

openheart Blood pressure target achievement and antihypertensive medication use in women and men after first-ever myocardial infarction: the Tromsø Study 1994–2016

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ABSTRACT

Background Recurrent cardiovascular events after myocardial infarction (MI) are frequent, and gender differences in blood pressure treatment have been reported. Despite increased focus on secondary prevention, recent reports indicate that treatment targets are not achieved. There is a need for gender-specific analyses of post-MI blood pressure treatment target achievement and antihypertensive medication adherence.

Design We investigated the change in systolic and diastolic blood pressure and antihypertensive drug use after first-ever MI over two time periods in a Norwegian population-based study.

Methods We followed 10 089 participants (55% women) attending the Tromsø Study in 1994–1995 (MI-cohort I) and 8412 participants (55% women) attending the Tromsø Study 2007–2008 (MI-cohort II) for first-ever MI up to their participation in 2007–2008 and 2015–2016, respectively. We used linear regression models to investigate sex and age differences in change in blood pressure.

Results A total of 396 participants in MI-cohort I and 131 participants in MI-cohort II had a first-ever MI in the observation periods. In MI-cohort I, 35% of the women and 52% of the men achieved the treatment targets of blood pressure <140/90 mm Hg (130/80 mm Hg if diabetic), while the proportions for MI-cohort II were 50% and 54% for women and men, respectively. Antihypertensive use was reported in 88% of women and 87% of men in MI-cohort I, and 76% of women and 81% of men in MI-cohort II.

Conclusions We found an overall low achievement of the treatment target. The findings call for better strategies for secondary prevention for both women and men.

INTRODUCTION

Lifestyle changes and treatment adherence after acute myocardial infarction (MI) are associated with improved prognosis and lower mortality¹; however, secondary prevention is still inadequate in many European countries, and the majority of MI patients do not achieve treatment goals.² In Norway,

Key messages

What is already known about this subject?

► Secondary prevention guidelines for myocardial infarction patient care are gender neutral, but recent studies from European countries show that women were less likely to achieve treatment goals compared with men.

What does this study add?

► Gender-specific analysis of achievement of blood pressure treatment target and antihypertensive medication use after myocardial infarction in a Norwegian general population.

How might this impact on clinical practice?

► Treatment target achievement is low in both women and men, and better strategies for secondary prevention are needed.

cardiovascular diseases (CVD) are the most common cause of inpatient hospitalisation.³ Long-standing decrease in MI case fatality over four decades,⁴ currently as low as 10%,⁵ leads to increase in the proportion of patients living with coronary heart disease complications.⁶ One of four acute MI hospitalisations are recurrent events, despite that >90% of all Norwegian MI patients are prescribed medical treatment such as antihypertensive drugs at hospital discharge,⁷ in accordance with European guidelines. The need for more intensive management of MI patients has previously been highlighted.^{8–11} Secondary prevention guidelines are gender neutral, and post-MI medications such as antihypertensive drug use have shown similar protection against CVD events in men and women.¹² However, a recently published study from the SWEDEHEART registry¹³ showed that Swedish women were less likely to achieve treatment



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goals for blood pressure, and a smaller proportion were on beta-blocker or ACE-inhibitor treatment compared with Swedish men. There is a need for gender-specific analysis of post-MI achievement of blood pressure treatment target and antihypertensive medication adherence in the Norwegian population.

AIM

We investigated the change in systolic and diastolic blood pressure levels and prevalence of antihypertensive drug use after MI among women and men in a Norwegian prospective cohort study followed in two time periods.

METHODS

Study population

The Tromsø Study⁹ is an ongoing population-based cohort study in the municipality of Tromsø, Northern Norway. The study includes seven waves of data collection (Tromsø 1: 1974; Tromsø 2: 1979–1980; Tromsø 3: 1986–1987; Tromsø 4: 1994–1995; Tromsø 5: 2001–2002; Tromsø 6: 2007–2008; Tromsø 7: 2015–2016) to which total birth cohorts and representative population samples were invited. Response rates were between 65% and 79%. A total of 45 473 women and men have participated in one or more waves of the study. The participants have given written informed consent.

