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Occurrence of Varicose Veins and Bidirectional Risk with Cardiovascular Diseases

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ACADEMIC DISSERTATION
To be presented, with the permission of
the Faculty of Medicine of the University of Tampere,
for public discussion in the Auditorium of
Tampere School of Public Health, Medisiinarinkatu 3,
Tampere, on October 31st, 2008, at 12 o'clock.

UNIVERSITY OF TAMPERE

To my Family

List of original publications

This dissertation is based on the following publications, which are referred to in the text by the Roman numerals I–IV. Some unpublished data is also presented.

I Mäkivaara LA, Jukkola TM, Sisto T, Luukkaala T, Hakama M and Laurikka JO (2004): Incidence of varicose veins in Finland. Vasa 33:159–163.

II Mäkivaara LA, Ahti TM, Luukkaala T, Hakama M and Laurikka JO (2008): Persons with varicose veins have a high subsequent incidence of arterial disease: A population based study in Tampere, Finland. Angiology 58:704–709.

III Mäkivaara LA, Ahti TM, Luukkaala T, Hakama M and Laurikka JO (2008): Arterial disease but not hypertension predisposes to varicose veins. Phlebology 23:142–146.

IV Mäkivaara LA, Ahti TM, Luukkaala T, Hakama M, Laurikka JO. The risk of congestive heart failure is increased in persons with varicose veins. (Submitted)

Abbreviations

AD	Arterial disease
AP	Angina pectoris
BMI	Body mass index
CEVD	Cerebrovascular disease
CHF	Congestive heart failure
HTN	Hypertension
IDR	Incidence density ratio
IOR	Incidence odds ratio
MI	Myocardial infarction
N	Number of subjects
OR	Odds ratio
PAD	Peripheral occlusive arterial disease
v.v.	Varicose veins

Abstract

The aim of the study was to find out the incidence of varicose veins in a middle-aged population and to assess the role of the sex, age, overweight and education in the etiology of varicose veins. The association between varicose veins and cardiovascular diseases (arterial disease, hypertension and congestive heart failure) was studied. The purpose was to examine the causal direction and common etiology of varicose veins and cardiovascular diseases.

A five-year follow-up study was conducted in a general population in Tampere, Finland. The study population included three complete age-cohorts (40-, 50- and 60-year-olds at entry), a total of 6,874 men and women. A questionnaire was used. The response rate was 81% (5,568 subjects responded) at the beginning of the study and of those 88% (4,903 subjects responded) after the follow-up period. The incidence of varicose veins was studied in those free of varicose veins at entry. The effects of sex, age, overweight and education on the prevalence and on the incidence of varicose veins were assessed. The association between varicose veins and cardiovascular diseases was studied through prevalence and incidence. The incidence of varicose veins was studied in subjects with and without cardiovascular disease at entry, and incidences of cardiovascular diseases were studied in those with and without varicose veins at entry to determine the direction of the effect and to find out if there could be some common factors in etiology.

The incidence of varicose veins was 13.5 per 1,000 person years. Female gender, higher age, overweight and lower education were risk factors of varicose veins according to the prevalence results. New varicose veins appeared more often in middle-aged women than in men, IOR 2.4 (1.7–3.4). Increasing age had no obvious effect on the incidence of varicose veins. The incidence was higher in the cohort of 50-year-olds than in other cohorts, IOR 1.6 (1.1.–2.3). The result was statistically significant only in women. Increasing BMI tended to increase the risk of new varicose veins. Compared to the leanest subjects (BMI≤21 kg/m^2), those with normal weight or overweight (21 kg/m^2<BMI≤30 kg/m^2) and obese subjects (BMI>30 kg/m^2) had elevated risk of new varicose veins, IORs 1.2 (0.7–2.1) and 1.8 (0.9–3.8) respectively. Subjects with lower level of education had somewhat decreased risk of new varicose veins compared to subjects with higher education, IOR 0.8 (0.6–1.2), but the effect was not statistically significant.

Subjects with arterial disease and with congestive heart failure, but not with hypertension, had significantly higher prevalence of varicose veins than those free of the disease. The incidence of varicose veins was significantly higher in women with arterial disease, IOR 2.2 (1.1.–4.5), but not in subjects with hypertension, IOR 1.1 (0.7–1.8), than in those without the disease. Subjects with varicose veins had increased risk of new arterial disease, IOR 2.1 (1.6–2.8), and of congestive heart failure, IOR 2.5 (1.4–4.6), but not of hypertension, IOR 1.0 (0.8–1.3) compared to those free of the disease.

In conclusion, new varicose veins also appeared in middle-aged population. Based on the proper design with follow-up and incidence rates female sex and overweight were risk factors of varicose veins. Higher age and level of education could not be confirmed as risk factors of varicose veins. There was an association between varicose veins and arterial disease and congestive heart failure but not between varicose veins and hypertension. No common risk factors explaining the association could be found. The association was strongest when varicose veins were the exposure and arterial disease or congestive heart failure the outcome, which indicates that varicose veins are a potential early consequence and arterial disease and congestive heart failure late consequences of a common etiological or pathogenetic component of these diseases.

Tiivistelmä

Tutkimuksen tarkoituksena oli selvittää suonikohjutaudin ilmaantuvuus keski-ikäisessä väestössä ja arvioida sukupuolen, iän, ylipainon sekä koulutuksen osuutta suoni-kohjutaudin etiologiassa. Suonikohjutaudin yhteyttä sydän- ja verisuonitauteihin (valtimotauti, verenpainetauti ja sydämen vajaatoiminta) ja sen suuntaa sekä mahdollista yhteistä etiologiaa arvioitiin.

Viiden vuoden väestöpohjainen seurantatutkimus toteutettiin Tampereella. Tutkimusväestönä olivat kolme ikäkohorttia (40-, 50- ja 60-vuotiaat), yhteensä 6874 miestä ja naista. Tutkimusmenetelmänä käytettiin kirjekyselyä. Tutkimuksen alussa vastausprosentti oli 81 % (5568 henkilöä vastasi) ja seuranta-ajan jälkeen 88 % (4903 henkilöä vastasi). Uusien suonikohjujen ilmaantuvuus tutkittiin henkilöillä, joilla ei ollut suonikohjuja seurannan alkaessa. Arvioitiin sukupuolen, iän, ylipainon ja koulutuksen vaikutusta suonikohjutaudin vallitsevuuteen ja ilmaantuvuuteen. Suonikohjujen ilmaantuvuus tutkittiin sydän- ja verisuonitautia sairastavilla ja sydän- ja verisuonitautien suhteen terveillä henkilöillä, ja sydän- ja verisuonitautien ilmaantuvuus tutkittiin suonikohjutautia sairastavilla ja sen suhteen terveillä henkilöillä tarkoituksena määrittää yhteyden suunta ja selvittää mahdollista yhteistä etiologiaa.

Suonikohjutaudin ilmaantuvuus oli 13.5/1000 henkilövuotta. Vallitsevuuslukujen perusteella naissukupuoli, ikä, ylipaino ja matala koulutustaso olivat suonikohjutaudin riskitekijöitä. Uudet suonikohjut ilmaantuivat useammin keski-ikäisille naisille kuin miehille, vetosuhde IOR 2.4 (1.7–3.4). Kasvavalla iällä ei ollut selvää vaikutusta suonikohjujen ilmaantuvuuteen. Ilmaantuvuus oli suurempi 50-vuotiaiden kohortissa kuin muissa ikäryhmissä, IOR 1.6 (1.1–2.3), mutta tilastollisesti merkitsevästi ainoastaan naisilla. Mitä suurempi painoindeksi (BMI), sitä suuremmalta vaikutti suonikohjutaudin riski. Hoikimpiin henkilöihin (BMI≤21 kg/m^2) verrattuna normaalipainoisilla tai ylipainoisilla (21 kg/m^2<BMI≤30 kg/m^2) sekä lihavilla (BMI>30 kg/m^2) oli kohonnut riski saada suonikohjut, IOR 1.2 (0.7–2.1) ensiksi mainitussa ja 1.8 (0.9–3.8) jälkimmäisessä ryhmässä. Matalammin koulutetuilla henkilöillä oli lievästi pienempi vaara suonikohjutaudin ilmaantumiseen kuin korkeammin koulutetuilla, mutta koulutustason merkitys ei ollut tilastollisesti merkitsevä, IOR 0.8 (0.6–1.2).

Suonikohjutaudin vallitsevuus oli suurempi valtimotautia tai sydämen vajaa-toimintaa sairastavilla kuin niiden sairauksien suhteen terveillä henkilöillä, mutta

vallitsevuudessa ei ollut eroa verenpainetautia sairastavilla tai sen suhteen terveillä henkilöillä. Suonikohjujen ilmaantuvuus oli merkitsevästi suurempi valtimotautia sairastavilla kuin valtimotaudin suhteen terveillä naisilla, IOR 2.2 (1.1–4.5). Ilmaantuvuudessa ei ollut eroa verenpainetautia sairastavilla ja verenpainetaudin suhteen terveillä henkilöillä, IOR 1.1 (0.7–1.8). Suonikohjutautia sairastavilla oli suurentunut vaara sairastua valtimotautiin, IOR 2.1 (1.6–2.8), ja sydämen vajaatoimintaan, IOR 2.5 (1.4–4.6), mutta ei verenpainetautiin, IOR 1.0 (0.8–1.3), verrattuna henkilöihin, jotka eivät raportoineet suonikohjutautia.

Johtopäätöksenä voidaan todeta, että uusia suonikohjutautitapauksia ilmaantuu myös keski-ikäisessä väestössä. Seurantatutkimusta voidaan pitää luotettavana tutkimusasetelmana ja ilmaantuvuuslukujen perusteella naissukupuoli ja ylipaino ovat suonikohjutaudin riskitekijöitä. Tulokset eivät vahvista kasvavan iän ja koulutus-tason merkitystä suonikohjujen riskitekijöinä. Suonikohjutaudin ja valtimotaudin sekä sydämen vajaatoiminnan välillä oli yhteys, mutta suonikohjujen ja verenpainetaudin välillä yhteyttä ei todettu. Yhteisiä riskitekijöitä, jotka selittäisivät yhteyden, ei löydetty. Yhteys oli vahvin kun suonikohjutauti oli altistus ja valtimotauti tai sydämen vajaatoiminta seuraus, minkä perusteella ne saattavat mahdollisesti johtua osittain yhteisistä syistä tai yhteisestä patofysiologiasta, josta suonikohjut ovat aikaisempi ja valtimotauti sekä sydämen vajaatoiminta myöhäisempiä ilmentymiä.

1. Introduction

Varicose veins of the lower extremities are subcutaneous permanently dilated veins equal to or more than 3 mm in diameter in upright position (Allegra et al. 2003). They are often tortuous, elongated and visible. They are among the most common conditions affecting general adult population and have a considerable economic impact on health care resources. Based on population based studies the prevalence of varicose veins varies mostly between 10% and 30% in men and between 25% and 50% in women (Callam 1994, Beebe-Dimmer et al. 2005, Robertson et al. 2008). Only few studies report the occurrence of new varicose veins in adult population (Brand et al. 1988, Cesarone et al. 2002) and there are no previous incidence estimates of varicose veins in Finland or in other Nordic countries. According to earlier studies on the etiology of varicose veins age, gender, obesity, parity and family history are suspected risk factors. The studies on the factors associated with the development of varicose veins are mainly cross-sectional and there are only a few follow-up studies. However, they are more reliable because of the possibility to observe time sequence.

Despite numerous studies, the pathophysiology of varicose veins is not well known. Vein-wall weakness, valvular incompetence and venous hypertension are regarded as the most important factors in the development of varicose veins (Naoum et al. 2007). There is a possibility of common pathophysiology or etiology of diseases of the circulatory system, including veins and arteries. The roles of endothelium, smooth muscle cells and extracellular matrix seem to be increasingly important in the pathogenesis of vascular diseases, for example atherosclerosis, hypertension and varicose veins (Jacob et al. 2001, Raffetto and Khalil 2008a). Established risk factors for arterial disease –obesity, smoking, physical inactivity, high cholesterol and diabetes- are also considered to be potential risk factors for varicose veins. We conducted a population-based study to explore the association between varicose veins and arterial diseases. Earlier studies on this topic are rare and the results are inconsistent.

2. Review of the literature

2.1 Prevalence of varicose veins

In review articles, the prevalence of varicose veins varies from 2% to 56% in men and from <1% to 73% in women. In Western populations prevalence estimates have been highest and mostly between 10% and 30% in men and between 25% and 50% in women. (Beaglehole 1986, De Backer 1997, Fowkes et al. 2001a, Jawien 2003, Beebe-Dimmer et al. 2005, Robertson et al. 2008) In a review by Callam (1994), the prevalence of visible varicose veins was estimated to vary from 10% to 15% in men and from 20% to 25% in women.

Studies in general populations. In Finland, there are two studies on the prevalence of varicose veins in general population. The Tampere Varicose Vein Study reported earlier a prevalence of varicose veins to be 18% in men and 42% in women (Laurikka 1992, Laurikka et al. 1993). The other study, a national health examination survey of 8,000 subjects aged 30 years and over, reported the prevalence of varicose veins diagnosed by a doctor to be 7% in men and 25% in women (Sisto et al. 1995).

In the Edinburgh Vein Study, the prevalence of trunk varices was 40% in men and 32% in women (Evans et al. 1999). In an earlier community study in London the prevalence of varicose veins was also 32% in women, but lower (17%) in men (Franks et al. 1992). In the Tecumseh Community Health Study in the USA, the prevalence of any varicose veins (prominent superficial veins) was 12.9% in men and 25.9% in women, and the prevalence of moderate or severe varicose veins was 7.4% and 16.7% respectively (Coon et al. 1973). In Italy, in a whole-population study of 30,000 subjects, The San Valentino Vascular Screening Project, the global prevalence of varicose veins was 7%. In subjects aged 41–50, 51–60 and 61–70 years the prevalence of varicose veins was 9% in each group. (Cesarone et al. 2002) In another study in general population in Italy, the prevalence of varicose veins was 27.4% in elderly subjects (Canonico et al. 1998). A study in adult population in France showed the prevalence of varicose veins to be 30.1% in men and 50.5% in women (Carpentier et al. 2004). In Turkey, total prevalence of varicose veins was 36.7% (34.5% in men and 38.3% in women) in a population aged 60 years and over (Komsuoglu et al. 1994).

Studies in other defined populations. In a study in England, the prevalence of varicose veins was 32% in women cotton workers aged 15–74 years (Mekky et al. 1969). In the Basle Study in Switzerland the prevalence of severe varices was 4.2% among employees, but if all forms of varicosities were included the prevalence was 62% (Da Silva et al. 1974).

In the USA, the prevalence of varicose veins was 15% in men and 28% in women among current and retired employees (Criqui et al. 2003). The prevalence of mild and moderate varicose veins was 26% in male employees aged 42–53 years in France (Ducimetiere et al. 1981).

Earlier studies show that the estimates of the prevalence of varicose veins vary widely, especially in men, in different studies in Western countries being mostly between 10% and 30% in men and between 25% and 50% in women. The variability is partly due to different methods (e.g. how varicose veins are defined) and different age groups. Table 1. summarizes prevalence estimates of varicose veins in Europe and in the USA.

Table 1. Prevalence of varicose veins (v.v.) in Finland and in other countries in Europe and in the USA.

Country and reference	N	Age (years)	Prevalence of v.v. (%) Men	Women
Finland				
Laurikka et al. 1993	6874	40-60	18	42
Sisto et al. 1995	8000	≥30	7	25
France				
Ducimetiere et al. 1981	7432	42-53	26	NA
Carpentier et al. 2004	8000	≥18	30	51
Italy				
Canonico et al. 1998	1319	>65	17	35
Cesarone et al. 2002	30000	Any	7 in all subjects	
Switzerland				
Da Silva et al. 1974	4422	20-70	57	68
Turkey				
Komsuoglu et al. 1994	856	≥60	35	38
United Kingdom				
Mekky et al. 1969	504	15-74	NA	32
Franks et al. 1992	2103	35-70	17	32
Evans et al. 1999	1566	18-64	40	32
USA				
Coon et al. 1973	6389	≥20	13	26
Criqui et al. 2003	2211	40-79	15	28

NA=Not available

2.2 Incidence of varicose veins

There are two follow-up studies on the appearance of new varicose veins. In the Framingham Study, two-year incidence was 39.4/1,000 in men and 51.9/1,000 in women aged 40–89 years in a general population of 3,822 subjects (Brand et al. 1988). The San Valentino Vascular Screening Project, a whole-population follow-up study of 30,000 subjects, showed the incidence (new cases per year) of varicose veins to be 0.22%. In the same study the incidence of varicose veins was 0.3–0.4% in each of the age groups 41–50, 51–60 and 61–70 year-olds (Cesarone et al. 2002). (Table 2.) As well as prevalence, the estimates of the incidence of varicose veins also vary in earlier studies; the risk of varicose veins was more than five times higher in the Framingham Study than in the San Valentino Vascular Screening Project in corresponding age groups.

Table 2. Follow-up studies on the incidence of varicose veins.

Reference	Country	N	Age range (years)	Follow-up (years)	Incidence (/1000 person years)
Brand et al. 1988	USA	3822	40–89	16	23.1
Cesarone et al. 2002	Italy	30000	Any	6	2.2

2.3 Risk factors of varicose veins

Most of the studies on the risk factors of varicose veins are cross-sectional. There are only a few follow-up studies which, however, can be considered more reliable etiological studies because of the possibility to observe the time relationship, a criterion of causality.

Gender. Varicose veins were more common in women than in men according to most of the existing studies (Weddell 1969, Coon et al. 1973, Abramson et al. 1981, Maffei et al. 1986, Franks et al. 1992, Scott et al. 1995, Sisto et al. 1995, Canonico et al. 1998, Laurikka et al. 2002, Criqui et al. 2003, Carpentier et al. 2004, Kroeger et al. 2004). However, contrary results have also been reported. Some of the studies did not show a significant difference in the risk of varicose veins between genders (Da Silva

et al. 1974, Komsuoglu et al. 1994, Cesarone et al. 2002) and some of the studies showed higher prevalence of varicose veins in men than in women (Stanhope 1975, Evans et al. 1999, Chiesa et al. 2005). A follow-up study showed higher incidence of varicose veins in women than in men, except in the oldest (aged 80-89 years) subjects (Brand et al. 1988).

Age. Earlier studies showed increasing prevalence of varicose veins with increasing age (Mekky et al. 1969, Weddell 1969, Malhotra 1972, Da Silva et al. 1974, Beaglehole et al. 1975, Abramson et al. 1981, Maffei et al. 1986, Franks et al. 1992, Komsuoglu et al. 1994, Evans et al. 1999, Cesarone et al. 2002, Laurikka et al. 2002, Criqui et al. 2003, Carpentier et al. 2004, Kroeger et al. 2004). In the national health examination survey in Finland the prevalence of varicose veins increased with age until old age in men but in women the highest prevalence was observed in the 55–64 year age group (Sisto et al. 1995). A study in Italy found similar prevalence of varicose veins throughout age groups in elderly subjects (more than 65 years) (Canonico et al. 1998) but, in Turkey, the prevalence of varicose veins also increased with increasing age in subjects aged over 60 years (Komsuoglu et al. 1994).

Older men were more likely to develop new varicose veins than younger men in the Normative Aging Study (Scott et al. 2004). In the Framingham Study, age had no obvious effect on the incidence of varicose veins. Varicose veins also appeared in older subjects. The incidence of varicose veins was highest in women aged 40–49 years. (Brand et al. 1988) Varicose veins are not lethal and appear throughout adult life, therefore, is it expected that the prevalence of varicose veins increases with increasing age.

