Peripheral arterial disease (PAD)

- A descriptive cost study with gender analyses.

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Peripheral Arterial Disease (PAD) is reaching pandemic levels, leading to a health economic burden as PAD affects a great amount of the Swedish population. The prevalence is higher than the estimate of people suffering from diabetes mellitus (DM) and breast cancer. Among elderly in Sweden, almost 20 % are affected and it is more common among women, although the gender specific prevalence is debated. The condition involves a decreased quality of life, with pain, functional impairment, risk of limb loss and an increased mortality rate, as PAD is highly associated with development of other cardiovascular conditions. Furthermore, PAD related health care cost are substantial and is predicted to increase. The aim of this study was to estimate PAD related health care costs for patients with PAD as primary diagnosis (defined by ICD-10). In 2005 to 2010, 3675 PAD patients were enrolled from Östergötland County. When studying health care costs gathered from The National KPP register (cost per patient), results reveal that men presents with higher cost than women, related to one individual health care appointment, however, when analysing total costs for PAD over this six-year time period, numbers are nearly equal between genders. The study indicates more but less expensive contacts for women and fewer but more costly contacts for men, which results in cost equality for both genders over time. The issue of cost is of highest health economic interest. As the life expectancy increases, elucidating PAD related health care costs is important for quality assurance and treatment of these patients. To answer the question why these differences exist, further studies need to be presented.

**Key words:** Ankle brachial index (ABI), co-morbidity, health care contact, health economic, KPP (cost per patient), peripheral arterial disease (PAD), prevalence, register, risk factor.
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ABBREVIATIONS

ABI- Ankle brachial index
CV- Cardiovascular
CVD- Cardiovascular disease
CLI- Critical limb ischemia
DM- Diabetes Mellitus
IC- Intermittent claudication
IHD- Ischemic heart disease
KPP- Cost per patient
MI- Myocardial infarction
PAD- Peripheral arterial disease
1. INTRODUCTION

Public health decision makers need to decide how to allocate health care resources, such as health care facilities, staff, material and time. Health economic research is one way to elucidate the health economic topic in order to optimize and prioritize limited resources. Globally cardiovascular disease (CVD) are increasing, by far, ischemic heart disease (IHD) and stroke are the main cause of death world wide (46 %) [1]. Lower limb arteries is one of the vascular territories and peripheral arterial disease (PAD) is defined as widespread arterial atherosclerosis from the aortic bifurcation and further more distal [2-4]. The disease is usually diagnosed with an ankle brachial index (ABI) below 0.90 with or without symptoms [5-6,7] although, far from all patients presents with symptoms, estimated to only between 10-30 %, yet, mortality rate are high [5,8].

PAD is common, in a recent performed population based study in Sweden, the prevalence was found to be 20 % among subjects over 60 years which indicates that almost half a million suffers from PAD today [9]. To put this in perspective is the estimate of people suffering from diabetes mellitus (DM) and breast cancer, 400.000 respectively 94.406 patients in Sweden which makes PAD a substantial health economic issue [10-11] and also a common global condition [3-4,12]. Interventions are often first performed when symptoms is presented to the patient, although the proceedings differs between countries [9]. The PAD prevalence increases significantly with higher age [13-14]. The gender specific prevalence is not yet defined but previous Swedish studies reveals that women are more likely to suffer from PAD than the male population [9,15]. Not much is known about sex differences in PAD prevalence [9], although, earlier studies show a higher prevalence for women when estimating ABI separately [1,15-17]. Egorova N. et. al, indicate gender differences in pathogenesis as well as clinical manifestations related to arterial disease [17].