The present analyses include two cohorts. This allows comparison with coinciding EUROASPIRE studies from the same time periods. The basis for the first cohort were all Tromsø 4 participants with no prevalent MI aged 25–74 in 1994 (n=24 984), of whom 10 154 also attended Tromsø 6 and formed cohort I. The basis for the second cohort were all Tromsø 6 participants with no prevalent MI aged 32–87 years in 2007 (n=12 358), and 8604 of these also attended Tromsø 7 and formed cohort II. We excluded subjects who did not consent to research (n=1) or did not have valid blood pressure measurements in Tromsø 4–6 (n=65) or Tromsø 6–7 (n=61), leaving 10 089 participants (55% women) in cohort I with baseline 1994–1995, and 8543 participants (55% women) in cohort II with baseline 2007–2008, to be followed for first-ever MI up to the next screening in 2007–2008 or 2015–2016, respectively. Among these, 396 participants (33% women) had a first-ever MI during 1994–2008 (MI-cohort I) and 131 participants (34% women) had a first-ever MI during 2007–2016 (MI-cohort II). To allow for change in risk factors, participants with an MI <3 months prior to their second screening were not included MI cohort I. Due to lack of validated MI endpoints after 2013, in MI-cohort II, participants with an MI <2 years before their second screening were not included in MI-cohort II. Among the 24 984 participants of the original Tromsø 4 invited to the Tromsø 6, 906 experienced a first-ever MI before 2008 and survived for at least 30 days, that is, 510 participants with MI from the original cohort did not attend the second screening. Of these, 65% were not invited to Tromsø 6 (due to emigration (13%), mortality

(33%) or not in the random sample invited to Tromsø 6 (20%)). Similarly, among the 12 358 participants of the original Tromsø 6, 235 experienced a first-ever MI before 2014 and survived for at least 30 days, that is, 104 participants with MI from the original cohort did not attend the second screening. Of these, 43% were not invited to Tromsø 7 (due to emigration (10%) or mortality (33%)). The non-attendees were older, had a higher systolic blood pressure and were more likely to be smokers than those who attended both waves (online supplementary table 1).

Measurements, questionnaires and event validation

Blood pressure was measured on the participant's right upper arm with a properly sized cuff based on arm circumference. Trained personnel performed all measurements. Blood pressure was measured three times with an oscillometric digital automatic device (in Tromsø 4: Dinamap Vital Signs Monitor; Critikon, Tampa, Florida, USA, and in Tromsø 6–7: Dinamap ProCare 300 monitor, GE Healthcare, Norway), measurements being separated by a 1 min interval after 2 min seated rest. The mean of the two final readings was used in the analysis. Antihypertensive drug use was always assessed through questionnaires and a written list of brand names of medications used on regular basis checked by health personnel at the study site (in Tromsø 4 only in individuals aged 55–74 years). Self-report of medication used regularly for chronic conditions is considered accurate.¹⁰ Incident cases of CHD were recorded from each participant's study entry in 1994–1995 until 31 December 2008 and 2007–2008 until 31 December 2013, respectively. Adjudication of hospitalised and out-of-hospital incident MI was based on all available information including medical records from hospitals, ambulance service, general practitioners, nursing homes, autopsy reports and death certificates. Validation of each event was based on modified WHO MONICA (Multinational MONItoring of trends and determinants in Cardiovascular disease/MORGAM (MONica Risk, Genetics, Archiving and Monograph)) criteria described elsewhere,¹⁴ and included clinical symptoms and signs, findings in ECGs, values of cardiac biomarkers and autopsy reports.