Weight and Height. Greater weight and obesity indicated an increased risk of varicose veins in many population based studies (Mekky et al. 1969, Abramson et al. 1981, Ducimetiere et al. 1981, Sisto et al. 1995, Laurikka et al. 2002). In studies in Italy (Canonico et al. 1998) and in the USA (Criqui et al. 2007) and in the Edinburgh Vein Study (Lee et al. 2003), obesity was related to varicose veins only in women. Another study in Italy showed that obese postmenopausal women had an increased risk of varicose veins compared to other women (Iannuzzi et al. 2002). There are also cross-sectional studies which did not show any association between varicose veins and overweight (Malhotra 1972, Da Silva et al. 1974, Komsuoglu et al. 1994, Carpentier et al. 2004, Kroeger et al. 2004).

Follow-up studies showed increased incidence of varicose veins in overweight women. In the Framingham Study, both overweight men and women had a higher incidence of varicose veins than others but the difference was statistically significant only in women (Brand et al. 1988). A follow-up study in the Netherlands also showed a higher risk of varicose veins in the overweight group compared to the control group

in women but not in men (Seidell et al. 1986). In a follow-up study in the USA, higher body mass index did not increase the incidence of varicose veins in men (Scott et al. 2004).

In studies in Finland, height was found to be at least a slight risk indicator of varicose veins (Sisto et al. 1995, Laurikka et al. 2002). In Scotland, height was related to venous reflux in men (Fowkes et al. 2001b) and to varicose veins in both sexes (Lee et al. 2003). This association between height and varicose veins was not confirmed in the studies from Turkey (Komsuoglu et al. 1994), from Israel (Abramson et al. 1981), or from Italy in women (Carpentier et al. 2004).

Social class and Education. The results on the association between varicose veins and social class, also measured by education or occupation, were not consistent. The prevalence of varicose veins increased with reported income (Sisto et al. 1995). On the other hand, a higher prevalence of varicose veins among lower social class men was found in France (Ducimetiere et al. 1981). In the Edinburgh Vein Study, lower level of education was associated with an increased risk of varicose veins in men (Lee et al. 2003). However, in the same population, there was no relation between varicose veins and occupation (Evans et al. 1999). Some of the earlier cross-sectional studies (Abramson et al. 1981, Laurikka 1992, Canonico et al. 1998, Carpentier et al. 2004) and a follow-up study (Scott et al 2004) showed no association between varicose veins and social class.

Family history. Family history of varicose veins was consistently associated with increased risk of varicose veins (Mekky et al. 1969, Laurikka 1992, Cornu-Thenard et al. 1994, Komsuoglu et al. 1994, Scott et al. 1995, Lee et al. 2003, Carpentier et al. 2004, Kroeger et al. 2004, Criqui et al. 2007). The lifetime risk of varicose veins was estimated to be 90% for those subjects both of whose parents had varicose veins and 20% for subjects both of whose parents were free of varicose veins (Cornu-Thenard et al. 1994).

Parity. Parity is usually considered to be a risk factor of varicose veins. In Tampere Varicose Veins Study, parity was independently associated with increased risk of varicose veins (Laurikka et al. 2002, Jukkola et al. 2006). A national health examination survey in Finland also reported that the prevalence of varicose veins increased linearly with number of births up to five children (Sisto et al. 1995). A significant association between a history of pregnancy and varicose veins was also found in other countries (Mekky et al. 1969, Weddell 1969, Beaglehole et al. 1975, Abramson et al. 1981, Maffei et al. 1986, Komsuoglu et al. 1994, Carpentier et al. 2004, Kroeger et al. 2004, Criqui et al. 2007). In a study in Italy, 40.5% of women affected by varicose veins reported the first appearance of varicosities after a pregnancy (Canonico et al. 1998). The Edinburgh Vein Study showed no association

between pregnancy and trunk varicosities, but less severe changes in veins were more common in women with pregnancies than in those without (Lee et al. 1999). Not all studies have reported an association between pregnancies and varicose veins (Coon et al. 1973).

Other risk factors. Men with varicose veins had significantly greater average caloric intake (Ducimetiere et al. 1981). Dietary fibre and constipation were not associated with varicose veins (Lee et al. 2001, Criqui et al. 2007). The results on the association between varicose veins and working position were not consistent. Standing at work was associated with higher prevalence of varicose veins (Mekky et al. 1969, Abramson et al. 1981, Sisto et al. 1995, Laurikka et al. 2002, Kroeger et al. 2004) but inconsistent results have also been reported (Weddell 1969, Maffei et al. 1986). Jobs that predominantly involved being seated were associated with a decreased risk of trunk varices in women (Lee et al. 2003), but the increasing number of hours in sedentary activities each day was also reported to increase the incidence of varicose veins in women (Brand et al. 1988). The association between varicose veins and use of oral contraceptives and postmenopausal hormone replacement therapy was studied with inconsistent results (Scott et al. 1995, Sisto et al. 1995, Lee et al. 1999, Kroeger et al. 2004, Jukkola et al. 2006). The association between varicose veins and arterial diseases, hypertension, congestive heart failure, physical activity, smoking, diabetes and cholesterol has also been studied and the studies are reviewed in the section "Varicose veins and cardiovascular diseases".

In summary, there are not many studies on the risk factors of varicose veins and there is a particular lack of follow-up studies. Earlier studies show inconsistent results with regard to the risk factors of varicose veins. Only family history was consistently associated with varicose veins.

2.4 Pathophysiology of varicose veins

Multiple etiology of varicose veins is to be expected, but despite numerous studies the specific causes of varicose veins are not known. The studies on the pathophysiology of varicose veins have shown three probable mechanisms: venous hypertension, valvular incompetence and vein wall weakness (Fan 2003, Pascarella and Schmid-Schönbein 2005, Bergan et al. 2006). In recent studies, the role of vein wall weakness has been emphasized; alterations in smooth muscle arrangements and changes in extracellular matrix and its components have been suggested to be important changes in the development of varicose veins (Naoum et al. 2007, Raffetto and Khalil 2008b).

Normal valves and muscle pumps ensure the proper functioning of the peripheral venous system. In the lower extremities, the deep vein system is the main conduit for venous blood and is a high pressure system mainly because of muscle pump. A superficial, low pressure, system conducts blood to the deep vein system. Perforator veins connect the deep vein system and the superficial vein system. The valves located throughout the deep and superficial veins prevent the reflux of the blood and the valves of the perforators normally do not allow the high pressure to be transmitted to the superficial system. (Beebe-Dimmer et al. 2005, Ebenhardt and Raffetto 2005) Failure of the valves allows retrograde blood flow and causes venous hypertension, and in addition, the failure of the valves of perforating veins or of the valves located at the junctions of the deep vein and superficial vein system allows high pressure to be transmitted to superficial veins leading to venous hypertension and venous dilatation. (Ebenhardt and Raffetto 2005) In addition to valve damage venous outflow obstruction, such as previous deep vein thrombosis, or failure of the calf-muscle pump can also lead to venous hypertension in the deep vein system. (Ebenhardt and Raffetto 2005, Bergan et al. 2006) Venous hypertension causes not only venous dilation and elongation, but venous hypertension is suggested also to cause inflammatory reaction in the vein wall (Schmid-Schönbein et al. 2001, Takase et al. 2004, Pascarella and Schmid-Schönbein 2005). Inflammatory processes have a role in causing adverse changes in the walls of the veins. Abnormal venous flow in varicose veins causes altered shear stress which promotes inflammatory and thrombotic processes. (Pascarella and Schmid-Schönbein 2005, Bergan et al. 2006)

The theory of primary valvular incompetence in the pathogenesis of varicose veins was challenged over twenty years ago (Rose and Ahmed 1986). However, there has been no consensus on whether primary valve incompetence is the initiating event in the pathogenesis of venous disease or if the valve incompetence is secondary to the changes in the vein wall (Beebe-Dimmer et al. 2005). Recent studies rather support the latter theory because there is some evidence that varicose veins may develop before or without valvular incompetence (Naoum et al. 2007, Raffetto and Khalil 2008b) and dilation of varicose veins is initially distal to the valve (London and Nash 2000). Studies show not only changes in valve anatomy but inflammation has also been observed (Takase et al. 2004, Pascarella and Schmid-Schönbein 2005, Bergan et al. 2008). Leukocyte adherence, activation and migration have been reported to be a part of a pathologic process which results in valve fibrosis and damage and too few valves (Bergan et al. 2001).

Recent observations suggest that varicose veins are caused by intrinsic changes within the venous wall (Naoum et al. 2007, Raffetto and Khalil 2008b). Primary weakness of the vein wall leading to dilation of the vein with resulting

separation of valve cups and valvular incompetence has been suggested as a cause of varicosity (Ibrahim et al. 1996, Vanhoutte et al. 1997, Golledge and Quigley 2003, Elsharawy et al. 2007). Changes in collagen content, smooth muscle cells and elastic fibres were found in the vein walls of varicose veins. There are both hypertrophic and atrophic segments in the vein walls caused by local differences in the balance of synthetic and degradative processes, for example, changes in the levels of matrix metalloproteinases, cytokines, proteolytic enzymes and their inhibitors. (Bergan et al. 2006) Matrix metalloproteinases and their inhibitors, which are important in the synthesis and degradation of extracellular matrix, have been consistently shown to have a role in the development of varicose veins (Jakob et al. 2001, Woodside et al. 2003, Hobeika et al. 2007, Raffetto and Khalil 2008a). A genetic defect in the regulation of the composition of extracellular matrix as a part of the pathogenesis of varicose veins was investigated (Kim et al. 2005). The role of endothelin receptors in the development of varicose veins was also studied (Agu et al. 2002). It was suggested that the dilation of the vein results from failure to contract adequately because of smooth muscle cell or endothelial dysfunction (Golledge and Quigley 2003). Hormonal involvement in the development of varicose veins was also investigated. Hormonal effects, at least sex hormone progesterone, were studied to cause excessive venous distension (Ebenhardt and Raffetto 2005). A study reported increased levels of sex-hormone, estrogen and progesterone, receptors in varicose segments of veins (Mashiah et al. 1999). However, external estrogen or progesterone in oral contraceptives and in hormone replacement therapy were not likely to increase the risk of varicose veins (Jukkola et al. 2006).

2.5 Varicose veins and cardiovascular diseases

2.5.1 Shared pathophysiology of veins and arteries

The extracellular matrix is a complex structure of collagens, elastins, laminins, fibronectins and proteoglycans which supports the cellular components of blood vessels. Matrix metalloproteinases, which are enzymes remodelling extracellular matrix, are important in many physiological and pathological vascular processes. Dysregulation of matrix metalloproteinase activity and extracellular matrix remodelling of the vascular wall have been associated with atherosclerosis and arterial disease and, recently, also with venous disease and varicose veins (Jakob et al. 2001, Lijnen 2003, Hobeika et al. 2007, Raffetto and Khalil 2008a). Hemodynamic forces, such as shear stress and increased intravascular blood pressure, strongly influence collagen metabolism through matrix metalloproteinases, which may cause vascular wall remodelling in both veins and arteries (Ishikawa et al. 2000). A study investigated the effect of statins, a class of cholesterol-lowering drugs, on the activity of matrix metalloproteinases in varicose veins and found that statins suppressed matrix metalloproteinase activity in ex vivo culture of varicose veins (Nomura et al. 2005).

It has been presented that varicose veins are the expression of a systemic pathology of the connective tissue. This hypothesis is supported by studies on the association between the pathology of matrix proteins in skin and in veins. Studies showed that the synthesis of collagen types I and III was dysregulated in dermal fibroblasts derived from individuals with varicose veins (Sansilvestri-Morel et al. 2002, Sansilvestri-Morel et al. 2003) and alterations of other components of extracellular matrix in varicose veins were also present in the skin (Sansilvestri-Morel et al. 2007). A few studies also reported that changes in matrix proteins in the skin correlated with changes in matrix proteins in the arterial wall (Berteretche et al. 1995, Gogly et al. 1998). A study reported an association between coronary artery ectasia and varicose veins and suggested that generalised defect of the entire vascular wall might explain the observed association (Androulakis et al. 2004). Raised levels of superoxide and biomarkers of oxidative stress and also altered relaxation in saphenous veins have been found in coronary artery patients (Al-Benna et al. 2006).

Recent studies suggested that there is probably an association between venous thromboembolism of unknown origin and atherosclerosis (Prandoni et al. 2003, Schulman et al. 2006). Patients with previous venous thromboembolism had increased risk of subsequent symptomatic atherosclerosis and arterial cardiovascular events. It was assumed that the association could be due to the activation of coagulation and inflammatory pathways in both the venous and the arterial system (Prandoni 2007).

To summarize, according to the published literature, there may be a systemic pathology of the entire vascular wall or even the connective tissue, possibly through matrix metalloproteinases or activation of coagulation or inflammatory pathways, leading to the diseases in veins and in arteries.

2.5.2 Potential common risk factors of varicose veins and cardiovascular diseases

In addition to a possible common pathophysiology of diseases of veins and arteries there are some factors, such as hypertension, which may be associated both with varicose veins and with arterial disease. At least the roles of obesity, physical inactivity, smoking, diabetes and cholesterol should be considered as potential common risk factors. The studies on the association between varicose veins and these factors are reviewed below, except for the studies on varicose veins and obesity which are found under the title "Risk factors of varicose veins".

Physical inactivity. In the Framingham Study, low physical activity was shown to be positively associated with varicose veins (Brand et al. 1988). In another study in the USA regular physical activity was not associated with venous disease (Criqui et al. 2007). A study in Italy showed that lack of exercise was a factor linked with varicose veins in men, but not in women (Carpentier et al. 2004).

Smoking. The results of studies on the association between varicose veins and smoking were inconsistent. Men with varicose veins smoked more cigarettes than those without (Ducimetiere et al. 1981, Brand et al. 1988), and a study reported an association between smoking and severe venous disease in men (Criqui et al. 2007). In a follow-up study, smokers were more likely to develop new varicose veins (Scott et al. 2004). In a case-control study, smoking was associated with lower limb venous insufficiency with a dose-effect relation (Gourgou et al. 2002). Some of the studies reported no association between varicose veins and smoking (Malhotra 1972, Abramson et al. 1981, Hirai et el. 1990, Franks et al. 1992, Laurikka 1992, Komsuoglu et al. 1994, Canonico et al. 1998, Lee et al. 2003, Carpentier 2004). A study in Finland found that female smokers had significantly lower prevalence of

varicose veins than non-smoking women, but in men there were no differences (Sisto et al. 1995), and a study in Germany reported lower prevalence of varicose veins in smokers than in non-smokers in both genders (Kroeger et al. 2004).

Diabetes. Most previous studies did not show any significant association between varicose veins and diabetes (Abramson et al. 1981, Ducimetire et al. 1981, Brand et al. 1988, Hirai et al. 1990, Franks et al. 1992, Laurikka 1992, Komsuoglu et al. 1994, Canonico et al. 1998, Scott et al. 2004). In a national health examination survey in Finland the prevalence of varicose veins was lower in diabetic men and women compared to other subjects but the result was statistically significant only in women whose varicose veins had been operated on (Sisto et al. 1995).

Cholesterol. In a follow-up study in the USA, subjects with lower cholesterol were more likely than others to develop new varicose veins (Scott et al. 2004). Other studies report no association between varicose veins and cholesterol (Ducimetiere et al. 1981, Brand et al. 1988, Hirai et al. 1990, Komsuoglu et al. 1994, Sisto et al. 1995).

In summary, overweight, low physical activity, smoking, diabetes and high cholesterol are risk factors of arterial diseases but, in earlier studies, only obesity in women was associated with varicose veins. The results on physical activity and smoking were inconsistent. Diabetes and higher cholesterol were not likely to be associated with varicose veins.

2.5.3 Varicose veins and arterial disease

The first results suggesting an association between arterial disease and varicose veins were reported by Lake et al. (1942) in the USA. They conducted a study among workers aged 40 years and over and found an increased prevalence of arteriosclerosis in leg arteries in men, but not in women, with varicose veins compared to those without varicose veins.

In the national health examination survey in Finland, subjects aged 30 years and over were included and those with coronary heart disease had somewhat, but not statistically significantly, higher prevalence of varicose veins than those without coronary heart disease (Sisto et al. 1995). A case-control study in the USA found no association between varicose veins and any form of heart disease in adult subjects (Scott et al. 1995). Another case-control study in the USA studied predictive factors for myocardial infarction and found a negative relation between varicose veins and myocardial infarction (Klatsky et al. 1976). A cross-sectional study in USA also reported less previous cardiovascular disease in 40 to 79-year-old subjects with moderate venous disease (Criqui et al. 2007). However, severe venous disease was

more common in women with previous cardiovascular disease than in other women in the same study. In a cross-sectional study in Turkey no association was found between varicose veins and angina pectoris or stroke in persons over 60 years of age (Komsuoglu et al. 1994). A community survey in Israel showed no association between coronary heart disease or between palpability of pedal pulses and varicose veins (Abramson et al. 1981).

There are three population based follow-up studies on the association between varicose veins and arterial diseases. Policemen aged 42–53 years with varicose veins had significantly higher incidence of severe coronary heart disease, at least in the lower social class, and intermittent claudication, but there was no association between varicose veins and incidence of angina pectoris. (Ducimetiere et al. 1981) In the Framingham Study coronary heart disease, congestive heart failure, stroke and intermittent claudication were taken into consideration as cardiovascular events. Men and women with varicose veins tended to have a higher incidence of coronary heart disease and intermittent claudication than those without. Significant additional risk was found only in women with coronary heart disease and the result was not significant after controlling for body mass and systolic blood pressure. (Brand et al. 1988) In the Normative Aging Study a reduced risk of symptomatic coronary heart disease was found in men with varicose veins compared to others over a follow-up of 35 years (Scott et al. 2004). In the same study those with a family history of heart disease were more likely than others to develop varicose veins.

2.5.4 Varicose veins and hypertension

In the Framingham Study women with varicose veins had significantly higher systolic blood pressure than other women (Brand et al. 1988). In France, 42 to 53-year-old men with varicose veins had higher values of diastolic, but not systolic, blood pressure than men without varicose veins (Ducimetiere et al. 1981). Hypertension has also been reported to be less prevalent in those subjects with varicose veins (Scott et al. 1995) and in subjects with moderate venous disease (Criqui et al. 2007) than in other subjects. However, in a study by Scott et al. (1995) the association seemed to be age-related. In a community survey in Israel, no association between systolic blood pressure and varicose veins was found. The same study showed a weak and marginal association between varicose veins and low diastolic blood pressure in women. (Abramson et al. 1981) Studies in elderly populations (66 to 96-year-olds) in Southern Italy (Canonico et al. 1998) and in Turkey (over 60-year-olds) (Komsuoglu et al. 1994) showed no significant association between varicose veins and hypertension. A result

of no association between varicose veins and hypertension was also found in a community study in England (Franks et al. 1992), in a cross-sectional study in Germany with subjects aged 20 to 70 years (Kroeger et al. 2004), in a cross-sectional study in Japanese women aged 15 to 90 years (Hirai et al. 1990), and in a national health survey in Finland (Sisto et al. 1995). However, a lower prevalence of varicose vein operations was found in hypertensive women in the same Finnish study.

In a follow-up study in the USA there was no association between diastolic blood pressure and the development of new varicose veins but those men with lower systolic blood pressure developed somewhat more often new varicose veins than other men (Scott et al. 2004).