The association between PAD and cardio- and cerebrovascular conditions is well known, even the asymptomatic stage [6-7,12,18]. Several studies indicate a strong relationship between PAD and later development of other cardiovascular disease (CVD) such as stroke or myocardial infarction (MI) [2,6,13,18-20]. PAD is also associated with increased cardiovascular mortality on par with symptomatically unstable angina pectoris [21-23]. Smoking, hypertension, and diabetes are some of the risk factors that patients with overall vascular disease can present with [8,12,14]. Patients who suffer from CLI are diabetic to a great extent and the critical connection
of cerebral- and cardiovascular events in addition as these patients often suffer from multiple illnesses initially, leads to a high mortality rate of PAD [6-7,12,24]. Intermittent claudication (IC) and critical limb ischemia (CLI) are the symptomatic stages and has both a considerable impact on quality on life [25]. Many patients experience a low quality of life, with pain and functional impairment, the condition is also the most common cause of amputation of limbs [7,26-28]. Functional decline also leads to an indirect economic societal burden as patients are forced to earn a living from medical insurance, due to reduced work capacity instead of employment and occupation [12,24].

In addition to patients decreased quality of life, care related cost to PAD is substantial [22,27-28]. Numbers reaches the same expenses relative to CVD and coronary artery disease (CAD) [28-29]. Sweden has well-developed and reliable data registers related to health care cost, among other parameters such as diagnosis, hospital care and use of medication. The KPP (cost per patient) register is a Swedish individual based register. This register provides information on e.g. patient data, hospital- and medical services (Figure 1.), which allow the identification of patients enrolled in this study and also, their medical resources utilization [30]. PAD reaches pandemic results worldwide, leading to a global burden [8,16,27-28]. From a treatment perspective, knowledge about possible differences in pathogenesis as well as symptoms between genders plays a crucial role [16]. Research is one way to enable treatment and enhance preventive care for patients in risk areas. The primary aim of this study was to estimate and identify PAD related health care costs during a six-year time period in Östergötland County with a special focus on gender differences.
2. MATERIALS AND METHODS

2.1 Ethical considerations
As the study is solely descriptive without personal data included and no journal review has been conducted, an ethical application is not relevant.

2.2 Identification of study population
From January 1st 2005 to December 31st 2010, 13,911 health care contacts from all patients in Östergötland County with PAD as primary diagnose code were gathered from the national KPP-register. Patients were identified with PAD from the International Classification of Disease-10 (ICD-10) with these following diagnose codes and their sub groups as primary diagnose;

- 170.2 Atherosclerosis of arteries of extremities
- 173.9 Peripheral vascular disease unspecified
- 174.3 Embolism and thrombosis of arteries of lower extremities
- 174.4 Embolism and thrombosis of arteries of extremities, unspecified
- 174.5 Embolism and thrombosis of iliac artery

2.3 Cost analyses
Costs were also collected from the individual-based national KPP-register. Data on costs were analysed by first identifying cost per contact, then proceeding with cost over time and cost per patient and year. To achieve more precise groups for comparison, patients were stratified for sex and age.

2.3 Register of Cost per Patient
The Swedish Association of Local Authorities and Regions (SKL) provide a database of cost per patient (KPP). Data registered in the KPP database is displayed in Figure 1. The KPP register is a Swedish individual based register and highly validated [30].
2.4 Statistical analyses
Student’s *t-Test* was carried out to analyse sex difference of age. Statistical analyses were performed using SPSS and Windows Excel. P-values below 0.05 were considered statistically significant.
3. RESULTS

The total number of health care contacts in Östergötland County, collected from the KPP database was 13,911. The age distribution of men and women are illustrated in Table 1. These contacts were equivalent to 3,675 patients, of these, 1,910 men and 1,765 women, giving the study cohort.

Table 1 Baseline characteristics of study cohort.