Statistics

Statistical analyses were performed using SAS V.9.4 (SAS Institute). Change in blood pressure was defined as the difference between the values in Tromsø 6 and Tromsø 4, and Tromsø 7 and Tromsø 6, respectively. Descriptive characteristics were reported with means (SD or 95% CIs) for continuous variables and proportions for binary variables. Test for differences in blood pressure between baseline (pre-MI) and second screening (post-MI) were assessed using pairwise t-tests. Multi-variable linear regression models were used to test for equality in blood pressure change between women and men, age groups and different groups defined by blood pressure levels in Tromsø 6 or Tromsø 7, respectively, or by levels of time between MI and the participation date

Table 1 Baseline characteristics by cohorts: the Tromsø Study 1994–2016

Characteristics	Cohort I, 1994–2008		Cohort II, 2007–2016	
	Total cohort	MI cohort	Total cohort	MI cohort
N	10 089	396	8543	131
Age (years)	46.8 (11.7)	56.1 (8.7)	57.4 (10.5)	64.1 (9.5)
Male (%)	45.3 (4575)	67.4 (267)	45.3 (3874)	66.4 (87)
Total cholesterol (mmol/L)	6.1 (1.3)	7.0 (1.1)	5.7 (1.1)	6.1 (1.0)
Low-density lipoprotein cholesterol (mmol/L)	3.9 (1.2)	4.8 (1.0)	3.4 (1.0)	4.0 (0.9)
High-density lipoprotein cholesterol (mmol/L)	1.5 (0.4)	1.4 (0.4)	1.5 (0.4)	1.4 (0.3)
Triglycerides (mmol/L)	1.5 (1.0)	2.0 (1.1)	1.5 (0.9)	1.7 (0.9)
Systolic blood pressure (mm Hg)	133 (18.0)	145 (20.0)	133 (21.6)	146 (23.6)
Diastolic blood pressure (mm Hg)	78.1 (11.6)	85.6 (11.4)	77.6 (10.5)	82.5 (10.6)
Body mass index (kg/m ²)	25.3 (3.7)	26.7 (3.4)	26.8 (4.2)	27.8 (4.5)
Daily smoking (%)	33.6 (3388)	44.2 (175)	17.9 (1517)	31.3 (41)

Values are mean (SD) or per cent (number).
MI, myocardial infarction.

in Tromsø 6 or Tromsø 7, respectively. Linear regression models were also used to calculate age-adjusted means between different groups. Logistic regression was used to test age-adjusted gender differences in achievement of treatment targets.

RESULTS

Mean age at first MI was 67 years in women and 63 years in men in MI-cohort I and 71 years in women and 65 years in men in MI-cohort II. Differences between the total and the MI-cohort for each period are presented in [table 1](#).

In MI-cohort I, the age-adjusted mean systolic blood pressure was 146.9 and 144.3 mm Hg at baseline ($P=0.22$), and 147.3 and 140.2 mm Hg at the second screening ($P=0.0048$), in women and men, respectively. The age-adjusted mean change in systolic blood pressure was 0.4 (95% CI -3.7 to 4.5) mm Hg in women and -4.1 (95% CI -7.0 to -1.3) mm Hg in men (P value for sex difference= 0.083)

([table 2](#)). In MI-cohort II, the age-adjusted mean systolic blood pressure was 146.5 and 146.5 mm Hg at baseline ($P=0.98$), and 138.6 and 133.5 mm Hg at the second screening ($P=0.29$), in women and men, respectively. The mean decrease in systolic blood pressure was -7.9 (95% CI -15.5 to -0.4) mm Hg in women and -13.0 (95% CI -18.3 to -7.7) mm Hg in men (P value for sex difference= 0.28) ([table 2](#)).