2.5.5 Varicose veins and congestive heart failure

There are a few studies on the association between varicose veins and congestive heart failure. In Turkey, subjects over 60 years of age were studied in a cross-sectional survey and congestive heart disease was not found to be associated with the prevalence of varicose veins (Komsuoglu et al. 1994). Nor did a cross-sectional community survey in Israel show any association between varicose veins and congestive cardiac failure (Abramson et al. 1981). In the USA, a case-control study found no association between varicose veins and any form of heart disease (Scott et al. 1995). In the follow-up to the Framingham Study, subjects with varicose veins tended to have higher incidence of congestive heart failure than those without varicose veins, but the result was not statistically significant (Brand et al. 1988).

As summarized in Table 3, the majority of cross-sectional studies showed no association between varicose veins and cardiovascular diseases and the results in the longitudinal studies were inconsistent.

Table 3. Studies on the association between varicose veins (v.v.) and arterial disease (AD), hypertension (HTN) and congestive heart failure (CHF).

Reference	Country	N	AD in subjects with v.v.	HTN in subjects with v.v.	CHF in subjects with v.v.
Longitudinal studies:					
Scott et al. 2004	USA	2280 men	Reduced risk of symptomatic coronary heart disease.	Lower systolic blood pressure.	NA
Brand et al. 1988	USA	3822	Higher risk of coronary heart disease in women. Higher, but non-significant, risk of intermittent claudication. No association with stroke.	Higher systolic blood pressure in women (cross-sectional result).	Higher, but non-significant, incidence of CHF.
Ducimetiere et al. 1981	France	7432 men	Higher risk of coronary heart disease and intermittent claudication but not of angina pectoris.	Higher diastolic blood pressure (cross-sectional result)	NA
Cross-sectional studies:					
Criqui et al. 2007	USA	2434	Less cardiovascular disease in men.	Less hypertension.	NA
Kroeger et al. 2004	Germany	6630	NA	No association.	NA
Canonico et al. 1998	Italy	1319	NA	No association.	NA
Sisto et al. 1995	Finland	8000	No significant association with coronary heart disease.	No association.	NA
Komsuoglu et al. 1994	Turkey	856	No association with angina pectoris or stroke.	No association.	No association.
Franks et al. 1992	England	2103	NA	No association.	NA
Hirai et al. 1990	Japan	541	NA	No association.	NA
Abramson et al. 1981	Israel	4888	No association with coronary heart disease or palpability of pedal pulses.	Lower diastolic blood pressure in women. No association with systolic blood pressure.	No association.
Lake et al. 1942	USA	536	More arteriosclerosis of the leg arteries in men.	NA	NA
Case-control studies:					
Scott et al. 1995	USA	335	No association with any form of heart disease.	No significant association.	No association with any form of heart disease.
Klatsky et al. 1976	USA	1392	Negative association with myocardial infarction.	NA	NA

NA=Not available

3. The purpose of the study

The follow-up study of varicose veins was established to ascertain the incidence of new varicose veins in a general middle-aged population and to assess the role of the specific risk factors in the etiology of varicose veins. The association between varicose veins and arterial disease, hypertension and congestive heart failure was studied at the beginning of the study, and the causal direction of the association was studied with incidences during the follow-up.

The specific purpose of the five-year follow-up study in a middle-aged Finnish population (40–65 years) was

1. to assess the incidence of new varicose veins.
2. to study the effect of potential risk factors sex, age, overweight and education on the occurrence of varicose veins.
3. to examine the causal direction and common etiology of varicose veins and cardiovascular diseases by studying the incidences of varicose veins and common diseases of arterial system (angina pectoris, myocardial infarction, peripheral occlusive arterial disease, cerebrovascular disease and hypertension) and congestive heart failure.

4. Population and methods

4.1 Population

The original population of the Tampere Varicose Vein Study included three complete age cohorts, 6,874 individuals (3,284 men and 3,590 women), of the residents of Tampere, a Finnish city with 171,307 inhabitants (in 1989). Subjects were born in 1929, 1939 and 1949, thus at the beginning of the study in 1989 they were 40-, 50- and 60-year-olds. The subjects were identified in the national population registry. Altogether 5,568 subjects (2,467 men and 3,101 women) responded in 1989 and the response rate was 81% (75% in men and 86% in women). The target population of the follow-up study comprised these respondents. Follow-up information was collected after a five-year interval from subjects who had responded in the first round and who were identified in the national population registry in 1994, altogether 5,351 individuals. One hundred and thirty-nine subjects died during the follow-up period and 78 subjects could not be identified in the registry. Causes of deaths were not followed-up. Altogether 4,903 subjects (2,049 men and 2,854 women) responded giving a response rate of 88% of the target population and 92% of those identified in the second evaluation. (Figure 1.)

In this study, prevalences were analysed in those who responded in the first evaluation (N=5,568) and, in the study concerning varicose veins and cardiovascular diseases or congestive heart failure, in those who responded in both evaluations (N=4,903). Incidences of varicose veins were analysed in those who reported not to have varicose veins at the beginning of the study in 1989 (N=3,065) and whose follow-up data collection was complete in 1994 (N=2,400). Incidences of arterial disease (N=3,032), angina pectoris (N=3,264), myocardial infarction (N=3,298), peripheral occlusive arterial disease (N=3,153), cerebrovascular disease (N=3,269), hypertension (N=2,915) and congestive heart failure (N=3,253) were analysed in those who at entry were free of the disease of interest and whose follow-up data was complete.

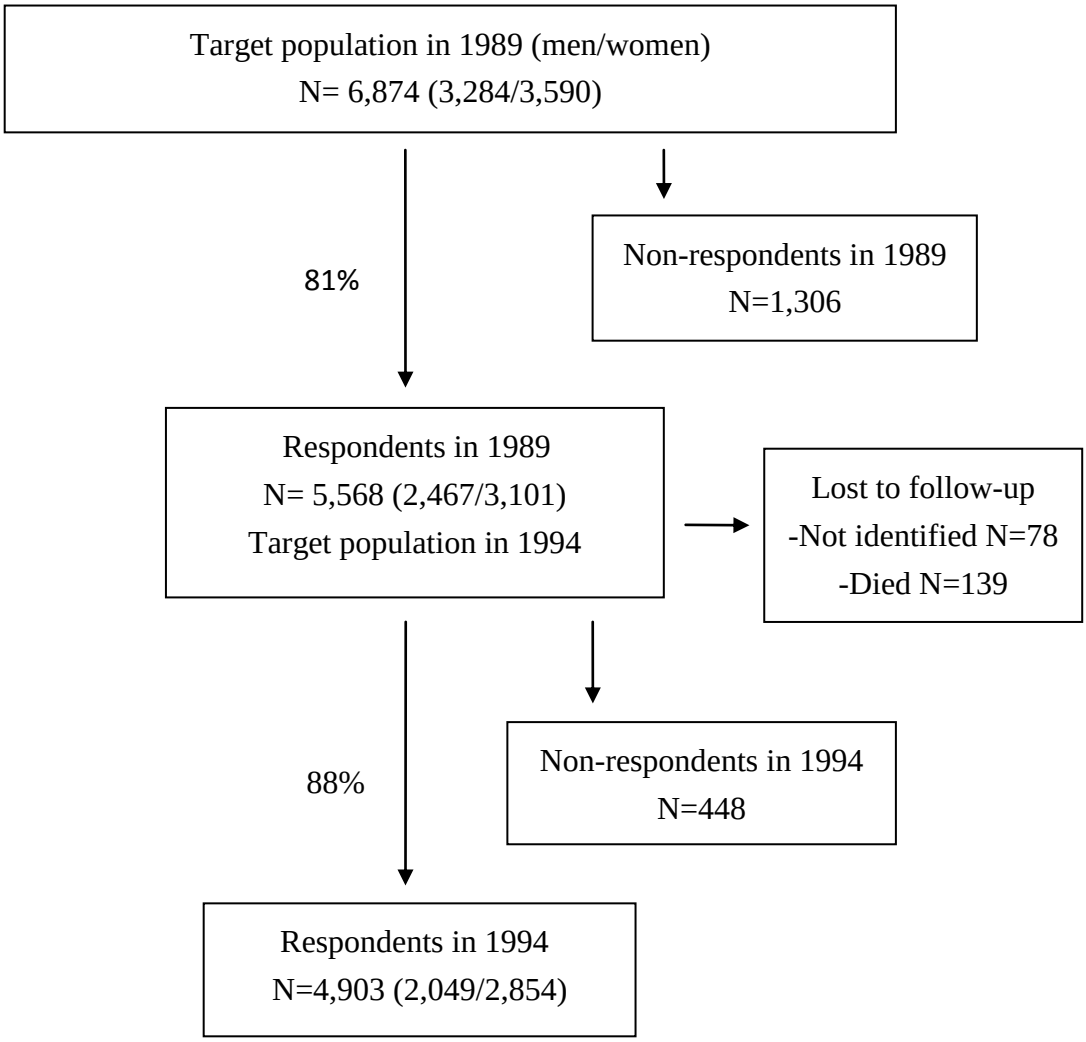


Figure 1. Target populations, participation rates (%) and numbers of respondents and non-respondents and those lost to follow-up in Tampere Varicose Vein Study in 1989 and in 1994.

4.2 Methods

A structured questionnaire was used. The questionnaire was similar in both surveys, questionnaires are provided in the Appendices. An identical questionnaire was mailed from one to two months later to the non-respondents in both surveys.

A common definition of varicose veins was used and the definition "clearly visible, dilated, tortuous, and possibly prominent subcutaneous veins of the lower extremities" was given in the questionnaire. It corresponds to the later published CEAP (C=clinical manifestations, E=etiologic factors, A=anatomic distribution, P=pathophysiologic condition) classification clinical class 2 (Porter and Moneta 1995). Subjects themselves assessed if they had varicose veins. The validity of the questionnaire based self-reported diagnosis of varicose veins was evaluated in a random sample of 166 50-year-old subjects in our population (Laurikka et al. 1993, Laurikka et al. 1995).

Body mass index (weight (kg)/[height (m)]^2) was used as an indicator of overweight. BMI was classified into three groups using 10 and 90 percentiles as cutpoints (P1: BMI≤21.2 kg/m^2, P2: 21.2 kg/m^2<BMI≤30.5 kg/m^2, P3: BMI>30.5 kg/m^2) when analysed as a potential risk factor of varicose veins, and BMI 25 as a cutpoint or as a continuous variable when analysed as a confounding factor. Weight and height were self-reported.

Level of education was classified into two groups; comprehensive and vocational school were defined as lower education level; high school, college and university were defined as higher education level. Sports was classified into two groups: irregularly (less than weekly) or regularly (daily or weekly). Smoking was classified as smoker or non-smoker as a confounding factor. Smokers were those who had ever smoked for longer than one year and, accordingly, ex-smokers were grouped with smokers.

Individuals were defined to have cardiovascular disease if they reported having arterial disease (angina pectoris, myocardial infarction, peripheral occlusive arterial disease or cerebrovascular disease), hypertension or congestive heart failure diagnosed by a doctor. These diseases were elicited with the alternatives "yes" or "no" in the questionnaire.

Prevalences of varicose veins, arterial disease, hypertension and congestive heart failure were defined as the proportion of those who reported ever having had the medical condition in question in relation to all respondents (lifetime prevalence) at entry, i.e. in 1989. Subjects with surgically treated varicose veins were defined as

having varicose veins. Odds ratios and multivariate-adjusted odds ratios with 95% confidence intervals were reported for prevalences.

The incidences of varicose veins, arterial disease, hypertension and congestive heart failure were estimated as the number of new cases of any of the diseases in question per 1,000 person-years during follow-up among those free of the condition at entry. Person-years at risk were estimated by assuming the new incident cases to appear on average at the midpoint of the five-year follow-up period. Incidence density ratios (IDR) were used as an indicator of risk and they were estimated as the ratio of incidence rate among exposed to non-exposed. A logistic regression analysis was performed to evaluate the simultaneous effects of the determinants on the disease studied. The indicator of the effect was multivariate-adjusted five-year incidence odds ratio (IOR). Estimates of IDRs and IORs were reported with 95% confidence intervals. Software packages SPSS 10.1 and SPSSwin 13 (SPSS, Chicago, IL, USA) were used in the analysis.

5. Results

Altogether 5,681 subjects returned the questionnaire in the first survey. One hundred and thirteen subjects were excluded from analysis because the information about varicose veins was missing. A total of 5,568 individuals were included for further analysis and follow-up. After the follow-up period 4,903 subjects responded. Varicose veins were less reported among those lost from follow-up than among follow-up respondents (women free of varicose veins 62.8% vs. 56.4%, p =0.02 and men free of varicose veins 84.4% vs.78.6%, p=0.46). Non-responders were more often in the youngest cohort than in the oldest cohort in both sexes.

5.1 Prevalence and incidence of varicose veins (I)

At the beginning of the study 1,748 subjects (454 men and 1,294 women) reported varicose veins (N=5,351). The prevalence of varicose veins was 32.6% among those who reported to have or not to have varicose veins (those who did not know were excluded). The incidence of varicose veins was studied in subjects responding in both evaluations and initially free of varicose veins (1,253 men and 1,147 women). Five years later 157 of these 2,400 respondents reported new varicose veins. The incidence of varicose veins in the population was 13.5 per 1,000 person years. (Table 4.)

Table 4. Size of populations (N), prevalent and incident cases, prevalence (%) and incidence (per 1,000 person years, pyrs) of varicose veins.

Sex	Prevalence			Incidence		
	N	Prevalent cases	%	N	Incident cases	/1000 person years
Men	2403	454	18.9	1253	52	8.5
Women	2948	1294	43.9	1147	105	19.2
Total	5351	1748	32.6	2400	157	13.5

5.2 Risk factors of varicose veins (I)

5.2.1 Sex

Women had statistically significantly higher prevalence of varicose veins than men (43.9% in women and 18.9% in men); OR 3.4 (3.0–3.8) and age, BMI and education adjusted OR 3.6 (3.2–4.1). The incidence of varicose veins was significantly higher in women (19.2 per 1,000 person years) than in men (8.5 per 1,000 person years); age, BMI and education adjusted IOR 2.4 (1.7–3.4). (Table 5.)

5.2.2 Age

The prevalence of varicose veins increased with increasing age. Varicose veins were reported by 23.0%, 36.6% and 42.8% of respondents in age groups 40-, 50- and 60-year-olds; sex, BMI and education adjusted odds ratio was 1.9 (1.7–2.3) in 50-year-olds and 2.5 (2.1–2.9) in 60-year-olds when a cohort of 40-year-olds was used as a reference group. The incidence was highest in the cohort of 50-year-olds, adjusted IOR 1.6 (1.1–2.3), both in men and in women, but the result was statistically significant only in women. Other cohorts, 40- and 60-year-olds, had nearly equal incidences of varicose veins (11.7 and 11.4 per 1,000 person years). (Table 5.)

5.2.3 Overweight

Based on prevalence higher BMI indicated higher risk of varicose veins. In the leanest decile (BMI≤21.2 kg/m^2) the prevalence of varicose veins was 30.2%, whereas in the heaviest decile (BMI>30.5 kg/m^2) it was 40.0%. Sex, age and education adjusted OR were 1.2 (1.0–1.5) and 1.5 (1.2–2.0) in the middle and heaviest decile with the leanest as the reference. Subjects with normal weight or overweight (21.2 kg/m^2<BMI≤30.5 kg/m^2) and obese subjects (BMI>30.5 kg/m^2) had similarly elevated, but not significant, risk of new varicose veins compared to the leanest subjects, adjusted IOR 1.2 (0.7–2.1) and 1.8 (0.9–3.8) respectively. (Table 5.)

5.2.4 Education

Those with lower education (comprehensive school or vocational school) had higher prevalence of varicose veins than those with higher education (high school or college or university); sex, age and BMI adjusted OR 1.2 (1.1–1.4). After the follow-up, there were no statistically significant differences in the incidences of varicose veins in the groups with higher or lower education. Subjects with lower education had somewhat less new varicose veins compared to others, adjusted IOR 0.8 (0.6–1.2). (Table 5.)

Table 5. Number of subjects (N) in prevalence and incidence studies, prevalent and incident cases of varicose veins (v.v) and multivariate adjusted (adjusted for the other variables in the table) odds ratios (OR) for the prevalence and incidence odds ratios (IOR) for the incidence of varicose veins with 95% confidence intervals (CI).

		Prevalence of v.v.			Incidence of v.v.		
Risk factor		N (5351)	Prev cases	Adjusted OR (CI)	N (2400)	Incid cases	Adjusted IOR (CI)
Sex							
	Men	2403	454	1	1253	52	1
	Women	2948	1294	3.6 (3.2-4.1)	1147	105	2.4 (1.7-3.4)
Age							
	40-45	2226	512	1	1141	65	1
	50-55	1627	595	1.9 (1.7-2.3)	718	62	1.6 (1.1-2.3)
	60-65	1498	641	2.5 (2.1-2.9)	541	30	1.0 (0.7-1.7)
BMI*							
	P1	513	155	1	243	16	1
	P2	4206	1346	1.2 (1.0-1.5)	1922	116	1.2 (0.7-2.1)
	P3	535	214	1.5 (1.2-2.0)	208	21	1.8 (0.9-3.8)
Education**							
	Higher	2819	891	1	886	63	1
	Lower	2168	722	1.2 (1.1-1.4)	1420	90	0.8 (0.6-1.2)

*Body mass index by 10 and 90 percentiles (P1: BMI≤21.2 kg/m^2, P2: 21.2 kg/m^2<BMI≤30.5 kg/m^2, P3: BMI>30.5 kg/m^2)

**Higher education: university, college and high school
Lower education: comprehensive school and vocational school

5.3 Varicose veins and cardiovascular diseases

5.3.1 Varicose veins and arterial disease (II,III)

Arterial disease was reported by 8.0% of subjects. Prevalence was 2.9% for angina pectoris, 1.2% for myocardial infarction, 3.3% for peripheral occlusive arterial disease and 2.2% for cerebrovascular disease. Eighty-four percent were free of these diseases. During follow-up, 265 subjects (110 men and 155 women) contracted new arterial disease. (Table 6.)

Those with arterial disease had higher prevalence of varicose veins (48.1%) than those without (31.3%), sex and age adjusted OR 1.7 (1.4–2.2), and also higher incidence of varicose veins (17.9 per 1,000 person years) than those without (13.0 per 1,000 person years), sex and age adjusted IOR 1.4 (0.8-2.7). The difference in the incidence was statistically significant in women, age-adjusted IOR of varicose veins by arterial disease was 2.2 (1.1–4.5). There were new occurrences of varicose veins in only two men with arterial disease, allowing no reliable conclusions; age-adjusted IOR 0.5 (0.1–2.2). (Table 7.) Sex, age and body mass index (as a categorical and continuous variable) -adjusted estimates of the incidence of varicose veins by arterial disease practically did not differ from the estimate adjusted for sex and age with IOR 1.5 (0.8–2.7).

Subjects with varicose veins at the beginning of the study contracted more new arterial diseases than subjects without varicose veins. The incidence of arterial disease was 30.3 and 13.2 per 1,000 person-years respectively and sex and age-adjusted incidence odds ratio was statistically significant, IOR 2.1 (1.6–2.8). Gender-specific analysis also revealed a significantly increased risk both in men (age-adjusted IOR 2.4 (1.5–3.8)) and in women (age-adjusted IOR 2.0 (1.4–2.8)) with varicose veins compared to others. (Table 8.) The effect of weight on the result was controlled for by adjusting for body mass index: sex, age and BMI adjusted IOR for the incidence of arterial disease by varicose veins was 2.0 (1.5–2.7), which was only marginally lower than the sex and age adjusted IOR. There was no confounding effect of sports (sex, age and sports adjusted IOR was the same 2.1 as sex and age-adjusted IOR) or smoking (sex, age and smoking adjusted IOR 2.1) on the relationship between varicose veins and arterial disease. The effect of deep vein thrombosis on the association between varicose veins and arterial disease was excluded by studying the incidence of arterial disease in those subjects with and without varicose veins who did not report previous deep vein thrombosis; the sex and age-adjusted IOR 2.0 (1.5–2.7) was also significant in this sub-population.

