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Protective Vascular Treatment of Patients with Peripheral Arterial Disease: Guideline Adherence According to Year, Age and Gender

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ABSTRACT

Objectives: To evaluate vasoprotective pharmacological treatment of patients with peripheral arterial disease (PAD) according to: 1) year, 2) age and 3) gender.

Methods: An observational retrospective study was conducted to evaluate the systemic vascular treatment of a population-based cohort of patients with PAD ≥50 years old, discharged from a tertiary-care teaching hospital between January 1, 1997 and December 11, 2006. Data were obtained from the Régie de l'assurance maladie du Québec. Drugs evaluated included antiplatelet agents (APs), statins (STs) and angiotensin converting enzyme inhibitors (ACEIs), and a combination of all three. Proportions of patients treated were compared according to year, age and gender using Chi-square.

Results: The mean age of the study population (5962 individuals) was 73.2 ± 9.1 years; 43.8% were women. After hospital discharge, 71.6%, 47.6%, 42.2% and 20.6% were taking respectively, an AP, statin, ACEI or all three. Protective treatment improved significantly from 1997 to 2006. Significantly more subjects 50-64 years used a statin or all three agents, compared to subjects ≥65 years (statins: 56.6% vs. 45.8%, all three: 26.2% vs. 19.5%; p<0.001). Significantly more men than women used statins (49.1% vs. 45.6%; p<0.001) and ACEIs (44.5% vs. 39.3%; p<0.001). Similarily, use of all three agents was 22.4% for men and 18.2% for women (p<0.001).

Conclusions: Although systemic vascular treatment received by patients with PAD has increased in the past years, it remains suboptimal, particularly for older patients and women. Strategies to improve adherence to treatment guidelines should be developed for these high-risk populations.

Key words: Peripheral arterial disease; secondary prevention; guideline adherence

Peripheral arterial disease (PAD) is now considered a CHD-risk equivalent.[1] Prevalence of PAD in Western populations is 12%,[2] increasing with age from 2.5% in persons <60 years to 18.8% in those 70-79 years.[3] Women have more asymptomatic disease, which may explain the historically higher prevalence of lower extremity disease in men in some studies.[4,5] However, recent population surveys report higher rates of PAD in women.[5-8]

Patients with PAD have a risk of cardiovascular (CV) morbidity and mortality comparable to that of patients with coronary heart disease (CHD).[9-11] Their risk for CV mortality is 3-5 times above baseline.[12] Prognosis in symptomatic PAD is even poorer, with 15-fold increased mortality at 10 years.[13]

Published recommendations specific for the treatment of these patients recognize the systemic nature of the disease; treatment recommendations include intensive risk factor reduction and systemic preventive treatment independent of risk factors.[14] According to the Canadian recommendations published in 2005, unless contraindicated, all PAD patients should receive an antiplatelet agent (AP), a statin (ST) and an angiotensin converting enzyme inhibitor (ACEI), irrespective of their risk factors. Research has demonstrated that each agent lowers incidences of cardiovascular mortality, myocardial infarction and cerebrovascular accident by 25%.[15-17] Effects are probably additive, attaining approximately 80% when combined with smoking cessation.[15-17]

Clinical care is often worse for PAD patients than CHD patients, although they have similar risk.[6,18-22] There is also evidence that gender[23,24] and age[25-27] biases exist in management of CHD,[28-30] as well as in secondary prevention for the elderly[27,31-33] and women.[34-37] Similar results have been found for treatment of stroke,[30,38-40] suggesting that gender and age bias could also lead to inadequate care for PAD patients.

There are limited data on age and gender difference in PAD. When this study began, there were no publications on age/gender bias in vascular preventive treatment of PAD, and no publications of any kind with data after 2005. Thus, the objective of this study was to evaluate the use of vascular protective treatment of patients with PAD, and determine if there were differences according to time period, age and sex.