In MI-cohort I, the age-adjusted mean diastolic blood pressure was 84.7 and 86.0 at baseline ($P=0.27$), and 75.3 and 77.4 mm Hg at the second screening ($P=0.071$), in women and men, respectively. The age-adjusted mean decrease in diastolic blood pressure was -9.4 (95% CI -11.6 to -7.3) mm Hg in women and -8.6 (95% CI -10.1 to -7.1) mm Hg in men (P value for sex difference= 0.41) ([table 3](#)). In MI-cohort II, the age-adjusted mean diastolic blood pressure was 78.9 and 84.3 mm Hg at baseline ($P=0.007$), and 73.4 and 73.7 mm Hg at the

Table 2 Systolic blood pressure levels after first-ever myocardial infarction (MI) by cohort, sex and age: the Tromsø Study 1994–2016

Age at MI	MI-cohort I, 1994–2008				MI-cohort II, 2007–2016			
	N	1994–1995	2007–2008	Change (95% CI)	N	2007–2008	2015–2016	Change (95% CI)
Overall	396	145.2 (20.0)	142.5 (24.1)	-2.7 (-5.0 to -0.4)	131	146.5 (23.6)	135.2 (26.1)	-11.3 (-15.5 to -7.1)
<65 years	217	141.2 (18.7)	137.6 (21.4)	-3.6 (-6.5 to -0.6)	54	137.9 (21.3)	128.8 (17.2)	-9.1 (-14.7 to -3.5)
≥65 years	179	150.0 (20.6)	148.4 (26.0)	-1.6 (-5.2 to 2.1)	77	152.5 (23.4)	139.7 (30.1)	-12.9 (-18.9 to -6.8)
Women								
Crude	129	149.0 (24.4)	149.7 (28.0)	0.7 (-4.1 to 5.5)	44	149.8 (28.4)	141.1 (27.8)	-8.7 (-14.8 to -2.6)
Age-adjusted	129	146.9 (24.4)	147.3 (28.0)	0.4 (-3.7 to 4.5)	44	146.5 (28.4)	138.6 (27.8)	-7.9 (-15.5 to -0.4)
Men								
Crude	267	143.3 (17.3)	139.0 (21.2)	-4.3 (-6.8 to -1.8)	87	144.8 (20.7)	132.2 (24.8)	-12.6 (-18.2 to -7.0)
Age-adjusted	267	144.3 (17.3)	140.2 (21.2)	-4.1 (-7.0 to -1.3)	87	146.5 (20.7)	133.5 (24.8)	-13.0 (-18.3 to -7.7)

Values are number, mean (SD or 95% CI) mm Hg.

Table 3 Diastolic blood pressure levels after first-ever myocardial infarction (MI) by cohort, sex and age: the Tromsø Study 1994–2016

Age at MI	MI-cohort I, 1994–2008				MI-cohort II, 2007–2016			
	N	1994–1995	2007–2008	Change (95% CI)	N	2007–2008	2015–2016	Change (95% CI)
Overall	396	85.6 (11.4)	76.7 (11.0)	–8.9 (–10.1 to –7.6)	131	82.5 (10.6)	73.6 (12.4)	–8.9 (–11.3 to –6.6)
<65 years	217	85.6 (11.8)	78.2 (10.8)	–7.3 (–9.1 to –5.6)	54	83.4 (13.0)	75.6 (11.0)	–7.9 (–11.2 to –4.5)
≥65 years	179	85.7 (10.9)	74.9 (11.0)	–10.8 (–12.5 to –9.0)	77	81.9 (8.60)	72.2 (13.2)	–9.7 (–13.0 to –6.4)
Women								
Crude	129	85.2 (13.0)	74.8 (11.8)	–10.4 (–12.7 to –8.1)	44	79.1 (9.1)	72.8 (10.9)	–6.3 (–9.7 to –2.9)
Age-adjusted	129	84.7 (13.0)	75.3 (11.8)	–9.4 (–11.6 to –7.3)	44	78.9 (9.1)	73.4 (10.9)	–5.5 (–9.7 to –1.4)
Men								
Crude	267	85.8 (10.5)	77.6 (10.5)	–8.1 (–9.6 to –6.7)	87	84.2 (11.0)	74.0 (13.1)	–10.3 (–13.3 to –7.2)
Age-adjusted	267	86.0 (10.5)	77.4 (10.5)	–8.6 (–10.1 to –7.1)	87	84.3 (11.0)	73.7 (13.1)	–10.6 (–13.6 to –7.7)

Values are number, mean (SD or 95% CI) mm Hg.

second screening ($P=0.89$), in men and women, respectively. The mean decrease in diastolic blood pressure was -5.5 (95% CI -9.7 to -1.4) mm Hg in women and -10.6 (95% CI -13.6 to -7.7) mm Hg in men (P value for sex difference= 0.056) (table 3).