The association between varicose veins and each type of arterial diseases was also studied, as described in more detail in Tables 9. and 10. Based on the prevalence there was significantly higher odds of varicose veins in those with peripheral occlusive arterial disease than in those without; sex and age-adjusted OR 3.9 (2.7–5.6). Subjects with angina pectoris, myocardial infarction or cerebrovascular disease did not have any significant increase in the risk of varicose veins; ORs 1.2 (0.8–1.7), 1.0 (0.6–1.9) and 0.9 (0.6–1.4) respectively. There was a small number of new varicose veins in those with angina pectoris, peripheral occlusive arterial disease or cerebrovascular disease and none in those with myocardial infarction (Table 9.), but the numbers of new arterial diseases in those with varicose veins were remarkably higher (Table 10.). During follow-up, subjects with varicose veins had statistically significantly higher incidence of peripheral occlusive arterial disease than subjects with no varicose veins; age and sex adjusted IOR 3.2 (2.3–4.6) (Table 10.). The result was statistically significant both in men, IOR 4.6 (2.6–8.0), and in women, IOR 2.7 (1.7–4.1). There was no significant difference in the incidence of angina pectoris, myocardial infarction or cerebrovascular disease in those with varicose veins at entry compared to those without; IORs 1.2 (0.8–1.9), 1.1 (0.5–2.6) and 1.2 (0.7–2.0) respectively (Table 10.).

5.3.2 Varicose veins and hypertension (II, III)

Among the subjects 18.2% reported hypertension and 77.2% reported no hypertension. Four hundred and three subjects (189 men and 214 women) contracted new hypertension during the five-year follow-up. (Table 6)

The prevalence of varicose veins was higher in respondents with hypertension (39.0%) than in others (31.9%), OR 1.4 (1.2–1.6), but sex and age-adjusted OR 1.1 (0.9–1.2) showed no association between hypertension and varicose veins. The incidence of varicose veins was not significantly higher (15.7 per 1,000 person-years) in those with hypertension than in those without (13.3 per 1,000 person-years), sex and age adjusted IOR 1.1 (0.7–1.8). The estimates of incidences of varicose veins by hypertension did not differ significantly when analysing genders separately: age adjusted IOR 1.3 (0.7–2.8) in men and 1.0 (0.6–1.8) in women. (Table 7)

The incidence of hypertension was nearly equal in those with varicose veins (30.5 per 1,000 person-years) and in those without varicose veins (28.9 per 1,000 person-years); sex and age-adjusted IOR 1.0 (0.8–1.3) (Table 8.), and adjusting for body mass index did not have any effect on the estimate.

5.3.3 Varicose veins and congestive heart failure (IV)

At the beginning of the study 2.1% of the study population reported having congestive heart failure and 89.6% reported not having this disease. Fifty-five respondents (35 men and 20 women) reported new congestive heart failure during follow-up. (Table 6)

The prevalence of congestive heart failure was higher in those with varicose veins (2.9%) than in those without varicose veins (1.9%), OR 1.6 (1.0–2.3). After adjusting for sex and age the increase in the risk of congestive heart failure in those with varicose veins was smaller and not statistically significant, OR 1.2 (0.8–1.9).

Only three out of 36 subjects with no varicose veins and reported congestive heart failure at entry reported new varicose veins during follow-up. The incidence of varicose veins was higher in those with congestive heart failure (17.4 per 1,000 person-years) than in others (13.5 per 1,000 person-years) but the result was not statistically significant; sex and age adjusted IOR 1.2 (0.4–4.0). All three new varicose veins occurred in women, and they had a higher incidence of varicose veins than women without heart failure; age adjusted IOR 1.8 (1.03–2.6). (Table 7.)

Subjects with varicose veins had higher incidence of congestive heart failure than those without varicose veins, 4.9 and 2.6 per 1,000 person-years respectively. The result was statistically significant with IOR 1.9 (1.1–2.9) and sex and age adjusted IOR 2.5 (1.4–4.6). The risk of new congestive heart failure was significantly increased in both men (age-adjusted IOR 2.2 (1.04–4.6)) and in women (age-adjusted IOR 3.5 (1.1–11.1)) with varicose veins. (Table 8.) BMI, arterial disease and hypertension were also taken into account as confounding factors, but none of these confounders accounted for the increased risk of congestive heart failure in those with varicose veins compared to others.

Subjects who reported ever having had deep vein thrombosis were excluded from the analysis and the incidence of congestive heart failure was studied in those with varicose veins and in those without; IOR 2.3 (1.2–4.4) showed only a minor effect of deep vein thrombosis on the result.

In summary, subjects with varicose veins had significantly higher incidence of arterial disease and congestive heart failure than subjects without varicose veins. The increased risk of arterial disease was mostly due to significantly higher incidence of peripheral occlusive arterial disease in subjects with than in subjects without varicose veins. The incidence of varicose veins was somewhat, but not significantly, higher in those with arterial disease than in those without arterial disease. The incidences did not show any association between varicose veins and hypertension. Sex, age, BMI, physical activity and smoking adjusted IORs are summarized in Figure 2.

Table 6. Prevalent cases and rates (%) and incident cases and rates (per 1,000 person years, pyrs) of varicose veins, arterial disease, hypertension and congestive heart failure in those responding in both evaluations.

Variable	Prevalent cases (%) (N=4903)		Incidence		
			N	Incident cases (/1000 pyrs)	
Varicose veins	1567	(32)	2400	157	(14)
Arterial disease	394	(8.0)	3032	265	(18)
AP	142	(2.9)	3264	99	(6.2)
MI	60	(1.2)	3298	32	(2.0)
PAD	161	(3.3)	3153	163	(11)
CEVD	108	(2.2)	3269	71	(4.4)
Hypertension	891	(18)	2915	403	(30)
Congestive heart failure	101	(2.1)	3253	55	(3.4)

AP=angina pectoris, MI=myocardial infarction, PAD=peripheral occlusive arterial disease, CEVD=cerebrovascular disease

Table 7. Incident cases (n) and adjusted incidence odd ratios (IOR) with 95% confidence intervals (CI) for incidence of varicose veins by arterial disease, hypertension and congestive heart failure (CHF).

Risk factor	Incidence of varicose veins					
	Men		Women		All	
	n	IOR* (CI)	n	IOR* (CI)	n	IOR** (CI)
Arterial disease						
No	45	1	88	1	133	1
Yes	2	0.5 (0.1-2.2)	11	2.2 (1.1-4.5)	13	1.4 (0.8-2.7)
Hypertension						
No	38	1	85	1	123	1
Yes	11	1.3 (0.7-2.8)	19	1.0 (0.6-1.8)	30	1.1 (0.7-1.8)
CHF						
No	47	-	98	1	145	1
Yes	0	-	3	1.8 (1.0-2.6)	3	1.2 (0.4-4.0)

N=2,400 *adjusted for age **adjusted for sex and age

Table 8. Incident cases (n) and adjusted incidence odds ratios (IOR) with 95% confidence intervals (CI) of arterial disease, hypertension and congestive heart failure by presence of varicose veins.

Risk factor	Incidence					
	Arterial disease (N=3032)		Hypertension (N=2915)		Congestive heart failure (N=3253)	
	n	IOR (CI)	n	IOR (CI)	n	IOR (CI)
Men*						
Varicose veins						
No	71	1	154	1	23	1
Yes	33	2.4 (1.5-3.8)	28	1.0 (0.6-1.5)	11	2.2 (1.04-4.6)
Women*						
Varicose veins						
No	57	1	116	1	4	
Yes	92	2.0 (1.4-2.8)	89	1.0 (0.8-1.4)	13	3.5 (1.1-11.1)
All**						
Varicose veins						
No	128	1	270	1	27	1
Yes	125	2.1 (1.6-2.8)	117	1.0 (0.8-1.3)	24	2.5 (1.4-4.6)

*adjusted for age **adjusted for sex and age

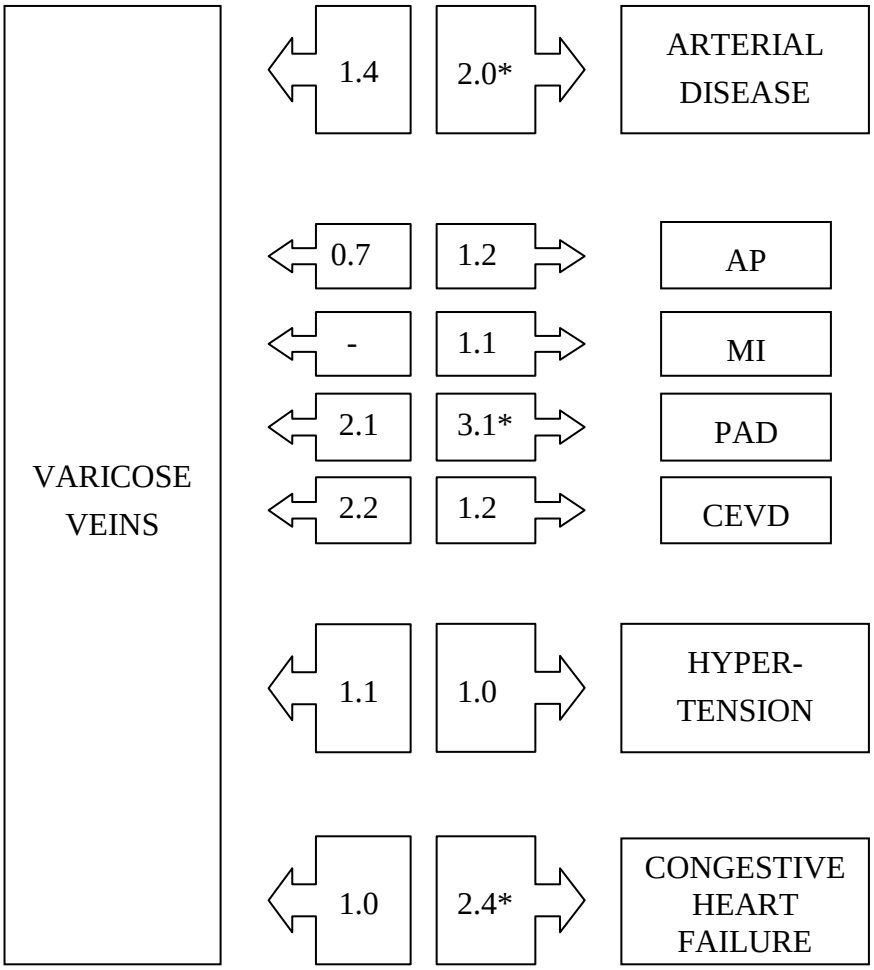
Table 9. Incident cases (n) of varicose veins (v.v). Sex and age-adjusted incidence odds ratios (IOR) with 95% confidence intervals (CI) for incidences of varicose veins by each arterial disease.

Risk factor	Incidence of v.v.	
	n	IOR (CI)
Angina pectoris		
No	146	1
Yes	3	0.7 (0.2-2.4)
Myocardial infarction		
No	148	-
Yes	0	-
Peripheral occlusive arterial disease		
No	140	1
Yes	5	1.9 (0.7-5.1)
Cerebrovascular disease		
No	140	1
Yes	6	2.1 (0.8-5.1)

N=2,400

Table 10. Incident cases (n) and sex and age-adjusted incidence odds ratios (IOR) with 95% confidence intervals (CI) of angina pectoris (AP), myocardial infarction (MI), peripheral occlusive arterial disease (PAD) and cerebrovascular disease (CEVD) by presence of varicose veins.

Risk factor	Incidence							
	AP (N=3264)		MI (N=3298)		PAD (N=3153)		CEVD (N=3269)	
	n	IOR (CI)	n	IOR (CI)	n	IOR (CI)	n	IOR (CI)
Varicose veins								
No	57	1	21	1	62	1	40	1
Yes	38	1.2 (0.8-1.9)	8	1.1 (0.5-2.6)	91	3.2 (2.3-4.6)	26	1.2 (0.7-2.0)



*statistically significant

Figure 2. Sex, age, body mass index, sports and smoking adjusted incidence odds ratios for the incidence of arterial disease, hypertension and congestive heart failure by presence of varicose veins and for the incidence of varicose veins by presence of arterial disease, hypertension and congestive heart failure. AP=angina pectoris, MI=myocardial infarction, PAD=peripheral occlusive arterial disease, CEVD=cerebrovascular disease.

6. Discussion

6.1 Population and methods

Our large study population gave us a sufficient number of prevalent and incident cases of varicose veins, arterial disease, hypertension and congestive heart failure to achieve reliable results. The response rates were good in both surveys (81% and 92%). The proportion of not known responses on the studied diseases varied between 4.7% and 8.3%. The number of subjects lost during follow-up and the proportion of not known responses were therefore at an acceptable level.

Diagnosis of varicose veins was self-reported and based on the definition given in the questionnaire. The questionnaire was validated earlier for the question on varicose veins in a sub-sample of 166 subjects aged 50 years. They visited the out-patient unit in Tampere University Hospital and were examined by a surgeon. Examination included inspection of the lower extremities and Trendelenburg tests with continuous wave (CW) Doppler reflux verifications. Nowadays, these tests have been largely superseded by colour duplex scanning (Bhasin and Scott 2006, Campbell 2006). However, hand-held Doppler assessment is still an adequate screening test of primary, previously untreated varicose veins (Campbell et al. 1997, Kim et al. 2000, Campbell 2006). A study compared the findings of CW Doppler with duplex ultrasound in the assessment of primary varicose veins and reported a sensitivity of 90–95% and a specificity of 93–100% (Darke et al. 1997). Another study compared hand-held Doppler assessment to colour duplex imaging and also reported high sensitivity (0.80–0.97) and specificity (0.73–0.92) (Kim et al. 2000).

The agreement between self-reports and clinical examination was relatively good in our population; the specificity was 0.93 in men and 0.91 in women and the sensitivity was 0.93 in men and 0.92 in women (Laurikka et al. 1995). A study in Italy also showed that the agreement between self-reports and clinical findings of varicose veins was good (prevalence of 29.6% vs 27.4%) (Canonico et al. 1998). In Israel (Abramson et al. 1981), an interview was controlled with a clinical examination of varicose veins and specificity (0.95 in men and 0.85 in women) was quite similar and sensitivity (0.47 in men and 0.67 in women) lower than in our survey. In Finland, the consistency of the answers to the questions about history of varicose veins was studied by a repeat questionnaire three months after the baseline evaluation and kappa

coefficients 0.71 in men and 0.83 in women were reported (Sisto et al. 1995). At least some of the good sensitivity in our study was probably due to social habits, for example sauna, and potentially also attributable to good health care services.

The critical point in our study was the lack of validation of the diagnosis of cardiovascular diseases. The questionnaire was not validated for the questions on arterial diseases, hypertension and congestive heart failure. These diseases were supposed to have been diagnosed by a doctor. We did not use any standard questionnaire for cardiovascular diseases. It is obvious that there are some individuals with disease but without diagnosis and vice versa and, therefore, some misclassification. Such a misclassification is true for any method, however, as it is impractical to apply clinical diagnostic methods to thousands of healthy people. Earlier studies on the validation of the questionnaire information show that self-report is more reliable for well-known diseases with clear diagnostic criteria and with regular controls (e.g. hypertension, coronary heart disease, cerebrovascular disease) than for diagnostically complex diseases (e.g. peripheral arterial disease and congestive heart failure), as reviewed below.

A study in Finland compared the agreement between questionnaire data and medical records in a middle-aged (45 to 73 year-old) population and reported substantial agreement for hypertension (kappa=0.78), myocardial infarction (kappa=0.77) and angina pectoris (kappa=0.73). For cerebral stroke or transient ischemic attack (kappa=0.62) and for claudication (kappa=0.30) the agreement was lower. (Haapanen et al. 1997) In the Women's Health Initiative self-report and adjudication of cardiovascular events were compared. They found substantial agreement between self-reports and doctors' opinions for myocardial infarction (kappa=0.64) and stroke (kappa=0.76), but the concordance was fair to moderate for angina (kappa=0.37), congestive heart failure (kappa=0.48) and peripheral vascular disease (kappa=0.53). (Heckbert et al. 2004) Another study in women, The Nurses' Health Study, validated the questionnaire information and reported confirmation rates for self-reported myocardial infarction to be 68% and for self-reported cerebrovascular accident 66% (Colditz et al. 1986). In the same study, among a random sample of women, all self-reports of hypertension were confirmed and 6.8% were false negatives. In a study by Okura et al. (2004) agreement between questionnaire responses and medical record diagnosis was assessed and was substantial for hypertension (kappa=0.75), myocardial infarction (kappa=0.80) and stroke (kappa=0.71) but not for heart failure (kappa=0.46). There was a high false-positive rate for heart failure.

Despite our large study population, there was quite small number of cases to study the effect of specific arterial diseases on the occurrence of varicose veins. We

combined ischemic heart disease (angina pectoris and myocardial infarction), peripheral occlusive arterial disease and cerebrovascular disease to represent atherosclerotic arterial disease to reduce random variation in the results. However, the analysis was also done for each of the arterial diseases separately. Although cerebrovascular disease is not always caused by atherosclerosis, all subjects who reported cerebrovascular disease were included in our analysis. Therefore the cerebrovascular disease group probably includes not only stroke but also cerebral hemorrhage.

We considered the effect of confounders in multivariate analyses. However, there may be some residual confounding because of crude classifications into few, such as two or three, classes. Moreover, it is inherent in non-experimental research that some confounders remain unidentified.

In our study on the risk factors of varicose veins and on the association between varicose veins and cardiovascular diseases, both prevalence and incidence estimates were studied, which allowed us an opportunity to evaluate if some of the inconsistencies can be accounted for by the design of the study. Cross-sectional design does not allow evaluation of the time relationship and, therefore, is not applicable to study the direction of the association. The prevalences give an average of the risks without the ability to distinguish the direction or differences in any bidirectional association. Furthermore, the results are more susceptible to bias. Therefore, in the results and in the discussion the main emphasis is on the incidences found by the follow-up design. The prevalences are used mainly to explain inconsistencies in the literature.

6.2 Results

6.2.1 Occurrence and risk factors of varicose veins

Prevalence estimates vary widely between different studies. Variability in populations, methods and definitions of varicose veins partly explain the differences in the estimates. The prevalence data of the total Tampere Varicose Vein Study population at entry has been published earlier in more detail (Laurikka 1992, Laurikka et al. 1993, Laurikka et al. 2002). The prevalence of varicose veins in our study population is within the limits of other studies. A national health examination survey in Finland (Sisto et al. 1995) reported lower prevalence rates than those in our study, but this is probably explained by age-groups and by the definition of varicose veins; in the Mini-

Finland Health Survey adults aged 30 years and over were included in the study and varicose veins were supposed to be diagnosed by a doctor.

There are few follow-up studies on the appearance of new varicose veins in a general population. The Framingham Study (Brand et al. 1988) reported the incidence of varicose veins per person-bienniums during a follow-up of 16 years. The Framingham Study included the same age-groups as our study, but also older subjects up to 89-year-olds. The incidence of varicose veins in our study (13.5 per 1,000 person-years) is slightly lower than the incidence in the Framingham Study (23.1 per 1,000 person-years). The incidence of varicose veins was 22.7 (18.9 in men and 26.2 in women) per 1,000 person-years in subjects aged from 40 to 69 years, therefore, older age-groups do not explain the higher incidence in the Framingham Study. The incidence of varicose veins in our study indicates substantially higher appearance of new varicose veins than the incidence of 2.2 per 1,000 person-years (3–4 in corresponding age-groups) reported in The San Valentino Vascular Screening Project in Italy (Cesarone et al. 2002). In the Framingham Study subjects were examined, and the definition of varicose veins (distended, tortuous, clearly visible veins in the lower limbs) was similar to the definition in our study. In Italy, subjects were evaluated by clinical assessment and duplex scanning.

