams JI, Young W. Inventory of studies on the accuracy of Canadian health administrative databases. Toronto: Institute of Clinical Evaluative Sciences. 96-03-TR, 1996.


Appendix 1: Validation Form

- Unique identifier:
- Chart number:
- Date of procedure as recorded in CIHI:

- Procedure coding in CIHI abstract:
  (Circle which procedure was included)

Bypass Surgery (CCP codes 51.25,51.29) match with patient chart Yes No
Amputation (CCP codes 96.11-96.15) match with patient chart Yes No

- Co-morbidities coding:

<table>
<thead>
<tr>
<th></th>
<th>CIHI abstract</th>
<th>Chart</th>
<th>CIHI match with chart</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Diabetes</td>
<td>present</td>
<td>absent</td>
<td>present absent</td>
</tr>
<tr>
<td>(ICD-9 Code 250)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Hypertension</td>
<td>present</td>
<td>absent</td>
<td>present absent</td>
</tr>
<tr>
<td>(ICD-9 codes 401-405)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- CAD</td>
<td>present</td>
<td>absent</td>
<td>present absent</td>
</tr>
<tr>
<td>(ICD-9 codes 410-414)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Hyperlipidaemia</td>
<td>present</td>
<td>absent</td>
<td>present absent</td>
</tr>
<tr>
<td>(ICD-9 codes 272)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Smoking history</td>
<td>NA</td>
<td>present absent</td>
<td>NA</td>
</tr>
</tbody>
</table>
MEMORANDUM

Te: Dr. D. Keesy
Vascular Surgery
Room E185

From: Philip Hébert MD

Date: December 11, 2000

Subject: Trends in the Surgical Management of Peripheral Vascular Disease in Ontario

Project Identification Number: 382-2000
Approval Date: December 11, 2000

The Research Ethics Board of Sunnybrook & Women's College Health Sciences Centre has conducted a review of the research protocol referenced above on the above captioned date and approved the involvement of human subjects as specified in the protocol.

The quorum for approval did not involve any member associated with this project.

The Research Ethics Board has procedures and responsibilities that are in accordance with the ICH Guidelines for Good Clinical Practice.

Should your study continue for more than one year you must request a renewal on or before one year from the approval date. Please advise the Board of the progress of your research annually and/or any adverse reactions or deviations which may occur in the future.

The above project identification number has been assigned to your study. Please refer to this number on all future correspondence.

Philip Hébert, MD, M.D., CCFP (C)
Chair, Research Ethics Board

106