In MI-cohort I, the age-adjusted prevalence of antihypertensive drug use was 11.8% in women and 8.3% in men at baseline, and 88% in women and 87% in men at the second screening. In MI-cohort II, the age-adjusted prevalence of antihypertensive drug use was 31% and 30% at baseline, and 76% and 81% at the second screening in women and men, respectively.

Table 4 shows the proportion of MI patients achieving the treatment target for prevention of recurrent events (systolic blood pressure <140 mm Hg (130 mm Hg if diabetic) and diastolic blood pressure <90 mm Hg (80 mm Hg if diabetic)). In MI-cohort I, the treatment target was achieved by 35% of the women compared with 52% of the men (age-adjusted $P=0.046$). In MI-cohort II, the treatment target was achieved by 50% of the women compared with 54% of the men (age-adjusted $P=0.68$). No consistency was found between blood pressure change and time interval between first-ever MI and second screening (online supplementary table 2–5).

DISCUSSION

In this study of MI patients from a general population followed in two study periods, we found an overall low achievement of the blood pressure treatment target, as well as some gender disparities in mean levels of blood pressure and treatment achievement.

Prevalence of antihypertensive drug use and overall achievement of treatment targets

Guidelines for control of various CVD risk factors for prevention of recurrent events have changed over time since the first Joint European Society guidelines (JESC) from 1994.¹⁵ An overall treatment target for blood pressure of 140/90 mm Hg was introduced in the JESC2

publication in 1998,¹⁶ with an additional treatment target of 130/80 mm Hg for very high-risk individuals (including patients with established CVD and/or diabetes) suggested from JESC3 in 2003¹⁷ and further. Although extensively discussed, these continued to be the overall treatment goals throughout this study period^{17–19} and further in the most recently published JESC6 from 2016.²⁰ In the third EUROASPIRE study conducted in 2006–2007,²¹ 80% of the MI patients used beta-blockers and 71% used ACE-inhibitors or angiotensin II receptor blockers, and 44% of all MI patients reached the treatment target of 140/90 mm Hg (or 130/80 mm Hg for patients with diabetes). In the fourth and most recent EUROASPIRE study from 2015,² the overall prevalence of all antihypertensive drug use was 78%, and 56% of all MI patients reached the treatment target of 140/90 mm Hg (or 130/80 mm Hg for patients with diabetes). On average, the proportion of MI patients achieving the treatment targets and reporting use of antihypertensive drugs was similar in our two study periods and the coinciding third and fourth EUROASPIRE studies.

Gender differences in secondary prevention

The higher incidence of MI in men compared with women has resulted in less awareness of prevention and treatment in women.²² A publication from EUROASPIRE III showed that women were 63% less likely to achieve appropriate secondary prevention than men,²³ and other previously published studies also show that women are less likely to use antihypertensive drugs and to achieve treatment targets for blood pressure control than men.^{13 23} In our study, there was a tendency (although not statistically significant in all analysis) towards women having higher systolic blood pressure, less decrease in blood pressure, less reported use of antihypertensives and lower achievement of the treatment targets at follow-up. Treatment guidelines do not differ by sex, and meta-analyses of the effectiveness of antihypertensive drug therapy do not report gender differences.¹² Gender

Table 4 Blood pressure levels after first-ever myocardial infarction (MI) by blood pressure levels in 2007–2008 or 2015–2016, respectively: the Tromsø Study 1994–2016