The risk profile of subjects with varicose veins at the beginning of the study (prevalent cases) may differ somewhat from the risk profile of subjects having no varicose veins at entry and reported new varicose veins during follow-up (incident cases) because the former group acquired varicose veins at a younger age. They may, for example, have a stronger hereditary component in the development of varicose veins than those without varicose veins until middle-age, or some other risk factors may also affect the pathogenesis of varicose veins earlier in life. Despite the study setting, female gender and overweight seemed to be risk indicators of varicose veins, but the results on age and education as risk factors were not that consistent and they were dependent on the design, as described in more detail below.

Female sex was an independent risk factor for varicose veins and the results have been rather consistent (Coon et al. 1973, Abramson et al. 1981, Maffei et al. 1986, Franks et al. 1992, Scott et al. 1995, Sisto et al. 1995, Canonico et al. 1998, Laurikka et al. 2002, Carpentier et al. 2004, Kroeger et al. 2004). It is not likely that the increased risk of varicose veins in women compared to men depends on external hormones (Jukkola et al. 2006). However, a recent study in Edinburgh showed varicose veins to be more prevalent in men than in women (Evans et al. 1999). In Edinburgh, the response rate (54%) was quite low, which may have affected the result.

As in most earlier studies (Mekky et al. 1969, Malhotra 1972, Da Silva et al. 1974, Beaglehole et al. 1975, Abramson et al. 1981, Maffei et al. 1986, Franks et al.

1992, Komsuoglu et al. 1994, Evans et al. 1999, Cesarone et al. 2002, Laurikka et al. 2002, Carpentier et al. 2004, Kroeger et al. 2004), our prevalence data showed increased prevalence of varicose veins with increasing age. Varicose veins accumulate with age in the population because they are usually chronic without treatment but not lethal. The cohort of 50-year-olds, especially women, had the highest incidence of new varicose veins in our study. In the Framingham Study, the highest incidence rate of varicose veins was in women aged 40–49 years (Brand et al. 1988). A study in Italy also showed the importance of menopausal age in the development of varicose veins when more than one third of women reported that varicose veins developed after the menopause (Canonico et al. 1998). It is possible that the incidence of varicose veins peaks middle-age, especially in women.

Most of the cross-sectional studies (Mekky et al. 1969, Abramson et al. 1981, Ducimetiere et al. 1981, Sisto et al. 1995, Canonico et al. 1998, Iannuzzi et al. 2002, Laurikka et al. 2002, Lee et al. 2003) and follow-up studies (Seidell et al. 1986, Brand et al. 1988) have shown that obese individuals, especially women, are more likely to develop varicose veins. In our study, obesity was consistently a significant risk indicator based on both cross sectional and longitudinal analyses, even if the risk of new varicose veins in subjects with higher body mass index did not reach statistical significance. Our results support the previously reported association between obesity and varicose veins.

There is no agreement as to whether education or occupation has an effect on the development of varicose veins (Abramson et al. 1981, Ducimetiere et al. 1981, Sisto et al. 1995, Canonico et al. 1998, Evans et al. 1999, Lee et al. 2003, Carpentier et al. 2004, Scott et al. 2004). In our study, lower level of education indicated somewhat increased prevalence of varicose veins but the effect was reverse and insignificant based on the incidence. The inconsistent results may be due to variation in design and other methodological approaches. Cross-sectional setting may overestimate the role of education in the occurrence of varicose veins, or the result may indicate that those with lower education (and related social co-factors) acquire varicose veins at a younger age.

6.2.2 Varicose veins and cardiovascular diseases

We hypothesized an association between varicose veins and other cardiovascular diseases based on rare existing epidemiological studies and studies on possible common pathophysiological mechanisms in the development of both venous and arterial diseases as described in the review of the literature. There are some cross

sectional studies (Lake et al. 1942, Abramson et al. 1981, Hirai et al. 1990, Franks et al. 1992, Komsuoglu et al. 1994, Sisto et al. 1995, Canonico et al. 1998, Kroeger et al. 2004, Criqui et al. 2007), two case-control studies (Klatsky et al. 1976, Scott et al. 1995) and three follow-up studies (Ducimetiere et al. 1981, Brand et al. 1988, Scott et al. 2004) on the association between varicose veins and cardiovascular diseases, with inconsistent results.

The questions about cardiovascular diseases were not validated in our questionnaire. In the following paragraphs the prevalence estimates (among those who responded to the question) in our study are compared to those reported in studies with clinical examination or structured interview. Some reasons which may have led to misclassification are discussed. If the disease is rare and misclassification is nondifferential with respect to exposure, the risk estimate will be driven towards one and rather underestimate the effect. If it is differential, the direction of bias is not known. It is possible that subjects have underestimated or overestimated both varicose veins and cardiovascular diseases, or contact with health care services because of one disease may increase the possibility of getting a diagnosis of another disease, which may lead to differential misclassification. On the other hand, subjects were asked to report cardiovascular diseases diagnosed by a doctor, which is likely to reduce misclassification and its differential characteristic.

Arterial disease. Coronary heart disease and cerebrovascular diseases are well-known chronic diseases and subjects are aware of their condition and report it quite reliably in questionnaire surveys, as reviewed at the beginning of the Discussion. Patients may not be as familiar with peripheral arterial disease as with other cardiovascular diseases and there may be some misunderstanding of the diagnosis causing misclassification.

In the Health 2000 study in Finland, the prevalence of angina pectoris, myocardial infarction and stroke in men and in women aged 30 to 64 years was 3.1% and 1.1%, 2.2% and 0.3%, 1.2% and 0.6% respectively (Aromaa et al. 2002). In the same study population the prevalence of angina pectoris symptoms was 4.2% in men and 5.6% in women and the prevalence of previous myocardial infarction 3.6% in men and 0.8% in women in subjects aged 45 to 64 years (Kattainen et al. 2006). The prevalences of angina pectoris, myocardial infarction and cerebrovascular disease in men and in women were 4.1% and 2.4%, 2.6% and 0.4%, 2.2% and 2.5% respectively in our population. If somewhat different age groups and definition of cerebrovascular disease are taken into consideration our prevalences are quite similar with those in the Health 2000 study supporting the reliability of our data.

Up to 5% of men and 2.5% of women aged 60 years and over have symptoms of intermittent claudication and the prevalence of peripheral arterial disease is

markedly higher when sensitive tests are used to make the diagnosis (Weitz et al. 1996) In an earlier study in Finland, according to a structured interview the prevalence of intermittent claudication was 1.9% in men aged 40 to 49 years and 4.6% in men aged 50 to 59 years. The prevalence was 1.6% and 2.8% in women respectively. (Reunanen et al. 1982) These prevalences are quite close to our estimates. The prevalence of peripheral occlusive arterial disease was 1.0% in 40-year-old men and 4.4% in 50-year-old men and 1.4% and 4.4% in women in corresponding age cohorts in our population. However, a prevalence of self-reported peripheral arterial disease diagnosed by a doctor in our study is not totally comparable with the prevalence of claudication reported by Reunanen et al. (1982). The majority of men and women with peripheral arterial disease diagnosed by ankle-brachial index do not have symptoms of claudication (McDermott 2006). Asymptomatic disease is not usually diagnosed and it is, therefore, probable that self-reported prevalence of peripheral arterial disease is close to the prevalence of symptoms. The prevalence of peripheral arterial disease increases with age and a recent Finnish study reported a prevalence of 22% among 90-year-old individuals while 85% of them had asymptomatic disease (Suominen et al. 2008). The Edinburgh Artery Study estimated that 8% of population has significant asymptomatic peripheral arterial disease in the age group from 55 to 74 years (Fowkes et al. 1991). Asymptomatic peripheral arterial disease may be more often diagnosed among subjects with than among subjects without varicose veins because often their lower extremities have been examined by a doctor and, in addition to venous disorder, usually arterial disease has also been considered.

In our study population, 17 % of those with arterial disease reported more than one manifestation i.e. had polyvascular disease. Symptomatic polyvascular disease was also common in the REACH Registry; 16% of patients with coronary artery disease, cerebrovascular disease or peripheral arterial disease had symptomatic involvement of 1 or 2 other arterial disease manifestations (Bhatt et al 2006).

We found an association between arterial disease and varicose veins based on prevalence and on incidence. Our follow-up results with incidences indicate that the association is mostly due to an association between varicose veins and peripheral occlusive arterial disease and less to an association between varicose veins and cerebrovascular disease. There seems to be only a weak, if any, positive association between varicose veins and ischemic heart disease. Our results on varicose veins and arterial disease are more or less consistent with the follow-up studies by Brand et al. (1988) and by Ducimetiere et al. (1981) who reported increased risk of intermittent claudication in those with varicose veins compared to others, but we could not demonstrate significantly increased risk of coronary heart disease as they did. Our

results on ischemic heart disease and varicose veins are not consistent with the results by Scott et al. (2004) who in a follow-up study reported a reduced risk of coronary heart disease.

The Framingham Study concluded that varicose veins are probably not independently atherogenic, but that the occurrence of varicose veins may be indicative of an atherogenic risk profile, primarily coexistent inactivity, obesity and hypertension (Brand et al. 1988). We found the same causal direction i.e. increased risk of arterial disease in those with varicose veins. However, in our study, physical inactivity, obesity and hypertension were taken into consideration as potential common causes of varicose veins and arterial disease by adjusting in the multivariate model but the association could not have been due to them. In addition, we adjusted for the confounding effect of smoking but we could not adjust for the effect of cholesterol. However, according to earlier cross-sectional studies, cholesterol is not strongly associated with varicose veins (Ducimetiere et al. 1981, Brand et al. 1988, Komsuoglu et al. 1994, Sisto et al. 1995) and, moreover, a follow-up study reported increased risk of varicose veins in those with lower cholesterol (Scott et al. 2004).

One proposed explanation for the association between varicose veins and arterial disease is coexistent disturbance in the fibrinolytic system (Ducimetiere et al. 1981, De Backer 1997). In our study, the observed association between varicose veins and arterial disease was similar in the sub-population without previous deep vein thrombosis.

Hypertension. There was probably some underdiagnosis of hypertension in our study population. At the time of the study, the statistics of the National Public Health Institute showed the self-reported prevalence of hypertension to be 20–25% in the corresponding age-groups (Berg et al. 1990). The prevalence of hypertension was 28% in men and 24% in women aged 30 to 64 years according to the interview in the more recent study, Health 2000, in Finland (Aromaa and Koskinen 2004). In another study by the National Public Health Institute in Finland, Finriski 2002, 35% of the study population aged 25 to 64 years reported that they had ever had elevated blood pressure, but only 13% of men and 11% of women had medication for hypertension (Laatikainen et al. 2003). Mean systolic blood pressure and the prevalence of hypertension have decreased significantly in recent decades in Finland. At the same time the proportion of subjects with hypertension who are unaware of their condition has also decreased markedly. (Kastarinen et al. 1998, Nissinen et al. 2004) Therefore, the prevalence of hypertension may rather have increased in the questionnaire surveys. The somewhat low prevalence of hypertension in our study is probably partly due to subjects' unawareness of their elevated blood pressure at the time of the study. In addition, the attitude towards elevated blood pressure may have become more

demanding in health care and people are well-informed about the risks of hypertension. Blood pressure may be measured and hypertension diagnosed more frequently nowadays than two decades ago.

We could not find any association between varicose veins and hypertension, which is consistent with cross-sectional studies (Hirai et al. 1990, Franks et al. 1992, Komsuoglu et al. 1994, Sisto et al. 1995, Canonico et al. 1998, Kroeger et al. 2004) and with a case-control study by Scott et al. (1995). The latter study reported less prevalent hypertension in subjects with varicose veins than in others in univariate analysis but, however, it seemed to be age-related and adjusting for age removed the effect. Abramson et al. (1981) reported somewhat lower diastolic blood pressure in women with varicose veins than in women without varicose veins. Cross-sectional results by Brand et al. (1988) showed higher systolic blood pressure and cross-sectional results by Ducimetiere et al. (1981) higher diastolic blood pressure in those with than in those without varicose veins. A cross-sectional study reported less venous disease in those with hypertension than in those without (Criqui et al. 2007). The only existing longitudinal study on hypertension and varicose veins reported lower systolic blood pressure in subjects with varicose veins than in those without varicose veins (Scott et al. 2004). It is likely that any causal relations between hypertension and varicose veins are minor or non-existent.

Congestive heart failure. The symptoms of congestive heart failure are non-specific and intermittent and the diagnosis is complex. Edema in the ankles and legs is a symptom of both congestive heart failure and varicose veins, making the diagnostics challenging and possibly leading to some underdiagnosis or overdiagnosis of these diseases. Patients may not be aware of their condition or they may confuse other heart diseases with congestive heart failure. This may impair the accuracy of self-reporting, as shown in earlier studies (Heckbert et al. 2004, Okura et al. 2004). Self-reports concerning congestive heart failure have usually led rather to some overdiagnosis (Heckbert et al. 2004, Okura et al. 2004). In the Health 2000 study (Aromaa and Koskinen 2004) the prevalence of self-reported heart failure was 1.4% in men and 1.1% in women aged 30–64 years. The prevalence of heart failure based on doctor's opinion was at lower 0.5% in men and 0.2% in women, but these low prevalence estimates are probably largely due to youngest subjects because in subjects aged 65 years and over the corresponding prevalence rates were 4.8% and 8.7% respectively. In our population the prevalence of congestive heart failure increased with age from 0.7% in the youngest cohort to 5.3% in the oldest cohort. Therefore, the prevalence (2.3% in men and 2.2% in women) in our population appears to be realistic. In addition, arterial disease and hypertension were predictors of congestive heart failure

in our population, as established in earlier studies, suggesting that the misclassification cannot be serious.

We found that those with varicose veins have higher risk of congestive heart failure than those without varicose veins. Consistent with our results, the only existing follow-up study, the Framingham Study, showed higher incidence of congestive heart failure in those with varicose veins than in others although the result in the USA was not significant (Brand et al. 1988). Our prevalence results could not show a significant association between varicose veins and congestive heart failure, nor could the cross-sectional study by Abramson et al. (1981) or by Komsuoglu et al. (1994) find any association between these two conditions. Therefore, the non-association results may rather be due to methodological deficiencies including cross-sectional setting. Given that there may be an association between varicose veins and arterial disease (Ducimetiere et al. 1981, Brand et al. 1988) and that arterial disease, especially myocardial infarction, is a risk factor for congestive heart failure (Kenchaiah et al. 2004), it could be postulated that arterial disease explains the increased risk of congestive heart failure in those with varicose veins compared to those without. In our study, however, only a minor part of the increased risk of congestive heart failure in those with varicose veins was accounted for by arterial disease. Deep vein thrombosis was also considered a potential confounding factor but it had only a minor effect on the results on the association between varicose veins and congestive heart failure. Therefore, it seems credible that those with varicose veins have an increased risk of congestive heart failure that cannot be accounted for by other risk factors of heart failure (sex, age, overweight, arterial disease and hypertension).

The direction of the association. We found an association between varicose veins and arterial disease and between varicose veins and congestive heart failure. Our results indicated the strongest association between varicose veins and cardiovascular disease when varicose veins preceded arterial disease or congestive heart failure, i.e. varicose veins were the exposure and arterial disease or congestive heart failure the outcome. Only the causal direction from cerebrovascular disease as exposure and varicose veins as outcome was stronger than the reverse one. Therefore, varicose veins in middle-age may indicate subsequent cardiovascular disease.

As varicose veins as such probably do not cause arterial disease or congestive heart failure, it is possible that varicose veins, arterial disease and congestive heart failure may have some common etiology or pathophysiology. We could not identify common etiological factors to explain the association. Therefore, common pathophysiological factors, affecting the entire vascular wall possibly through matrix metalloproteinases or activation of coagulation or inflammatory pathways, may explain the association observed. For the time being, no direct observations have been

reported on such relationships. Because the strength of the association, measured by IORs, was stronger from varicose veins to arterial disease and to congestive heart failure than from arterial disease or congestive heart failure to varicose veins, it is likely that varicose veins is an early and cardiovascular disease a late manifestation of such a process.

7. Summary and Conclusions

The incidence of varicose veins was studied with a mailed questionnaire in a general population during a five-year follow-up to assess the appearance of new varicose veins in a middle-aged population in the city of Tampere, Finland. The study population included three complete age-cohorts (40-, 50- and 60-year-olds at entry), altogether 6,874 men and women. The effects of sex, age, overweight and education on the occurrence of varicose veins were assessed to ascertain their role in the etiology of varicose veins. The association between varicose veins and cardiovascular diseases was estimated with incident cases during follow-up to establish the direction of the effect and to make inferences if these diseases could have common factors in etiology or in pathophysiology.

The incidence of varicose veins was 13.5 per 1,000 person years. Women had higher risk of varicose veins than men, but there was no consistent age effect. Men and women aged 50–55 years reported more new varicose veins than subjects aged 40–45 years or 60–65 years, and the result was statistically significant in women. Overweight seemed to be a significant risk factor of varicose veins. Level of education could not be confirmed as a risk factor of varicose veins.

There was an association between varicose veins and arterial disease. The association was strongest when varicose veins were assumed as an exposure and arterial disease as an outcome. The association was independent of hypertension, smoking and physical activity, and the impact of overweight was marginal. There was also an association between varicose veins and congestive heart failure. People with varicose veins reported significantly more new congestive heart failure than others. There was no association between varicose veins and hypertension. The results indicate that varicose veins may be an early and arterial disease and congestive heart failure late consequences of the common etiology or pathophysiology. However, the known risk factors of arterial disease (overweight, hypertension, smoking, physical inactivity) and congestive heart failure (overweight, hypertension, arterial disease) are not likely to be those common causes (etiological components) as the results were adjusted for their confounding effect.

In conclusion,

1. Incidence of varicose veins was assessed in a middle-aged population and it was 13.5 per 1,000 person-years. This indicates that new varicose veins also occur in middle-aged population.

2. The effects of sex, age, overweight and education on the appearance of varicose veins were studied. Female sex and overweight were found to be risk factors of varicose veins. Higher age and level of education were not significant risk factors.

3. Associations between varicose veins and arterial disease and between varicose veins and congestive heart failure were found. The causal direction from varicose veins to arterial disease and to congestive heart failure was stronger than from cardiovascular diseases to varicose veins and, therefore, they possibly have some common etiology or pathophysiology in which varicose veins precede arterial disease and congestive heart failure. However, no common etiological components of varicose veins and cardiovascular diseases explaining the observed association could be found.

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10. Appendices

Questionnaires

QUESTIONNAIRE ON CIRCULATORY PROBLEMS IN THE LOWER EXTREMITIES (1989) (Translated from Finnish)

SURNAME_____ (FORMER NAME_____)

FORENAME_____ 1.SOCIAL SECURITY NUMBER __ __ __ - ____

2.GENDER [ ] male [ ] female

3.PROFESSION_____ RETIRED [ ]

ADDRESS _____

4.Weight _____ kg Height _____ cm

5.Do any of your closest relatives (parents, grandparents or siblings) have varicose veins?
[ ] NO / [ ] DON'T KNOW
[ ] YES, who _____

6.Have you ever given birth?
[ ] NO / [ ] YES, how many times? ____ , year of the first birth ____.

7.Have you ever used contraceptive pills?
[ ] NO / [ ] YES, how many years? ____.