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) at enrolment (mean)</td>
<td>73.8</td>
<td>77</td>
<td>75.4</td>
<td></td>
</tr>
<tr>
<td>Numbers of patients (n)</td>
<td>1910 (51 %)</td>
<td>1765</td>
<td>3675</td>
<td></td>
</tr>
<tr>
<td>Age groups</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 65 (%)</td>
<td>416 (11.3)</td>
<td>300 (8.1)</td>
<td>716 (19.5)</td>
<td>0.06</td>
</tr>
<tr>
<td>65-74 (%)</td>
<td>549 (14.9)</td>
<td>343 (9.3)</td>
<td>892 (24.3)</td>
<td>0.0005</td>
</tr>
<tr>
<td>75-84 (%)</td>
<td>567 (15.4)</td>
<td>632 (17.2)</td>
<td>1199 (32.6)</td>
<td>0.54</td>
</tr>
<tr>
<td>&gt; 85 (%)</td>
<td>313 (8.5)</td>
<td>555 (15.1)</td>
<td>868 (23.4)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Figure 2 illustrates cost per contact, related to one specific health care admission. Men presents with higher cost than women in all age group beside in group 75-84 year.

Figure 2. Cost (SEK) per contact for PAD (mean) separated by age and sex.
The cost (mean) per patient and year during the total study time period is shown in Figure 3. Men and women present similar cost in age group 65-74 years and 75-84 years. A greater difference can be seen in patients that are older than 85 years old; where men cost approximately 10,000 SEK (mean) more than women.

Figure 3. Cost (SEK) per patient per year for PAD (mean) separated by age and sex.

Figure 4 presents total cost (mean) per patient per year, separated by sex. The diagram illustrates the time trend over the total study period (2005-1010) and result show that PAD cost has increased in both men and women without dramatically differences between sexes. Women cost 28 % more in 2010 than in 2005, and men respectively, 56 % more.

Figure 4. Cost (SEK) per patient per year divided by sex (mean).
Different types of health care admissions are presented in Table 2. Men are more prone to seek doctor appointment than women. The major difference between genders is appointments for medical treatment, which women seek much more frequently than men, 793 contacts for women and 389 for men.

Table 2. Total numbers of contacts separated by type of health care admission and sex. (Number of (mean) contact per patient)

<table>
<thead>
<tr>
<th>Type of contact</th>
<th>Men</th>
<th>Women</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalization</td>
<td>1395 (0.73)</td>
<td>1252 (0.70)</td>
<td>2647</td>
</tr>
<tr>
<td>Doctors appointment</td>
<td>5045 (2.6)</td>
<td>4385 (2.5)</td>
<td>9430</td>
</tr>
<tr>
<td>Medical treatment</td>
<td>389 (0.2)</td>
<td>793 (0.4)</td>
<td>1182</td>
</tr>
<tr>
<td>Others*</td>
<td>358 (0.18)</td>
<td>294 (0.2)</td>
<td>652</td>
</tr>
</tbody>
</table>

*IDA= indirect doctor appointment (contact via telephone etc.), IMT = indirect medical treatment (care contact with another health care provider without the physical presence of the patient).

Table 3 shows total cost divided by type of health care appointment and sex. Men presents with higher cost in hospitalization events compared women, but the major cost difference are seen in the medical treatment group were women cost more than 100 % more than men.

Table 3. Cost (SEK) divided by type of health care contact and sex (mean).

<table>
<thead>
<tr>
<th>Type of contact</th>
<th>Men</th>
<th>Women</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalization</td>
<td>93412</td>
<td>89538</td>
<td>91475</td>
</tr>
<tr>
<td>Doctors appointment</td>
<td>11073</td>
<td>11180</td>
<td>11127</td>
</tr>
<tr>
<td>Medical treatment</td>
<td>983</td>
<td>2445</td>
<td>1714</td>
</tr>
<tr>
<td>Others*</td>
<td>380</td>
<td>267</td>
<td>324</td>
</tr>
</tbody>
</table>

*IDA= indirect doctor appointment (contact via telephone etc.), IMT= indirect medical treatment (care contact with another health care provider without the physical presence of the patient)
4. DISCUSSION