METHODS

Study design, data sources and study population

As part of a larger, population-based study focusing on 12 months compliance to treatment, this observational retrospective study identified people 50 years old with PAD from a tertiary-care hospital research database. Medical insurance numbers of patients discharged between January 1, 1997 and November 11, 2006, with

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Figure 1. Flow chart for selection of participants with peripheral arterial disease, including inclusion and exclusion criteria
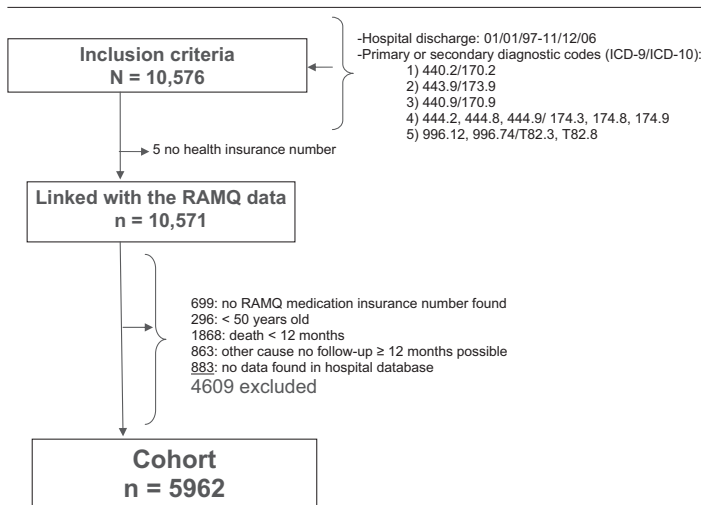
primary or secondary diagnosis of PAD indentified using the ninth or tenth International Classification of Diseases (ICD-9 or ICD-10 classification) were linked to the administrative databases of the Régie de l'assurance maladie du Québec (RAMQ). Data from January 1, 1996 to December 31, 2007 were retrieved, including demographic data, information on diagnostic tests, surgical procedures, and comorbidity, as well as prescribed medications as listed in the pharmaceutical file. This file, previously validated for research,[41] gives information for all individuals ≥65 years, and for others insured under the public drug plan including welfare recipients and people without access to private insurance.

Variables

Evaluated treatment included APs, STs, ACEIs, and concurrent use of all three. We considered that participants were adherent to treatment recommendations if they had filled their prescription at least once within the first 90-day period after hospital discharge. We also developed a treatment concordance score. Patients using all medications recommended received a score of 3, patients using two of the three drugs received a score of 2, those taking only one of the recommended agents had a score of 1 and if none of the three recommended agents was being used the score was 0. The higher the score the better was adherence to treatment recommendations.

Statistical analysis

We compared treatment according to three selected time periods: before April 2002, between April 2002 and December 2004, and after January 1, 2005. Results were also compared according to three age groups: 50-64 years old, 65-79 years old and ≥80 years old. Furthermore, we compared treatment between men and women, with and without stratifying for age. Proportions of patients treated were compared using Chi-square. Analyses were performed with SAS Software version 9.0 and SPSS Software version 16.0. Results are expressed as percentages of people treated. The level of significance used was $p<0.05$.

Ethical considerations

Approval for this study was obtained from the ethics board of the care centre where the study participants had been hospitalized. The

Table 1. Baseline Characteristics of PAD Patients (n=5962)

Characteristic	n (%)*
Age, years (mean ± SD)	73.2 ± 9.1
Age group (years)	
50-64	990 (16.6)
65-79	3439 (57.7)
≥80	1533 (25.7)
Gender	
Women	2610 (43.8)
Marital status	
Married or common-law spouse	3019 (50.7)
Risk factors†	
Hypertension	3974 (66.7)
Diabetes	1767 (29.6)
Hypercholesteremia	2483 (41.6)
Smoking	No data available
Vascular interventions (non-cardiac)†	
No intervention	4405 (73.9)
Angioplasty	718 (12.0)
Bypass	1045 (17.5)
Other	76 (1.3)
Inclusion criteria†	
Diagnostics: (ICD-9/ICD-10)	
Peripheral atherosclerosis (440.2/I70.2)	1316 (22.1)
Peripheral arterial disease (443.9/I73.9)	1188 (19.9)
Atherosclerosis (not heart/brain) (440.9/I70.9)	5218 (87.5)
Arterial embolism or thrombosis (not heart/brain) (other ICD codes included; see figure 1)	782 (13.1)

* Data are presented as numbers (%) unless otherwise specified.
† Total is more than 100% because some patients have more than one risk factor, intervention or diagnosis.