DIET AND HABITS:

8.What kind of milk do you drink?
[ ] whole milk / [ ] semi-skimmed milk / [ ] skimmed milk /
[ ] other, what kind? _____
How many glasses (2dl) of milk daily? _____ glasses
Do you use (e.g. in food and on bread) [ ] BUTTER /[ ] MARGARINE /[ ] VEGETABLE OIL
[ ] NONE OF THESE
For how many times each week do you eat meals of meat or sausages? _____ times

How many slices of bread do you eat each day? _____ slices

9.Have you ever smoked for longer than one year?

[ ] NEVER
[ ] I HAVE STOPPED SMOKING, at what age did you start ____ and stop ____?
[ ] I NOW SMOKE; -at what age did you start? _____
-do you smoke [ ] cigarettes or [ ] cigars
[ ] pipe
-how much each day? ____ cigarettes/cigars/pipefuls

10.Do you use alcohol?

[ ] NOT AT ALL OR OCCASIONALLY
[ ] YES, how much per week
beer in bottles (1/3 l) ____
wine in bottles (3/4 l) ____ or in glasses (12 cl) ____
spirits in bottles (1/2 l) ____ or in glasses (4 cl) ____

11.Do you get any physical exercise when not at work?
[ ] NOT AT ALL / [ ] OCCASIONALLY / [ ] EACH WEEK / [ ] SEVERAL TIMES A WEEK,
which exercise?_____

12.Which of the following applies to the posture normally assumed in your main (past or present) occupation?

[ ] SITTING WITH LESS THAN ½ HOUR OF STANDING IN A DAY
[ ] MAINLY SITTING, WITH LESS THAN HALF THE WORKING DAY SPENT STANDING
[ ] STANDING FOR OVER HALF OF THE WORKING DAY
[ ] OTHER, what posture _____

IF YOU WORKED ON YOUR FEET, DID YOU WORK IN A STATIC STANDING POSTURE?
[ ] NO
[ ] YES, for how many hours daily (on average)? _____ hours
HOW MANY YEARS? ____ years

PREVIOUS HEALTH:

13.Have you ever suffered conditions requiring medical care?

[ ] NO

[ ] YES, which of these?

-diabetes [ ] NO [ ] YES, since _____
-high blood pressure [ ] NO [ ] YES, since _____
-cardiac infarct [ ] NO [ ] YES, since _____
-angina pectoris [ ] NO [ ] YES, since _____
-insufficiency of the heart [ ] NO [ ] YES, since _____
-pulmonary diseases [ ] NO [ ] YES, which disease _____
-superficial thrombosis in lower extremities [ ] NO [ ] YES, since _____
in which leg? [ ] right/[ ]left
-deep venous thrombosis in lower extremities [ ] NO [ ] YES, since _____
in which leg? [_] right/[_]left
-pulmonary embolism [ ] NO [ ] YES, since _____
-sciatica or other back problems [ ] NO [ ] YES, since _____
-renal diseases [ ] NO [ ] YES, since _____
-fractures in lower extremities [ ] NO [ ] YES, when _____
in which leg? [ ] right/[ ]left
in which part of the leg?_____
-major contusions with prolonged healing [ ] NO [ ] YES, when _____
in lower extremities in which leg? [ ] right/[ ]left
-problems in arterial circulation of the legs [ ] NO [ ] YES, since _____
in which leg? [ ] right/[ ]left
-cerebral circulatory problems [ ] NO [ ] YES, since _____
-ulceration in leg [ ] NO [ ] YES, since _____
in which leg? [ ] right/[ ]left
-other chronic or severe disease, which disease? _____, since _____

14.Have you had a frequent or prolonged experience of the following conditions? (In which leg?)

-sensation of heavy leg(s) in the afternoon [ ] NO [ ] YES -> [ ]RIGHT/[ ]LEFT
-pain or prickly sensation in leg(s) during the daytime [ ] NO [ ] YES -> [ ]RIGHT/[ ]LEFT
-swelling of ankle or leg(s) [ ] NO [ ] YES -> [ ]RIGHT/[ ]LEFT
-swelling of thigh(s) [ ] NO [ ] YES -> [ ]RIGHT/[ ]LEFT
-considerable leg-pain while standing [ ] NO [ ] YES -> [ ]RIGHT/[ ]LEFT
-cold legs [ ] NO [ ] YES -> [ ]RIGHT/[ ]LEFT
-numbness in leg(s) [ ] NO [ ] YES -> [ ]RIGHT/[ ]LEFT
-cramps in leg(s) [ ] NO [ ] YES -> [ ]RIGHT/[ ]LEFT
-permanent change in the color of the skin in ankle or leg [ ] NO [ ] YES -> [ ]RIGHT/[ ]LEFT
-intermittent claudication (explained) [ ] NO [ ] YES -> [ ]RIGHT/[ ]LEFT
-lower-extremity pain while at rest [ ] NO [ ] YES -> [ ]RIGHT/[ ]LEFT
-longstanding ulceration or necrosis in foot or leg [ ] NO [ ] YES -> [ ]RIGHT/[ ]LEFT
-if any of the symptoms have occurred, does it help when you
elevate the legs? [ ] NO [ ] YES
let the legs hang? [ ] NO [ ] YES
-any other symptom?_____
_____

15.Are you on permanent medication?

[ ] NO

[ ] YES, for/medication is

[ ] diabetes
[ ] hypertension
[ ] coronary disease
[ ] arrhythmia
[ ] insufficiency of the heart
[ ] pulmonary disease
[ ] coagulation
[ ] aid to the circulation
[ ] pain
[ ] constipation
[ ] other disease, for which _____
[ ] cortisone (tablets or injections)
[ ] sex hormones

Names of the drugs:_____
_____
_____
_____
_____
_____
_____

16.Do you now have or have you ever had <u>varicose veins</u> in the lower extremities?

(Varicose veins are clearly visible, dilated, tortuous and possibly prominent subcutaneous veins of the lower extremities).

[ ] NO
[ ] DON'T KNOW
[] YES

Where do the varicose veins exist? [ ] in left thigh / [ ] in left leg / [ ] in right thigh / [ ] in right leg
For how many years have they existed?_____ years.
When did they appear (for example after trauma/childbirth/other)?

_____

Do you now have varicose veins?	[ ] NO	[ ] YES
Are the varicose veins a cosmetic problem?	[ ] NO	[ ] YES

Have you been operated on for varicose veins?
[ ] NO
[ ] YES in left ___ times, years_____
in right ___ times, years_____

Have you received injections for varicose veins?
[ ] NO
[ ] YES in left ___ times, years_____
in right ___ times, years_____

Have you been treated for varicose veins with <u>compressive stocking</u> for more than one month?
[ ] NO
[ ] YES, for_____ months

Have you been treated for varicose veins with <u>support stocking</u>?
[ ] NO
[ ] YES, for_____ months

Have varicose veins reappeared after treatment?
[ ] NO
[ ] YES,_____ months/_____ years after the treatment.

Do you now need treatment for varicose veins?
[ ] NO [ ] YES [_] DON'T KNOW

17.Have you been operated on for any other disease?
[] NO
[] YES, which disease and when:

year _____ which operation _____

year _____ which operation _____

year _____ which operation _____

##########
Please check that you have answered all questions. A stamped and addressed envelope is included. Mail the questionnaire soon. Thank you!
##########

1989

TUTKIMUSKAAVAKE VERENKIERTOHAIRIÖISTA ALARAAJOISSA

****

SUKUNIMI _____ (ENTINEN _____)

ETUNIMET _____ **1.HENKILÖTUNNUS** __ __ __ -____
(esim.sairausvakuutuskortista)

2.SUKUPUOLI [] mies [] nainen ⌊_⌋

3.AMMATTI _____ ELÄKKEELLÄ [] ⌊_⌋⌊_⌋⌊_⌋
(nykyinen tai entinen pitkäaikainen)

OSOITE _____

4.Painonne ___ kiloa **Pituutenne** ___ senttimetriä ⌊_⌋⌊_⌋⌊_⌋

5.Onko lähisukulaisillanne (vanhemmat, isovanhemmat, sisarukset) suonikohjuja? ⌊_⌋⌊_⌋⌊_⌋
[] EI / [] EN TIEDÄ/
[] KYLLÄ,kenellä
(sukulaisuuden laatu, esim. isällä) _____ ⌊_⌋

6. Onko Teillä ollut synnytyksiä?
[] EI / [] KYLLÄ, synnytyksiä ___ kappaletta,ensimmäinen vuonna _____. ⌊_⌋⌊_⌋

7. Oletteko milloinkaan käyttänyt ehkäisypillereitä? ⌊_⌋⌊_⌋
[] EN /[] KYLLÄ, montako vuotta ___ ⌊_⌋⌊_⌋

RAVINTOAINEET JA ELINTAVAT:

8.Minkälaista maitoa käytätte?
[] Kulutusmaitoa/ []Kevytmaitoa/ [] Rasvatonta maitoa/ ⌊_⌋
[] Muuta,mitä_____
Montako lasillista (2 dl) maitoa käytätte päivässä? _____lasillista. ⌊_⌋⌊_⌋
Käytättekö ruuissanne (mm.leivässä) [] VOITA /[] MARGARIINIA/[] KASVISÖLJYÄ
[] EN KÄYTÄ NIITÄ ⌊_⌋
Montako kertaa viikon aikana syötte liha- tai makkararuokia? ____ kertaa. ⌊_⌋⌊_⌋

Montako leipäviipaletta käytätte päivässä? __ viipaletta. ⌊_⌋⌊_⌋

9.Oletteko tupakoinut säännöllisesti yli vuoden ajan elämässänne? ⌊_⌋
[] EN OLE MILLOINKAAN
[] OLEN NYT LOPETTANUT, minkä ikäisenä aloititte___ ja lopetitte___? ⌊_⌋⌊_⌋
[] TUPAKOIN; -minkä ikäisenä aloititte? _____ ikäisenä. ⌊_⌋⌊_⌋
-mitä tupakoitte [] savukkeita tai [] sikareita
[] piippua ⌊_⌋
-paljonko tupakoitte päivässä? ___ savuketta/sikaria/piipullista ⌊_⌋⌊_⌋

10.Käytättekö alkoholipitoisia juomia?

[] EN LAINKAAN TAI SATUNNAISESTI ⌊_⌋
[] KYLLÄ,paljonko seuraavista viikossa
olutta ____ pulloa(1/3 l)
viiniä ____ pulloa(3/4 l) tai ____lasillista (12 cl) ⌊_⌋⌊_⌋⌊_⌋
viinaa ____ pulloa (½ l) tai ____lasillista (4 cl)

11.Harrastatteko vapaa-aikana liikuntaa?

[] EN LAINKAAN/ [] SATUNNAISESTI/[] VIIKOITTAIN/[] USEITA KERTOJA VIIKOSSA, ⌊_⌋
mitä_____

12.Eniten tekemänne työ on/oli pääasiassa mielestänne

[] ISTUMATYÖTÄ, JOSSA TYÖPÄIVÄN AIKANA LIIKUNTAA TAI SEISOMISTA VÄHÄN (alle½t)
[] ISTUMATYÖTÄ, JOSSA TYÖPÄIVÄN AIKANA SEISOMISTA ALLE PUOLET AJASTA
[] YLI PUOLET TYÖPÄIVÄSTÄ SEISOMATYÖTÄ, ISTUMISTA AJOITTAIN TAI EI LAINKAAN
[] MUUTA KUIN EDELLÄ,minkälaista_____

JOS TEITTE SEISOMATYÖTÄ, OLIKO SEISOMATYÖSSÄ PAIKALLAANOLOA?
[]EI
[]KYLLÄ,montako tuntia päivässä keskimäärin? ___ tuntia.
MONTAKO VUOTTA TEITTE TÄTÄ TYÖTÄ? _____ vuotta.

AIKAISEMPI TERVEYDENTILANNE:

13.Onko Teillä esiintynyt pitempää lääkärinhoitoa vaatineita sairauksia?

[] EI

[] KYLLÄ (vastaa seuraaviin; rastita EI ruutu, jos kysyttyä sairautta ei ole Teillä ollut, KYLLÄ vaihtoehdoissa vastaa myös lisäkysymyksiin)

ONKO TEILLÄ OLLUT TAI ONKO NYT

- sokeritautia [] EI [] KYLLÄ,milloin alk._____
- kohonnutta verenpainetta [] EI [] KYLLÄ,milloin alk._____
- sydäninfarktia [] EI [] KYLLÄ,milloin _____
- sydämen sepelvaltimosairautta (=angina pectoris) [] EI [] KYLLÄ,milloin alk._____
- sydämen vajaatoimintaa [] EI [] KYLLÄ
- hengityselinten sairautta [] EI [] KYLLÄ,mikä _____
- alaraajan pinnallista laskimotukosta [] EI [] KYLLÄ,milloin _____ kumpi jalka []oikea/ []vasen
- alaraajan syvää laskimotukosta [] EI [] KYLLÄ,milloin _____ kumpi jalka []oikea/ []vasen
- keuhkoveritulppaa [] EI [] KYLLÄ,milloin _____
- selkäsairautta tai iskiasta [] EI [] KYLLÄ,milloin _____
- munuaissairautta [] EI [] KYLLÄ
- alaraajojen murtumia [] EI [] KYLLÄ,milloin_____ kumpi jalka []oikea/ []vasen
  missä kohdassa? _____
- alaraajojen ruhjeitten aiheuttamia pitkäaikaisia vammoja? [] EI [] KYLLÄ,milloin_____ kumpi jalka []oikea/ []vasen
- alaraajojen valtimoverenkiertohäiriöitä [] EI [] KYLLÄ,milloin alk. _____ kumpi jalka []oikea/ []vasen
- aivoverenkiertohäiriöitä [] EI [] KYLLÄ,milloin _____
- säärihaavaa [] EI [] KYLLÄ,milloin alk._____ kumpi jalka []oikea/ []vasen
- muu pitkäaikainen tai vaikea sairaus, mikä_____
  milloin_____

14.Onko Teillä esiintynyt useamman kerran tai pitkäaikaisesti alaraajoissa jokin seuraavista (jos vastaat KYLLÄ, rastita kummassa jalassa)

- jalka tuntuu raskaalta iltaa kohden [] EI [] KYLLÄ -[]OIKEA/[]VASEN
- särkyä, pistelyä päivän mittaan [] EI [] KYLLÄ -[]OIKEA/[]VASEN
- turvotusta nilkan tai säären alueella [] EI [] KYLLÄ -[]OIKEA/[]VASEN
- turvotusta reiden alueella [] EI [] KYLLÄ -[]OIKEA/[]VASEN
- aina seistessä ilmenevä säären voimakas kipu [] EI [] KYLLÄ -[]OIKEA/[]VASEN
- jalkojen palelua [] EI [] KYLLÄ -[]OIKEA/[]VASEN
- jalkojen puutumista [] EI [] KYLLÄ -[]OIKEA/[]VASEN
- suonenvetoa jaloissa [] EI [] KYLLÄ -[]OIKEA/[]VASEN
- tummanruskea ja pysyvä värimuutos nilkan tai säären ihossa [] EI [] KYLLÄ -[]OIKEA/[]VASEN
- katkokävelyoire (kävellessä pysähtymään pakottava kipu pohkeessa tai pakarassa) [] EI [] KYLLÄ -[]OIKEA/[]VASEN
- levossa ollessa kipua jalassa [] EI [] KYLLÄ -[]OIKEA/[]VASEN
- pitkäaikainen haavauma tai kuolio jalkaterän tai säären alueella [] EI [] KYLLÄ -[]OIKEA/[]VASEN
- jos jaloissa on joitakin kysytyistä oireista,
  helpottaako jalan kohottaminen oireita? [] EI [] KYLLÄ
  helpottaako jalan riiputtaminen oireita? [] EI [] KYLLÄ
- jokin muu oire, mikä_____
  _____

15.Käytättekö säännöllistä lääkitystä?

[]EN

[]KYLLÄ, mihin sairauteen tai minkä lääkeaineryhmän lääkkeitä?

[] sokeritautiin
[] verenpaineeseen
[] sepelvaltimotautiin
[] rytmihäiriöihin
[] sydämen vajaatoimintaan
[] hengityselinten sairauteen
[] veren hyytymiseen
[] verenkierron parantamiseen
[] särkyihin (mukaanlukien mm. Aspirin)
[] ummetukseen
[] muuhun sairauteen, mihin _____
[] kortisonia (tabletteina tai pistoksina)
[] nais- tai miessukuhormonia

Lääkkeiden nimet:_____
_____
_____
_____
_____
_____
_____

16.Onko Teillä nyt tai onko ollut alaraajoissa suonikohjuja?

(Suonikohjuilla tarkoitetaan selvästi näkyvää, laajentunutta, mutkittelevaa ja mahdollisesti pullottavaa alaraajan ihonalaista laskimosuonta).

[] EI(siirry kys.17.)
[] EN TIEDÄ
[] ON NYT TAI ON OLLUT)vastatkaa seuraaviin:
Millä kohdalla? []vasen reisi/ []vasen sääri/ []oikea reisi/ []oikea sääri ___
Kuinka kauan kohjut ovat olleet? _____vuotta. ___
Missä yhteydessä kohjut tulivat (esim. vamman/raskauden/muun jälkeen)?

_____

Onko Teillä tällä hetkellä suonikohjuja? [] EI [] KYLLÄ ___
Onko kohjuista Teille ulkonäöllistä haittaa? [] EI [] KYLLÄ ___

Onko Teitä leikattu suonikohjujen takia?
[] EI
[] KYLLÄ vasen jalka __ kertaa,vuosina _____ ___
oikea jalka __ kertaa,vuosina _____ ___
Onko suonikohjuja hoidettu lääkeainetta ruiskuttamalla?
[] EI
[] KYLLÄ vasen jalka __ kertaa, vuosina _____ ___
oikea jalka __ kertaa, vuosina _____ ___
Onko suonikohjuihin käytetty puristussukkahoitoa säännöllisesti yli kuukauden ajan?(ei tarkoiteta ns. tukisukkaa)
[]EI
[]KYLLÄ,___ kk ajan ___

Onko suonikohjuihin käytetty ns. tukisukkaa?
[] EI
[] KYLLÄ, ___ kk ajan. ___

Ovatko suonikohjut uusiutuneet hoitojen (leikkaukset,ruiskutukset ym.) jälkeen?
[]EIVÄT
[]KYLLÄ, kuinka pian:_____kuukautta tai ____ vuotta hoidon jälkeen ____

Tarvitsetteko mielestänne tällä hetkellä hoitoa suonikohjujen takia?
[] EN []KYLLÄ [] EN OSAA SANOA ___

17.Onko Teitä leikattu muun sairauden takia?
[] EI
[] KYLLÄ, minkä ja milloin:

v._____ leikkaus_____

v._____ leikkaus_____

v._____ leikkaus_____
(jatka tarvittaessa)

##########

OLKAA HYVÄ JA TARKISTAKAA, ETTÄ VASTASITTE KAIKKIIN KOHTIIN OHJEIDEN MUKAISESTI. SULKEKAA KYSYMYSLOMAKE (4 SIVUA) MUKANA SEURANNEESEEN OSOITTEELLA VARUSTETTUUN KIRJEKUOREEN (POSTIMAKSU ON MAKSETTU) JA JÄTTÄKÄÄ SE POSTIIN PIAN. KIITOS!