This study investigated cost for PAD with respect to gender differences. Results revealed that men presented with higher cost in almost every age group than women when analyzing one specific health care admission. Number of various type of health care contacts seem to differ between gender, women tend to seek health care more often than men, however, to a great extent, less costly contacts. Men are more likely to be admitted to hospital than women and seen in this study, hospitalization events are the most expensive contacts in provided PAD health care. Interpretation of these differences is complex. As this study is exclusively a descriptive cost study with health economic as center point, only speculations regarding why possible gender inequalities in PAD related health care cost exists can be expressed. Although, discussion on this topic is highly important for several reasons, most essential to allocate health care resources, enhance prevention-based care and to evaluate health economics in Sweden for the future. PAD-related health care cost is substantial; the total cost of cardiovascular disease in 2010, estimated to 61.5 billion SEK [31], letting us understand the magnitude of these conditions from a health economic perspective. In addition to this, costs are expected to rise in expenses in years ahead. Due to an increased life expectancy and with interventions being more advanced, carried out more frequently and more expensive today compared with previous years [28,32]. This reflects the increase in portion of gross national product (GNP) offered to health care between 2005 with 9.1 % of GNP to 9.5 % in 2010 [33]. This trend can also be interpreted in Figure 4.

The issue of gender differences in health care has grown in importance in light of recent studies that raises the topic on gender inequalities in several patient populations. For example, a Swedish, recently published study, describe cost difference between men and women regarding myocardial infarction and appendicitis [34]. When highlighting these differences, differences in health care can therefore be noticed and evaluated and form the basis for health care improvement. One interesting result presented in this study was that men cost more than women when presenting cost per contact and almost equal numbers over time. The answer to this could be of many reasons; earlier studies as well as the Swedish vascular register (SwedVasc), a register on cardiovascular conditions and statistics, indicates that CI is more commonly diagnosed amongst men [19,35] whilst CLL is more likely to occur in women [3,15-17,36-37]. This is a liable outcome even in this study as the study population is equivalent to a great amount of PAD patients in Östergötland County. This study presents information on health care costs subdivided into different types of health care admissions. Women are shown to seek medical
treatment more often than men; one factor could be that women tend to live longer [9] and offered more conservative therapy due to more permanent damage to their limbs. Table 1 illustrates a higher number of women in age group > 85 years (p-value 0.0001) which may reflect reality. Another reason could be that symptoms of women are misinterpreted as arthritis or osteoporosis, also, women seem to seek medical care later in progression of disease than men and are therefore more often in need of limb amputation earlier in health care contact than men, which decreases hospitalization events [17]. This could also indicate that women show atypical symptoms which delays time to diagnose. As several studies show that prevalence of PAD is higher in women [9,15].

There are well-known limitations to this study. First, lack of data on co-morbidities making analyses of cost differences difficult, thus leaving to speculation. Risk factors and underlying disease such as diabetes, hypertension and smoking must be considered when analysing costs [34]. Second, the costs presented are only divided into type of health care appointments. No data on costs of interventions is shown, this could help to analyse treatment patterns regarding possible gender differences in conservative or surgical interventions. Finally, the strength in number of patients in this study cohort is hard to value. Östergötland County was chosen as a possible model for PAD patients in total in Sweden as participating rates in the KPP database were high in this region. However, there may be several unreported PAD patients especially in outpatients were health contacts not always receive a diagnose code as hospitalization do. If these 3765 patients correspond to total Swedish PAD-population remains unclear. To answer these questions, further studies must be undertaken.

To date, to our knowledge, this study presents data never before investigated. The data is robust, furthermore, costs are solid figures, which make the precision of the results definitive and reliable. In addition, the function of medical registers in Sweden is solid as well as the registry participation from many Swedish hospitals. The KPP-register is one of many validated registers and the study cohort enrolled for this study is all represented in this database, as level of participation here is high [30]. When analysing costs, the gender perspective was taken into account. To identify health care costs is of highest interest; as the life expectancy increases, diabetes and obesity are predicted to grow [38], knowledge about PAD, its consequences and costs is crucial for evaluating and planning the health economic future in Sweden and to evolve preventive care to imped development of cardiovascular disease and to optimize treatment.
5. CONCLUSION

When estimating PAD related health care costs, results present a minor cost difference between genders related to PAD health care when analysing individual health care appointments. However, in total, men and women seem to cost equally when health care contacts are merged over time. As the health care costs associated with PAD are expected to increase the upcoming years, further health economic analyses need to be performed for the best health decisions to be made how to improve treatment of these patients and for sustainable quality assurance in PAD health care.