Blood pressure treatment goal	MI-cohort I, 1994–2008				MI-cohort II, 2007–2016			
	N	%	Systolic blood pressure change	Diastolic blood pressure change	N	%	Systolic blood pressure change	Diastolic blood pressure change
Overall								
No	213	53.8	7.8 (4.7 to 10.8)	-6.9 (-8.6 to -5.1)	62	47.3	-2.7 (-7.1 to 1.8)	-4.5 (-7.4 to -1.6)
Yes	183	46.2	-14.8 (-17.4 to -12.2)	-11.2 (-12.9 to -9.5)	69	52.7	-19.1 (-25.5 to -12.6)	-12.9 (-16.3 to -9.5)
Women								
No	84	65.1	8.2 (2.3 to 14.2)	-8.8 (-11.7 to -6.0)	22	50.0	-2.2 (-10.2 to 5.8)	-2.3 (-6.9 to 2.3)
Yes	45	34.9	-13.4 (-19.6 to -7.2)	-13.3 (-17.3 to -9.4)	22	50.0	-15.2 (-23.8 to -6.7)	-10.3 (-14.9 to -5.7)
Men								
No	129	48.3	7.5 (4.2 to 10.7)	-5.6 (-7.8 to -3.4)	40	46.0	-2.9 (-8.4 to 2.5)	-5.7 (-9.4 to -1.9)
Yes	138	51.7	-15.3 (-18.0 to -12.5)	-10.5 (-12.4 to -8.7)	47	54.0	-20.8 (-29.4 to -12.3)	-14.1 (-18.6 to -9.7)

Values are number, mean (95% CI) mm Hg or per cent (number). Blood pressure treatment target: systolic blood pressure ≤ 140 (≤ 130 if diabetic) mm Hg and diastolic blood pressure ≤ 90 (≤ 80 if diabetic) mm Hg.

differences in antihypertensive drug use could be the result of lower initiation of treatment or lower adherence to treatment. Lower treatment initiation after MI among women compared with men has been reported in several studies.^{24 25} Gender differences in adherence to antihypertensive drug use after MI show various results; some studies report women to be less adherent to antihypertensive drug use compared with men,^{24 26 27} others do not report gender differences in antihypertensive drug adherence.²⁷ Overall, women tend to experience MI somewhat later in life than men, and elderly MI patients are less likely to receive secondary prevention, although treatment of the elderly is highly beneficial.²⁸ This could suggest an age–sex interaction responsible for the lower use of secondary prevention in women.^{24 25} Lower initiation of antihypertensive treatment in women compared with men, and higher blood pressure at hospital discharge, has also been found in young MI patients.²⁵

Study limitations

Only 44% and 55% of the surviving MI patients in the original cohorts attended Tromsø 6 and Tromsø 7, respectively. Non-responders among MI patients in the original Tromsø 4 and Tromsø 6 cohorts had higher baseline systolic blood pressure than responders. We assume that participants that did not attend Tromsø 6 or Tromsø 7, respectively, due to death, disease or other causes were more prone to have a less favourable blood pressure profile. Thus, our results can be biased towards more favourable blood pressure levels than in the average MI population. Further, no analyses of predictors for change in blood pressure or medication use were included in this study.

CONCLUSION

In this descriptive study of change in blood pressure after MI over time, we found an overall low achievement of the long-standing treatment target, consistent with previous studies. A larger proportion of women reached the treatment goals in the last study period compared with the first. However, compared with men, women had higher follow-up mean systolic blood pressure levels in the second study period. The findings call for better treatment strategies for secondary prevention in both women and men.

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Contributors LAH and TW contributed to the conception and design. TW performed the data analysis. LAH drafted the manuscript. AEE, M-LL, EBM, AN, IN and TW critically revised the manuscript. All authors contributed to the acquisition

and interpretations of data, and gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

Competing interests None declared.

Patient consent Obtained.

Ethics approval The Tromsø Study has been approved by the Regional Committee of Medical and Health Research Ethics (REC North) (approval number 2015/1778) and the Norwegian Data Protection Authority, and performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement The data that support the findings of this study are available from the Tromsø Study but restrictions apply to the availability of these data, which were used under licence for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of the Tromsø Study.

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