##########

QUESTIONNAIRE ON CIRCULATORY PROBLEMS IN THE LOWER EXTREMITIES (1994) (Translated from Finnish)

SURNAME_____ FORENAME_____ GENDER [_] male [_] female

DATE OF BIRTH OR SOCIAL SECURITY NUMBER __ __ __ - ____

Address _____
Profession _____

[_] senior clerical worker
[_] clerical worker
[_] worker
[_] other _____

Education:
[_] University
[_] College
[_] Vocational school
[_] High school
[_] Comprehensive school
[_] Other _____

Weight _____ kg and Height _____ cm

DIET AND HABITS:

What kind of milk do you drink?
[_] WHOLE MILK
[_] SEMI-SKIMMED MILK
[_] SKIMMED MILK
[_] OTHER, WHAT KIND? _____
How many glasses (2dl) of milk daily? _____ GLASSES
Do you use (e.g. in food and on bread)
[_] BUTTER
[_] MARGARINE
[_] VEGETABLE OIL
[_] NONE OF THESE

For how many times each week do you eat meals of meat or sausages? _____ times
How many slices of bread do you eat each day? _____ slices

Have you ever smoked for longer than one year?
[_] NEVER
[_] I HAVE STOPPED SMOKING, at what age did you start ____ and stop ____?
[_] I NOW SMOKE, at what age did you start? _____
Do you smoke
[_] CIGARETTES, [_] CIGARS OR [_] PIPE ?
How much each day? ____ cigarettes/cigars/pipefuls

Do you use alcohol?
[_] NOT AT ALL OR OCCASIONALLY
[_] YES, how much per week
beer in bottles (1/3 l) ____
wine in bottles (3/4 l) ____ or in glasses (12 cl) ____
spirits in bottles (1/2 l) ____ or in glasses (4 cl) ____

Women: Have you ever given birth?
[_] NO [_] YES, HOW MANY TIMES? ____ , YEAR OF THE FIRST BIRTH ____.

Women: Have you ever used contraceptive pills?
[_] NO
[_] YES, how many years? ____.
At what ages did you start using contraceptive pills? __ At what ages did you stop using contraceptive pills? __

Women: Have you ever used hormone replacement therapy?
[_] NO
[_] YES, how many years? ____.
At what ages did you start using contraceptive pills? __ At what ages did you stop using contraceptive pills? __

Which of the following applies to the posture normally assumed in your main (past or present) occupation?
[_] SITTING WITH LESS THAN ½ HOUR OF STANDING IN A DAY.
[_] MAINLY SITTING, WITH LESS THAN HALF THE WORKING DAY SPENT STANDING.
[_] STANDING FOR OVER HALF OF THE WORKING DAY.
[_] OTHER, what posture _____

How many years? ____ years
If you worked on your feet, did you work in a static standing posture?
[_] NO [_] YES, for how many hours daily (on average)? _____ hours

PREVIOUS HEALTH:

Have you ever suffered following conditions requiring medical care?
[_] NO
[_] YES, which of these?

-diabetes	[_] NO [_] YES, since _____
-high blood pressure	[_] NO [_] YES, since _____
-cardiac infarct	[_] NO [_] YES, since _____
-angina pectoris	[_] NO [_] YES, since _____
-insufficiency of the heart	[_] NO [_] YES, since _____
-pulmonary diseases	[_] NO [_] YES, which disease _____
-superficial thrombosis in lower extremities	[_] NO [_] YES, since _____ in which leg? [_] right/[_]left
-deep venous thrombosis in lower extremities	[_] NO [_] YES, since _____ in which leg? [_] right/[_]left
-pulmonary embolism	[_] NO [_] YES, since _____
-sciatica or other back problems	[_] NO [_] YES, since _____
-renal diseases	[_] NO [_] YES, since _____
-problems in arterial circulation of the legs	[_] NO [_] YES, since _____ in which leg? [_] right/[_]left
-cerebral circulatory problems	[_] NO [_] YES, since _____
-ulceration in leg	[_] NO [_] YES, since _____ in which leg? [_] right/[_]left

-other chronic or severe disease, which disease? _____, since _____

Have you had a frequent or prolonged experience of the following conditions during last month? (In which leg?)

-sensation of heavy leg(s) in the afternoon	[_] NO [_] YES -> [_]RIGHT/[_]LEFT
-pain or prickly sensation in leg(s) during the daytime	[_] NO [_] YES -> [_]RIGHT/[_]LEFT
-swelling of ankle or leg(s)	[_] NO [_] YES -> [_]RIGHT/[_]LEFT
-swelling of thigh(s)	[_] NO [_] YES -> [_]RIGHT/[_]LEFT
-considerable leg-pain while standing	[_] NO [_] YES -> [_]RIGHT/[_]LEFT
-cold legs	[_] NO [_] YES -> [_]RIGHT/[_]LEFT
-numbness in leg(s)	[_] NO [_] YES -> [_]RIGHT/[_]LEFT
-cramps in leg(s)	[_] NO [_] YES -> [_]RIGHT/[_]LEFT
-permanent change in the color of the skin in ankle or leg	[_] NO [_] YES -> [_]RIGHT/[_]LEFT
-intermittent claudication (explained)	[_] NO [_] YES -> [_]RIGHT/[_]LEFT
-lower-extremity pain while at rest	[_] NO [_] YES -> [_]RIGHT/[_]LEFT
-longstanding ulceration or necrosis in foot or leg	[_] NO [_] YES -> [_]RIGHT/[_]LEFT

[_] NONE OF THE ABOVEMENTIONED SYMPTOMS

Are you on permanent medication?
[_] NO
[_] YES, for/medication is

[_] diabetes
[_] hypertension
[_] coronary disease
[_] arrhythmia
[_] insufficiency of the heart
[_] pulmonary disease
[_] coagulation
[_] aid to the circulation
[_] pain
[_] constipation
[_] other disease, for which _____
[_] cortisone (tablets or injections)
[_] sex hormones

List the names of the drugs: _____
_____
_____
_____
_____
_____
_____
_____

Do you now have or have you ever had varicose veins in the lower extremities?

(Varicose veins are clearly visible, dilated, tortuous and possibly prominent subcutaneous veins of the lower extremities).
[_] NO
[_] DON'T KNOW
[_] YES
[_] YES, BUT NOT ANYMORE, BECAUSE THEY [_] HAVE BEEN OPERATED ON /[_] HAVE DISAPPEARED

Where do the varicose veins exist?
[_] in left thigh
[_] in left leg
[_] in right thigh
[_] in right leg

How old were you when varicose veins appeared? _____ years old

Are the varicose veins a cosmetic problem?
[_] NO [_] YES

Have you been operated on for varicose veins?
[_] NO [_] YES, how many times? _____, when? (years) _____

Where have you been operated on for varicose veins?
[_] in a regional hospital
[_] in Hatanpää City Hospital
[_] in Tampere University Hospital
[_] in another central hospital, which _____
[_] in a private hospital
[_] in another hospital, which_____

Have you received injections for varicose veins?
[_] NO [_] YES

Where have you received injections for varicose veins?

[_] in a regional hospital
[_] in Hatanpää City Hospital
[_] in Tampere University Hospital
[_] in another central hospital, which _____
[_] in a private hospital
[_] in another hospital, which_____

Have varicose veins reappeared after treatment?
[_] NO [_] YES

Do you now need treatment for varicose veins?
[_] NO [_] DON'T KNOW [_] YES,
What kind of treatment?
[_] counseling
[_] examination or treatment
[_] other, what? _____

Are you waiting for treatment for varicose veins?
[_] NO
[_] YES, [_] operation [_] other treatment

Have you been treated for varicose veins with compressive stocking for more than one month?
[_] NO [_] YES

Have you been treated for varicose veins with support stocking?
[_] NO [_] YES

Do you closest relatives (parents, grandparents or siblings) have varicose veins?
[_] NO [_] DON'T KNOW [_] YES, who _____

Have you been operated on for any other disease?
[_] NO
[_] YES, which disease and when:

year _____ which operation _____

year _____ which operation _____

year _____ which operation _____

##########
Please check that you have answered all questions. A stamped and addressed envelope is included. Mail the questionnaire soon. Thank you!
##########

1994

TUTKIMUSLOMAKE VERENKIERTOHÄIRIÖISTÄ ALARAAJOISSA

****

SUKUNIMI _____ **ETUNIMET** _____ **SUKUPUOLI** [_] mies [_] nainen

SYNTYMÄAIKA/SOTU (esim.sairausvakuutuskortista) __ __ __ -___

Osoitteenne _____

Ammattinne _____

Oletteko viimeisimmän ammattinne mukaisesti :
[_] YLEMPI TOIMIHENKILÖ
[_] ALEMPI TOIMIHENKILÖ
[_] TYÖNTEKIJÄ
[_] MUU, MIKÄ?_____

Koulutuksenne on
[_] YLIOPISTO TAI KORKEAKOULU
[_] OPISTOTASOINEN KOULUTUS
[_] AMMATTIKOULU TAI VASTAAVA
[_] LUKIO TAI OPPIKOULU
[_] KANSAKOULU,
[_] MUU, MIKÄ _____

Nykypainonne ___ kiloa ja **Pituutenne** ___ senttimetriä

RAVINTOAINEET JA ELINTAVAT:

Minkälaista maitoa käytätte?
[_] KULUTUSMAITOA
[_] KEVYTMAITOA
[_] RASVATONTA MAITOA/
[_] MUUTA,MITÄ_____
Montako lasillista (2 dl) maitoa käytätte päivässä? ____LASILLISTA.
Käytättekö ruuissanne (mm.leivässä)
[_] VOITA
[_] MARGARIINIA
[_] KASVISÖLJYÄ
[_] EN KÄYTÄ NIITÄ

Montako kertaa viikon aikana syötte liha- tai makkararuokia? ____ kertaa.
Montako leipäviipaletta käytätte päivässä? __ viipaletta.

Oletteko tupakoinut säännöllisesti yli vuoden ajan elämässänne?
[_] EN OLE MILLOINKAAN
[_] OLEN NYT LOPETTANUT, minkä ikäisenä aloititte___ ja lopetitte___?
[_] TUPAKOIN EDELLEEN; minkä ikäisenä aloititte? _____ Ikäisenä.
Mitä tupakoitte?
[_] SAVUKKEITA , [_] SIKAREITA VAI [_] PIIPPUA
Paljonko tupakoitte päivässä? ___ **savuketta/sikaria/piipullista**

Käytättekö alkoholipitoisia juomia?
[_] EN LAINKAAN TAI SATUNNAISESTI
[_] KYLLÄ,paljonko seuraavista viikossa
olutta ____ pulloa(1/3 l)
viiniä ____ pulloa(3/4 l) tai ____lasillista (12 cl)
viinaa ____ pulloa (½ l) tai ____lasillista (4 cl)

Naiset: Onko **Teillä ollut synnytyksiä?**
[_] EI [_] KYLLÄ, SYNNYTYKSIÄ ___ KAPPALETTA, ENSIMMÄINEN VUONNA _____.

Naiset: Oletteko milloinkaan käyttänyt ehkäisypillereitä ?
[_] EN
[_] KYLLÄ, montako vuotta ___.
Minkä ikäisenä aloititte pillerit? ____Vuotiaana. Minkä ikäisenä lopetitte ne? ____Vuotiaana.

Naiset: Oletteko milloinkaan käyttänyt naissukuhormonia ?
[_] EN
[_] KYLLÄ, montako vuotta ___.
Minkä ikäisenä aloititte ? ____Vuotiaana. Minkä ikäisenä lopetitte ? ____Vuotiaana.

Eniten tekemänne työ on/oli pääasiassa mielestänne
[_] ISTUMATYÖTÄ, JOSSA TYÖPÄIVÄN AIKANA LIIKUNTAA TAI SEISOMISTA VÄHÄN (alle ½ t)
[_] ISTUMATYÖTÄ, JOSSA TYÖPÄIVÄN AIKANA SEISOMISTA ALLE PUOLET AJASTA
[_] YLI PUOLET TYÖPÄIVÄSTÄ SEISOMATYÖTÄ, ISTUMISTA AJOITTAIN TAI EI LAINKAAN
[_] MUUTA KUIN EDELLÄ,minkälaista_____

Montako vuotta teitte tätä ilmoittamaanne työtä? _____ vuotta.
Jos teitte seisomatyötä, oliko seisomatyössänne paikallaanoloa?
[_]EI [_]KYLLÄ, montako tuntia päivässä keskimäärin? ___ tuntia.

AIKAISEMPI TERVEYDENTILANNE:

Onko Teillä esiintynyt allalueteltuja, pitempää lääkärinhoitoa vaatineita sairauksia?
[_] EI
[_] KYLLÄ (vastatkaa seuraaviin; rastittakaa EI ruutu, jos kysyttyä sairautta ei ole Teillä ollut, KYLLÄ vaihtoehdoissa vastatkaa myös lisäkysymyksiin)

ONKO TEILLÄ OLLUT TAI ONKO NYT

- sokeritautia [_] EI [_] KYLLÄ,milloin alk._____
- kohonnutta verenpainetta [_] EI [_] KYLLÄ,milloin alk._____
- sydäninfarktia [_] EI [_] KYLLÄ,milloin _____
- sydämen sepelvaltimosairautta (=angina pectoris) [_] EI [_] KYLLÄ,milloin alk._____
- sydämen vajaatoimintaa [_] EI [_] KYLLÄ, -"- _____
- hengityselinten sairautta [_] EI [_] KYLLÄ,mikä _____
- alaraajan pinnallista laskimotukosta [_] EI [_] KYLLÄ,milloin _____ kumpi jalka [_]oikea/ [_]vasen
- alaraajan syvää laskimotukosta [_] EI [_] KYLLÄ,milloin _____ kumpi jalka [_]oikea/ [_]vasen
- keuhkoveritulppaa [_] EI [_] KYLLÄ,milloin _____
- selkäsairautta tai iskiasta [_] EI [_] KYLLÄ,milloin _____
- munuaissairautta [_] EI [_] KYLLÄ -"- _____
- alaraajojen valtimoverenkiertohäiriöitä [_] EI [_] KYLLÄ,milloin alk. _____ kumpi jalka [_]oikea/ [_]vasen
- aivohalvausta tai muuta aivoverenkiertohäiriöitä [_] EI [_] KYLLÄ,milloin _____
- säärihaavaa [_] EI [_] KYLLÄ,milloin alk._____ kumpi jalka [_]oikea/ [_]vasen
- muuta pitkäaikaista tai vaikeaa sairautta, mikä_____ milloin todettu? Vuonna _____

Onko Teillä esiintynyt useamman kerran tai pitkäaikaisesti alaraajoissa viimeksi kuluneen kuukauden aikana jokin seuraavista
(jos vastaatte KYLLÄ, rastittakaa kummassa jalassa)

- jalka tuntuu raskaalta iltaa kohden [_] EI [_] KYLLÄ ->[_]OIKEA/[_]VASEN
- särkyä, pistelyä päivän mittaan [_] EI [_] KYLLÄ ->[_]OIKEA/[_]VASEN
- turvotusta nilkan tai säären alueella [_] EI [_] KYLLÄ ->[_]OIKEA/[_]VASEN
- turvotusta reiden alueella [_] EI [_] KYLLÄ ->[_]OIKEA/[_]VASEN
- aina seistessä ilmenevä säären voimakas kipu [_] EI [_] KYLLÄ ->[_]OIKEA/[_]VASEN
- jalkojen palelua [_] EI [_] KYLLÄ ->[_]OIKEA/[_]VASEN
- jalkojen puutumista [_] EI [_] KYLLÄ ->[_]OIKEA/[_]VASEN
- suonenvetoa jaloissa [_] EI [_] KYLLÄ ->[_]OIKEA/[_]VASEN
- tummanruskea ja pysyvä värimuutos nilkan tai säären ihossa [_] EI [_] KYLLÄ ->[_]OIKEA/[_]VASEN
- katkokävelyoire (kävellessä pysähtymään pakottava kipu pohkeessa tai pakarassa) [_] EI [_] KYLLÄ ->[_]OIKEA/[_]VASEN
- levossa ollessa kipua jalassa [_] EI [_] KYLLÄ ->[_]OIKEA/[_]VASEN
- pitkäaikainen haavauma tai kuolio jalkaterän tai säären alueella [_] EI [_] KYLLÄ ->[_]OIKEA/[_]VASEN

[_] EI MITÄÄN EDELLÄLUETELLUISTA OIREISTA

Käytättekö nyt säännöllistä lääkitystä?
[_]EN
[_]KYLLÄ, mihin sairauteen tai minkä lääkeaineryhmän lääkkeitä?

[_] sokeritautiin
[_] verenpaineeseen
[_] sepelvaltimotautiin
[_] rytmihäiriöihin
[_] sydämen vajaatoimintaan
[_] hengityselinten sairauteen
[_] veren hyytymiseen
[_] verenkierron parantamiseen
[_] särkyihin (mukaanlukien mm. Aspirin)
[_] ummetukseen
[_] muuhun sairauteen, mihin _____
[_] kortisonia (tabletteina tai pistoksina)
[_] nais- tai miessukuhormonia

Lääkkeidenne nimet: _____
_____
_____
_____
_____
_____
_____
_____

Onko Teillä nyt tai onko joskus ollut alaraajoissa suonikohjuja?

(Suonikohjuilla tarkoitetaan selvästi näkyvää, laajentunutta, mutkittelevaa ja mahdollisesti pullottavaa alaraajan ihonalaista laskimosuonta).
[_] EI
[_] EN TIEDÄ
[_] ON NYT
[_] ON OLLUT, MUTTA NYT EI KOSKA NE OVAT [_] HOIDETUT /[_] HÄVINNEET ITSESTÄÄN

Missä suonikohjuja on (rastittakaa kaikki esiintymispaikat)?
[_]vasen reisi
[_]vasen sääri
[_]oikea reisi
[_]oikea sääri

Missä iässä suonikohjut tulivat? _____vuotiaana.

Onko kohjuista Teille ulkonäöllistä haittaa?
[_] EI [_] KYLLÄ

Onko Teitä milloinkaan leikattu suonikohjujen takia?
[_] EI [_] KYLLÄ, montako kertaa? _____, minä vuosina?_____

Missä leikkaus tai leikkaukset tehtiin (valitkaa kaikki Teihin sopivat vaihtoehdot)?
[_] aluesairaalassa
[_] Hatanpään sairaalassa
[_] Tampereen keskussairaalassa/TAYSissa
[_] muussa keskussairaalassa, missä_____
[_] yksityissairaalassa Suomessa
[_] muussa paikassa(esim ulkomailla), missä? _____

Onko suonikohjuja hoidettu ruiskuttamalla lääkettä niihin?
[_] EI [_] KYLLÄ, vuosina _____

Missä ruiskutus tehtiin (valitkaa kaikki Teihin sopivat vaihtoehdot)?
[_] aluesairaalassa
[_] Hatanpään sairaalassa
[_] Tampereen keskussairaalassa/TAYSissa
[_] muussa keskussairaalassa, missä_____
[_] yksityissairaalassa Suomessa
[_] muussa, (esim ulkomailla), missä? _____

Ovatko suonikohjut uusiutuneet hoitojen (leikkaukset,ruiskutukset ym.) jälkeen?
[_]EIVÄT [_]KYLLÄ

Tarvitsetteko mielestänne tällä hetkellä hoitoa suonikohjujen takia?
[_] EN [_] EN OSAA SANOA [_]KYLLÄ
Jos vastasitte kyllä, minkälaista hoitoa?
[_] neuvontaa esim terveydenhoitajalta
[_] lääkärintutkimusta tai -hoitoa
[_] muuta, mitä _____

Oletteko tällä hetkellä odottamassa lääkärin määräämää hoitoa suonikohjujen takia?
[_] EN
[_] KYLLÄ, OLEN [_] suonikohjuleikkausjonossa [_] muuta suonikohjujen hoitoa odottamassa

Oletteko suonikohjujen takia käyttänyt mittojen mukaan valittua puristussukkaa yli kuukauden ajan?
[_]EN [_]KYLLÄ

Oletteko käyttänyt kevyempiä ns. tukisukkia?
[_] EN [_] KYLLÄ

Onko lähisukulaisillanne (vanhemmat, isovanhemmat, sisarukset) suonikohjuja?
[_] EI [_] EN TIEDÄ [_] KYLLÄ,kenellä (sukulaisuuden laatu, esim. isällä)_____

Onko Teitä leikattu muun sairauden takia?
[_] EI
[_] KYLLÄ, minkä ja milloin:

v._____ leikkaus_____

v._____ leikkaus_____

v._____ leikkaus_____ (jatkakaa tarvittaessa)

##########

OLKAA HYVÄ JA TARKISTAKAA, ETTÄ VASTASITTE KAIKKIIN KOHTIIN OHJEIDEN MUKAISESTI. SULKEKAA KYSYMYSLOMAKE (4 SIVUA) MUKANA SEURANNEESEEN OSOITTEELLA VARUSTETTUUN KIRJEKUOREEN JA JÄTTÄKÄÄ SE POSTIIN PIAN. KIITOS!