6. ACKNOWLEDGEMENTS

I would like to thank my supervisor Dr. Birgitta Sigvant for your knowledge, guidance and the great amount of support throughout this process. Also thank you to Dr. Antonio Pereira Filho for helping me gathering data and for taking time from your busy schedule.
7. REFERENCES


34. Määttä S, Schenk-Gustafsson K, Trollvik M, Karlsson Å, Evengård Å. Men cost more than women regarding myocardial infarction and appendicitis. Läkartidningen. 2015;112:DEYT.


Ethical considerations

Ethics are an important subject when it comes to research and scientific studies. These considerations make up the framework in which research can be performed. As humans and sometimes animals are involved in several experiments, consideration on the topic of ethics is central when it comes to safety and health for example. The research should be performed with good intentions, and in some way lead to a positive result. The ethical “rules” are crucial during the entire process, from brainstorming research projects to methods, study design and in writing. All scientific projects must be ethically approved before execution, however, in this specific project entitled "Peripheral Arterial Disease – a descriptive study from a gender perspective", the study design allows research without ethical consent. As it is a descriptive study without journal reviews and no personal data is included, an ethical consideration is not relevant.

Maintaining anonymity of test individuals is often a goal in the research area. Also, to maintain integrity with the study population is often of great interest when handling surveys etc. Also, to implement your study, one has to ask for permission. Participating individuals in a specific project must be offered informed consent when initiating project and should be able to leave the experiment if they do not want to proceed.

Ethical considerations can be seen from an individual- or from a group perspective. How is the aim of this study affecting the participants? On an individual basis, or in a group perspective? The focus for ethical studies is to obtain a positive outcome for society in general. The participants have to be protected from potential risks of experiment.

Research must be based on former studies and knowledge on the subject to indicate new studies and projects and the risk should not exceed the benefit of the study.
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**Letter of intent**

January 7, 2016  

Dr. Vasc  
Editor in chief, Journal of Vascular Surgery

Dear editor,

Attached to this paper I would like to submit the manuscript entitled- “Peripheral Arterial Disease (PAD)- a descriptive study with a gender perspective” to be considered for publication in the Journal of Vascular Surgery.

This descriptive cost study presents health care costs from 3675 PAD-patients in Östergötland County, data never before investigated and analysed and therefore I believe is of highest interest to be elucidated in your journal.

The study indicates presence of gender inequalities in health economic in PAD-related care. It is important to highlight this topic in medical journals, as awareness in clinicians and researchers can prevent inequality in health care between men and women and for quality assurance in treatment of these individuals, and additionally, maintain the sustainability in health economics.

This study is original and is not being published elsewhere.  
Sincerely,  
Rebecka Wästgård
PRESSMEDDELANDE

- "Nya data gällande hälsovårdskostnader för perifer benartärsjukdom pekar mot kostnadsskillnader mellan män och kvinnor".

Benartärsjukdom (BAS) är ett mycket vanligt tillstånd globalt och är en av de mest kostsamma kardiovaskulära sjukdomarna. Tillståndet leder till kraftigt sänkt livskvalitet för patienterna med smärta, funktionsnedsättning samt hotande amputationsrisk. BAS har även en stark koppling till senare utveckling av kardio- samt cerebrovaskulära tillstånd som stroke och hjärtinfarkt med en ökad dödighet som följd.


Att analysera kostnader från ett könsperspektiv leder till att förekomst av ojämlig vård tas upp till ytan och ger möjlighet till förbättringsarbete inom hälso- och sjukvård. Ämnet står högt på agendan då ett flertal tidigare studier pekat åt samma håll gällande andra sjukdomstillstånd. Att säkerställa kvalitet inom vården är viktigt, samt att de faktiska
vårdkostnaderna presenteras och kan stå till grund för en mer effektiv och hållbar hälsoekonomi i Sverige.