"Commission d'accès à l'information du Québec" also gave approval for use of the databases obtained from the Régie d'assurance maladie du Québec. Researchers replaced the health insurance numbers by an encrypted number specific for each patient in order to protect confidentiality.

RESULTS

Figure 1 shows selection of the study population. Characteristics of the study population appear in Table 1. The mean age of the study population (n=5962) was 73.2 ± 9.1 years; 43.8% were women. Overall use of APs, STs, ACEIs or all three together was respectively 71.6%, 47.6%, 42.2% and 20.6%. Interestingly, 14% of the patients in our study used none of the three medications recommended, while 31.2% and 34.2% used only one or two of the agents respectively.

When comparing use of vasoprotective treatment for the three time periods, we observed significantly higher rates after March 2002, as seen in Figure 2. For STs, a statistically significant difference was also seen between the period ending in 2004 and the one starting in 2005. Thus "better" treatment seems to precede publication of the 2005 recommendations by several months. With time, there was also a significant shift in the treatment concordance score (results not shown). A progression was seen with people taking one, then two and finally more taking all three agents. Before April 2002, 37.2% used only one agent and 32.2% used two, whereas between April 2002 and January 2005, 23.4% and 36.7% were using one and two agents respectively. The highest rate of people taking all three agents was seen after 2005.
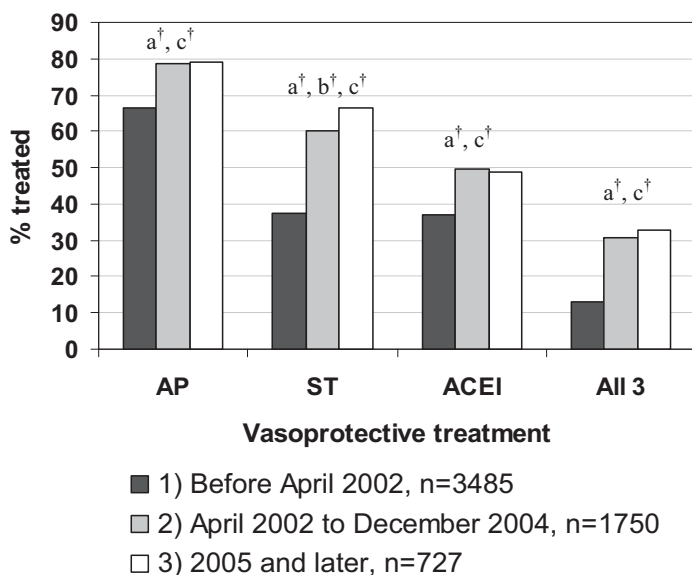
When comparing age groups, we found no differences in the use of APs (Figure 3). For STs and for concurrent use of all three medications, we observed a significant difference between each age group. Younger people used all vascular treatments recommended more often. Figure 3 also reveals that while people ≥80 years used fewer ACEIs, there was no significant difference between the 50-64

Table 2. Comparison of Vasoprotective Treatment According to Gender and Stratified for Age

Age (years)	Sex	AP (% treated)	ST (% treated)	ACEI (% treated)	All 3 (% treated)
All	F (n=2610)	1887 (72.3)	1189 (45.6) †	1027 (39.3) †	475 (18.2) †
	M (n=3352)	2383 (71.1)	1647 (49.1)	1491 (44.5)	752 (22.4)
50-64	F (n=362)	267 (73.8)	205 (56.6)	135 (37.3) †	83 (22.9)
	M (n=628)	440 (70.1)	355 (56.5)	296 (47.1)	176 (28.0)
65-79	F (n=1378)	1003 (72.8)	706 (51.2)	560 (40.6) *	293 (21.3)
	M (n=2061)	1473 (71.5)	1059 (51.4)	921 (44.7)	472 (22.9)
≥80	F (n=870)	617 (70.9)	278 (31.9)	332 (38.2)	99 (11.4) *
	M (n=663)	470 (70.9)	233 (35.1)	274 (41.3)	104 (15.7)

* p<0.05; † p<0.005

Figure 2. Use of vasoprotective treatment according to time period. Comparison of time periods: a compares 1 vs. 2, b compares 2 vs. 3, c compares 1 vs. 3

1) Before April 2002, n=3485
2) April 2002 to December 2004, n=1750
3) 2005 and later, n=727