##########

Original publications

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Incidence of varicose veins in Finland

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Summary

Background: Incidence of varicose veins in the population is unknown. The study aimed at estimating the incidence of varicose veins in complete cohorts of 40–60 year-olds in a general population.

Patients and methods: The study was conducted in the city of Tampere, Finland. A validated questionnaire (with 93% sensitivity and 92% specificity) was used in a general population of 6874 individuals (aged 40, 50 or 60). Initially, 3065 of them had no varicose veins and 78% were followed-up for 5 years.

Results: 157 individuals reported new varicose veins during the follow-up. The overall incidence was 13.5 per 1000 person years (8.5 for men and 19.2 for women). Female sex was an independent and statistically significant risk indicator of varicose veins (adjusted odds ratio, OR 2.4). The incidence was significantly higher at the age of 50–55 years (OR 1.6). Higher body mass index seemed to be related to higher risk of new varicose veins (OR 1.2–1.8), but the association failed to reach statistical significance. The level of education did not affect the incidence.

Conclusions: New varicose veins appear also in the middle-aged population, and the rate is linked with the female gender, especially at the beginning of the 6th decade.

Key words

Varicose veins, incidence, population, risk factors

Zusammenfassung

Inzidenz von Varizen in Finnland

Hintergrund: Die Inzidenz von Varizen in der Allgemeinbevölkerung ist unbekannt. Diese Studie wurde konzipiert, um die Inzidenz in einer kompletten Kohorte von 40- bis 60-Jährigen zu bestimmen.

Patienten und Methoden: Die Studie wurde in der Stadt Tampere in Finnland durchgeführt. Es wurde ein validierter Fragebogen mit einer Sensitivität von 93% und einer Spezifität von 92% zur Befragung von 6874 Individuen im Alter von 40, 50 oder 60 Jahren benützt. Zu Beginn der Untersuchung hatten 3065 Personen keine Varikose. 78% wurden über 5 Jahre beobachtet.

Ergebnisse: Während dieses Zeitraumes berichteten 157 Personen von einer neu aufgetretenen Varikose. Die gesamte Inzidenz betrug 13,5 pro 1000 Personenjahre (8,5 für Männer und 19,2 für Frauen). Das weibliche Geschlecht war ein unabhängiger und statistisch signifikanter Risikofaktor (odds ratio 2,4). Die Inzidenz war im Alter von 50–55 Jahren signifikant höher (odds ratio 1,6). Ein höherer Body-Mass-Index schien mit einem höheren Risiko verbunden zu sein (odds ratio 1,2–1,8), wenn auch eine statistische Signifikanz nicht erreicht wurde. Der Bildungsgrad hat keinen Einfluss.

Schlussfolgerungen: Varizen treten auch in der mittelalten Population auf. Die Inzidenz ist korreliert mit dem weiblichen Geschlecht insbesondere am Anfang der 6. Dekade.

Introduction

Varicose veins are a common chronic condition in the caucasian populations. World Health Organization has defined primary varicose veins as "saccular or cylindrical widened superficial veins where the widening may be circumscribed or segmental" [7]. Visible, dilated, tortuous and elongated/prominent subcutaneous lower limb veins have been considered pathological and the description has been used to define superficial venous incompetence in many epidemiological studies of larger populations [1, 2, 3, 12, 13, 15], where detailed ultrasonic examination of vein trunks has been difficult and possibly too time consuming to perform. Prevalence of varicose veins has varied between 10% and 17% in men and 20% and 35% in women in Western adult populations [4, 5]. A national health survey in Finland reported 25% prevalence of varicose veins in women and 7% in men [15], and in Tampere study of 40, 50 and 60-year-old cohorts an overall life-time prevalence was 42% in women and 18% in men [10].

Despite the fact that varicose veins are a common condition and cause significant need for surgery only a few studies report incidences of varicose veins. Since the incidence of varicose veins in the Scandinavian population is entirely unknown, and the proportion of the population in older age groups is expected still to increase, we wanted to get more detailed information on the number of individuals in whom varicose veins develop in the middle age or later in life. Therefore we performed a 5-year follow-up study of three defined middle-aged cohorts in Tampere; in this study we report the first follow-up data on the indi-

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viduals, who originally had no varicose veins at the beginning of the follow-up.

Patients and methods

Our study included complete cohorts of all forty, fifty and sixty-year-old residents in Tampere, a city with 171 307 inhabitants in Southern Finland. The same population was evaluated twice during the study. Originally, the population consisted of 3284 men and 3590 women who were identified in the population registry and they were mailed a structured questionnaire [10]. In the first study the response rate was 75% (2467) among men and 86% (3101) among women; the results of the prevalences have been published earlier. Follow-up information was gathered with a similar questionnaire five years later; 2049 men and 2854 women of the original responders replied to it. Analysis was focused on individuals not having varicose veins (n = 3065) in the initial evaluation at start of the follow-up. Follow-up data collection was complete in 2400, yielding a secondary response rate of 78% (i.e. 1253 men and 1147 women replied). We aimed at reaching as high return rate as possible, and a similar questionnaire was mailed one to two months later to the non-responders in both evaluations. Diagnostic criteria were based on the subjects themselves assessing whether they had varicose veins (or not) and they were given the definition in the questionnaire ("dilated tortuous and elongated superficial veins of the lower extremities"). We used the existing common definition of varicose veins as described originally by Arnoldi [1] and adopted to other population studies and to WHO [2, 3, 7, 12, 13, 16]; it corresponds to the CEAP clinical class 2, but the CEAP classification was published later [14]. The questionnaire also included detailed clinical questions such as medical history, medication, weight, and height, and information on dietary, family and socioeconomic status was also recorded. The validation of the questionnaire based self-assessed diagnosis was performed against surgeon's diagnosis in randomly picked 166 50-year olds participating in our population survey. The examination involved inspection of both uncovered lower extremities by one surgeon (J.L.) in good illumination during an outpatient clinic visit (in Tampere University Hospital); the examiner did not know the self-diagnosis the individual had given. Additional clinical Trendelenburg tests with CW Doppler reflux verifications of the long and short saphenous veins and visible tributaries were performed to discover superficial venous reflux. In all patients both of the legs and thighs were studied. The results of this validation have been published earlier and showed the accuracy of the self-assessed diagnosis to be relatively high with a specificity of 0.9 (the 95% confidence interval 0.8–1.0) and sensitivity of 0.9 (95% CI 0.7–1.0) in men and of 0.9 (95% CI 0.8–1.0) in women [9]. The prevalence of varicose veins was defined as the proportion of the individuals who reported having ever had varicose veins during their life time out of all respondents (lifetime prevalence). The incidence of varicose veins was the number of new varicose vein cases per 1000 person years of follow-up. Individuals with surgically cured varicose veins were defined as having varicose veins and were excluded from the follow-up analysis. Body mass index (weight (kg)/[height (m)]^2) was analysed in decile groups, and in the final analysis three groups were formed by using 10 and 90 percentiles as cut-points (P1: BMI $\leq$ 21.2 kg/m^2, P2: 21.2 kg/m^2 < BMI $\leq$ 30.5 kg/m^2, P3: BMI > 30.5 kg/m^2). Education level was classified in two groups; comprehensive and vocational school were determined as lower education level; university, college and high school education were determined as higher education level.

Univariate analysis was performed first to delineate potential risk factors of varicose veins. Mantel-Haenszel test was applied in the stratified analysis of the odds ratios and, finally, logistic regression analysis was performed to evaluate the independent effects of the determinants of varicose veins in the model. Estimates of odds ratios were reported with 95% confidence intervals, as reported from a logistic regression analysis with statistical software package SPSS.

The study protocol was approved by the Ethics committees in Tampere University Hospital and in the Tampere City Department of Health, and the study conformed to the principles of the Declaration of Helsinki.

Results

The estimates of both prevalence and incidence were calculated to determine if prevalent cases have differing risk pattern to incident cases. The prevalence of varicose veins at the beginning of the follow-up was 32.6% (1744 individuals reported varicose veins); 1253 men and 1147 women of the target population were initially free of varicose veins (Table I). 157 of them reported varicose veins after the follow-up of five-years. The overall incidence of varicose veins in the population was 13.5 per 1000 person-years (8.5 for men and 19.2 for women) (Table I). The effects of risk factors were estimated from odds ratios (OR). Women had significantly higher incidence than men (OR 2.4, 95% confidence interval, CI 1.7–3.4). All risk determinants with odds ratios are presented in Table II.

The highest incidence was observed in the initial cohort of 50-year-olds, OR 1.6 (CI 1.1–2.3). Incidence peak was noted in both sexes but the difference was statistically significant only in women. 40- and 60-year-old cohorts at the beginning of the study had closely equal incidences of varicose veins (OR 1.0 in both groups). This result differs from the prevalences noticed at the beginning of the follow-up, where the association of varicose veins with age was more clear and was consistently related with increasing age (OR 1.9 for 50-year-olds and OR 2.5 for 60-year-olds).

Higher incidence of varicose veins was seen when body mass index (BMI) increased. Obese persons (with BMI > 30.5 kg/m^2 in the heaviest decile) had the highest incidence (OR 1.8). Persons with normal weight or mild obesity were in slightly elevated risk of getting varicose veins (OR 1.2) when compared to lean individuals with low BMI (BMI $\leq$ 21.2 kg/m^2 in the leanest decile). Also at the beginning of the follow-up individuals with obesity had more often varicose veins. Similarly, individuals with lower level of edu-

Table I: The numbers of individuals in varicose vein prevalence and incidence studies; incidence study included only individuals initially free from varicose veins. Prevalences indicate life-time occurrence of varicose veins (%) out of all individuals at the beginning of the study whereas incidences indicate new cases of varicose veins during follow-up (per 1 000 person years, pyrs).

Risk factor		Prevalence			Incidence		
		Size of population	N	%	Size of population	N	Per 1000 p/yrs
Sex	Male	2403	454	18.9	1253	52	8.5
	Female	2948	1294	43.9	1147	105	19.2
	Total	5351	1748	32.6	2400	157	13.5
Age	40–45	2226	512	23.0	1141	65	11.7
	50–55	1627	595	36.6	718	62	18.0
	60–65	1498	641	42.8	541	30	11.4
	Total	5351	1748	32.6	2400	157	13.5
BMI[1]	P1	513	155	30.2	243	16	13.6
	P2	4206	1346	32.0	1922	116	12.4
	P3	535	214	40.0	208	21	21.3
	Total	5254	1715	32.6	2373	153	13.3
Education	Higher[2]	2819	891	31.6	886	63	14.7
	Lower[3]	2168	722	33.3	1420	90	13.1
	Total	4987	1613	32.4	2306	153	13.7

[1] Body mass index by 10 and 90 percentiles (P1: BMI ≤ 21.19 kg/m², P2: 21.19 g/m²,< BMI ≤ 30.48 kg/m², P3: BMI > 30.48 kg/m²).
[2] Higher education includes university, college and high school.
[3] Lower education includes comprehensive school and vocational school.

Table II: Odds ratios (OR, in univariate analysis) and adjusted odds ratios (in logistic regression analysis; adjusted for the other determinants) in the prevalent cases with varicose veins (v.v.) at the beginning of the study and in individuals with new varicose veins during the follow-up.

Risk factor		OR for prevalence of.v.v.	Adjusted* OR for prevalence of v.v.	OR for incidence of v.v.	Adjusted* OR for incidence of v.v.
Sex	Male	1	1	1	1
	Female	3.4 (3.0–3.8)	3.6 (3.2–4.1)	2.3 (1.7–3.3)	2.4 (1.7–3.4)
Age	40–45	1	1	1	1
	50–55	1.9 (1.7–2.2)	1.9 (1.7–2.3)	1.6 (1.1–2.2)	1.6 (1.1–2.3)
	60–65	2.5 (2.2–2.9)	2.5 (2.1–2.9)	1.0 (0.6–1.5)	1.0 (0.7–1.7)
BMI[1]	P1	1	1	1	1
	P2	1.1 (0.9–1.3)	1.2 (1.0–1.5)	0.9 (0.5–1.6)	1.2 (0.7–2.1)
	P3	1.5 (1.2–2.0)	1.5 (1.2–2.0)	1.6 (0.8–3.1)	1.8 (0.9–3.8)
Education	Higher[2]	1	1	1	1
	Lower[3]	1.1 (1.0–1.2)	1.2 (1.1–1.4)	0.9 (0.6–1.2)	0.8 (0.6–1.2)

* Adjusted for the other variables in the table.
[1] Body mass index by 10 and 90 percentiles (P1: BMI(21.2 kg/m2, P2: 21.2 kg/m2<BMI(30.5 kg/m2, P3: BMI>30.5 kg/m2).
[2] Higher education includes university, college and high school.
[3] Lower education includes comprehensive school and vocational school.

cation (up to vocational or comprehensive school) had significantly more often varicose veins. Interestingly, during the follow-up this difference disappeared and there were no statistically significant differences in the incidences of varicose veins in the groups with higher or lower education. In fact, the results indicate that the risk was slightly lower in the less educated individuals.

We also analysed the available information we had about the individuals we lost from the follow-up. In the group of non-responders to the follow-up, who had responded at the beginning of the study, varicose veins were less reported than among the follow-up responders. In women the non-responders were slightly more likely (62.8% vs. 56.4%, p = 0.02) to be initially free from varicose veins but in men the difference was not significant (84.4% vs.78.6%, p = 0.46). There were no significant differences in the parity in women or obesity among the responders and non-responders, but non-responders were significantly more often blue-collar than white-collar workers, although the over-representation was only 4.9% in women and 5.2% in men. Non-responders were also more often in the youngest cohort than in the oldest cohort in both sexes.

Discussion

Female sex, higher age, and obesity with higher body mass index together with social co-factors have been regarded as risks for later varicose veins [2, 3, 9, 11, 12]. Our study

aimed at estimating for the first time in Scandinavia the incidence rates of varicose veins in general population. Only limited information on the incidence of varicose veins exist, and is based on the results from the North American study in Framingham [3] and on the results from Italy [6]; in Italy the reported incidence was 0.22% per year which indicates lower appearance of new varicose veins than in our population [6]. In Framingham, the incidence of varicose veins was determined per person-bienniums in 40- to 89-year-olds and this differs from our study where we report incidences by person years in three cohorts. Therefore, the actual numbers differ slightly and despite of the differences in population ages and the study methods the incidence of varicose veins in our study (13.5 per 1000 person years) was only slightly lower than what was found in Framingham (23.1 per 1000 person years).

Varicose veins seem to be significantly related to female gender [3, 4, 10, 11, 12, 15], although discordant findings do exist [8]. In our population the female gender effect was less (as judged from the OR) in the incident cases as compared to the prevalent cases, who had varicose veins at younger age. In our study there was a peak of incidence in the middle cohort (50-year-old at start of follow-up), and this was especially in women. We do not know the cause and it occurred in both genders; however, it may be related to menopause in women. Earlier prevalence studies have not revealed this because of the continuing accumulation of varicose veins with age in the population. The accumulation is evident since varicose veins are not likely to cause deaths and they are permanent (if not treated). Also other cohort effects, such as the childhood during the wartime may have affected the level of physical exercise or nutritional status but we have no data in Finland to prove this.

The effect of obesity on varicose veins was studied by comparing ten equal-sized groups. In the leanest decile and in the most obese decile of the population there was a significant difference in both the prevalence and the incidence of varicose veins. The same trend was noted also when we divided the groups into four and used quartile analysis: the higher the body mass index the higher the risk for new varicose veins. Also prevalence analysis confirms the association of obesity with varicose veins. In the logistic regression analysis body mass index was linked with the second highest risk for new varicose veins during the follow-up, although due to the small number of new cases the risk did not reach significant level.

In our study population work dominated by standing was related to higher prevalence of varicose veins [11]. These results are in accordance to many studies but also discordant findings have been reported [4]. Work is closely associated with other social determinants, and we used education to approximate social status. At the beginning, individuals having less education (to vocational or comprehensive school level) had higher prevalence of varicose veins but during the follow-up education (with related social co-factors) did not affect the development of new varicose veins and we were unable to confirm differences in incidences during the follow-up. It may reflect the fact that educational status together with working conditions and other social factors affect in the pathogenesis earlier in life than in the later middle age. It is also possible that education per se does not reflect protective or adverse life habits as much as we expect. It is noteworthy, that our incidence-based findings also derive from the part of the study population not having varicose veins at the start of the study whereas the earlier results from individuals already having varicose veins at the beginning of the study (prevalent cases) may include different pattern of risk factors.

Most of the studies on varicose veins are based on cross-sectional structure yielding prevalence rates potentially specified by a set of risk indicators. The inferences on effects of such risk factors may be biased as the curability and other types of selection bias affect the prevalence. Therefore, incidence rates are to be preferred when conclusions on aetiology in terms of risk factors are made. The comparison of prevalence-based and incidence-based odds ratios in this study showed that the cross-sectional prevalence design overestimated the effect of female sex, increasing age, and low education on the risk of varicose veins. On the other hand, the effect of obesity is probably stronger than indicated by prevalence odds ratios. While cross-sectional studies may be valid for many purposes in provision of health services they may be severely biased for etiological research.

The role of misclassification bias has already been approximated in our previous prevalence studies. It may affect the figures, but based on the accuracy evaluation we performed its effect should be small when the comparison was made against the CEAP classification class C2. However, during the follow-up we lost 22% of the eligible follow-up population, and the loss predominated in the younger cohorts and in individuals initially not having varicose veins. Legislation in Finland prevents us from getting hospital-based (or any other) information from the target population originally not responding to our surveys. If all individuals recognizable for follow-up had stayed healthy (with regard to varicose veins) and participated in the follow-up, the overall incidence of varicose veins in our population would have been 15.1 per 1000 person-years in women and 7.0 per 1000 person-years in men (i.e. indicating at maximum a surplus of incidence by 21% in women and by 16% in men). Even though the calculated incidence (per 1000 person years) lies between 15.1–19.2 in women and between 7.1–8.5 in men, we cannot expect our figures to be under-representative to the true incidence.

In conclusion, we were able to confirm that middle-aged (40–60) women have a higher risk of new varicose veins than men. Also high body mass index could contribute to the increased risk but in our study the increase in risk was not significant. Even though the varicose vein prevalence is increasing by age, our results showed higher appearance only during the menopausal age range. The results indicate that the effect of socio-economic factors (as determined by the level of education) on varicose veins is not of major importance. New varicose veins appear also in the middle aged Finnish population, and the rate is linked with female gender and immediate postmenopausal age. Prevention of varicose veins could be focused on weight reduction, especially in women.

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