* p<0.05; † p<0.005

Figure 3. Use of vascular protective treatment according to age group. Comparison of age groups: a compares 1 vs. 2, b compares 2 vs. 3, c compares 1 vs. 3

1) 50-64 years, n=990
2) 65-79 years, n=3439
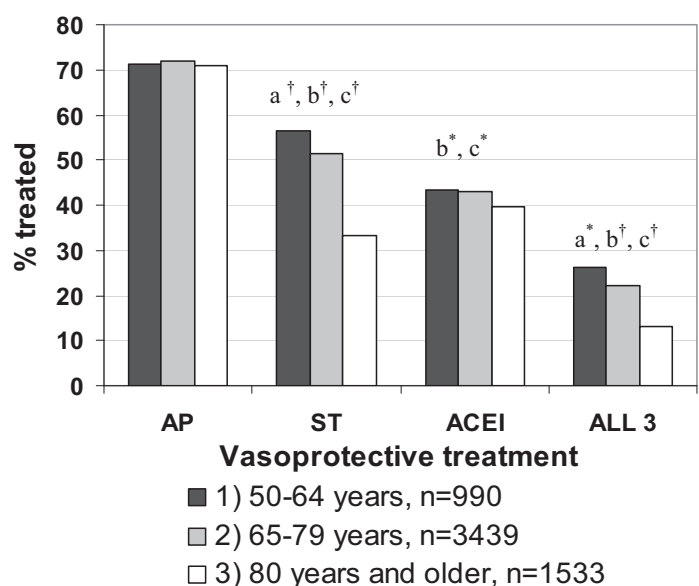3) 80 years and older, n=1533

* p<0.05; † p<0.005

and 65-79 year age groups. The treatment concordance scores show an inverse relationship between treatment and age with the younger age group having more optimal treatment (p<0.05). People aged 65 to 79 more often used two compared to one of the three recommended agents (35.4% vs. 28.8%). In the ≥80 age group, patients more often used only one drug (32.0% used two vs. 40.1% used one).

As seen in Table 2, except for antiplatelet use which is similar for men and women, men appear to be better treated than women. Whereas more men used all three medications significantly more often (p<0.005), a similar proportion use two (34.6% for women vs. 33.9% for men) and more women than men use only one (33.4% vs. 30.0%) of the recommended agents. When stratifying for age, gender difference is no longer significant for statins. Table 2 also reveals that use of ACEIs is significantly less for women than men in the two youngest age groups, and that use of all three pharmacological agents at the same time is significantly less frequent for women ≥80 years old.

DISCUSSION

Regarding vascular protective treatment, Canadian recommendations specific for patients with PAD were published in 2005. These recommendations are presumed to be the cause of the significant increase that was noted around that time in the use, by PAD patients, of APs, STs, ACEIs or all three medications. At the same period, there was also a favourable shift in the number of agents received, people receiving more often two of the three agents instead of only one. However, although there has been an improvement, vascular protective treatment is still suboptimal, as has been observed in other studies.[14,21,22]

To our knowledge, this is the first study specifically examining age and gender bias of atherosclerotic protective treatment in PAD patients, and confirming that both biases are present. Recently, it has been reported elsewhere that use of drugs with the potential of preventing cardiovascular disease in patients with PAD was more common among men than women.[42]

Populations have aged as life expectancy at birth has considerably increased in the 20th century. In Canada, life expectancy is now 83.4 years for women and 76.4 for men.[43] Consequently, elderly women outnumber elderly men. PAD is highly prevalent in that age category. Women and older people with peripheral arterial disease represent high-risk patients with a particular risk for cardiovascular complications, yet they are under-represented in drug admission studies. Also, there is little evidence-based data to guide

us in determining appropriate secondary preventive therapies that can be used for patients older than 75 years.[44] Comorbidity and use of complex pharmacological treatment complicate the issue and may also explain undertreatment of older patients. More research is needed for both this age group and for women in order to determine the best treatment for all patients.

Observations in this study may not be generalized to the overall target population of PAD patients for several reasons. First, the study is monocentric. Moreover, because of the numerous exclusion criteria applied, the study cohort was composed of only 5,962 people of the 10,576 who were initially included, as illustrated in Figure 1. Also, we evaluated treatment of patients diagnosed with PAD after hospital discharge. More than half of people with peripheral arterial disease are asymptomatic and many remain undiagnosed.[2] People with less severe disease, probably even more undertreated, were not considered. On the other hand, we have no information on treatment contraindication, which could explain why some patients do not receive the recommended drugs. For example, although oral anticoagulants are not recommended for patients with PAD,[14] some patients may receive them for another medical condition such as atrial fibrillation. The risk associated with the addition of an antiplatelet could outweigh the benefit. Antiplatelet treatment may also be underevaluated since aspirin is an over-the-counter drug.

We assumed in this study that people who have a treatment prescribed after hospital discharge buy the suggested medication, and that those who fill out their prescriptions use the medication appropriately. This may not be so. Our study also looks at use of medication during hospitalization, and adherence and persistence to treatment over a 12-month period, but these results will be presented elsewhere. We will also look at use of angiotensin receptor antagonists (ARAs). Insufficient data on effects of ARAs were available at the time that the recommendations were published, so this class is not included in guidelines published up to now. We may suspect, however, that some patients receive ARAs instead of ACEIs and this could explain, at least partly, the undertreatment of patients observed in this study.

CONCLUSION

PAD is a marker for premature cardiovascular events, with increased risk of cardiovascular morbidity and mortality in the absence of aggressive secondary preventive treatment. However, use of the recommended vascular protective treatment is suboptimal.

This study shows that systemic vascular treatment of PAD patients has improved in the last several years, but older people and women receive the recommended therapy less often. Interventions in clinical practice and increased public awareness[45] are important in order to improve treatment of these high-risk patients. Strategies should be developed to improve guideline adherence in clinical practice, and should take account of the treatment differences we have observed. Future research should also be conducted to study determinants of guideline adherence.

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RÉSUMÉ

Objectifs : Évaluer l'utilisation du traitement pharmacologique vasoprotecteur de patients atteints de la maladie vasculaire artérielle périphérique (MVAP) et plus spécifiquement comparer le traitement selon : 1) l'année, 2) l'âge et 3) le sexe.

Méthode : Nous avons mené une étude observationnelle rétrospective pour évaluer le traitement vasoprotecteur d'une cohorte de patients de ≥50 ans atteints de la MVAP, ayant reçu leur congé d'un hôpital universitaire tertiaire entre le 1er janvier 1997 et le 11 décembre 2006. Les données ont été obtenues de la Régie de l'assurance maladie du Québec. Le traitement pharmacologique évalué incluait l'utilisation d'antiplaquettaires (AP), de statines (ST), d'inhibiteurs de l'enzyme de conversion de l'angiotensine (IECA) et des trois à la fois. Les proportions de patients traités étaient comparées selon le temps, l'âge et le sexe à l'aide du test du khi-carré.

Résultats : L'âge moyen de la population (n=5 962) était de 73,2 ± 9,1 ans, dont 43,8 % de femmes. Après le congé hospitalier, respectivement 71,6 %, 47,6 %, 42,2 % et 20,6 % prenaient un antiplaquettaire, une statine, un IECA ou les trois agents. L'utilisation du traitement vasoprotecteur augmente significativement de 1997 à 2006. Plus de patients jeunes, de 50-64 ans, utilisent une ST ou les trois agents simultanément comparativement aux patients de ≥65 ans (statine : 56,6 % comparativement à 45,8 %, les trois : 26,2 % comparativement à 19,5 %; p<0,001). Significativement plus d'hommes que de femmes utilisaient une ST (49,1 % contre 45,6 %; p<0,001) et un IECA (44,5 % contre 39,3 %; p<0,001). De façon similaire, 22,4 % d'hommes comparativement à 18,2 % de femmes utilisaient les trois agents en même temps (p<0,001).

Conclusions : Malgré une amélioration dans les dernières années, l'utilisation du traitement vasoprotecteur des patients atteints de MVAP demeure sous-optimal, particulièrement en ce qui concerne les femmes et les personnes âgées. Des stratégies pour augmenter l'adhésion aux recommandations émises pour le traitement vasoprotecteur de ces personnes à haut risque vasculaire devraient être élaborées.

Mots clés : maladies vasculaires périphériques; prévention secondaire; adhésion aux directives