Cardiovascular risk management in old age

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Time-trends in preventive drug treatment after myocardial infarction in community-dwelling elderly patients

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Submitted

Abstract

Background: Undertreatment with preventive drugs in elderly patients with a history of myocardial infarction ('post-MI patients') is widespread.
Aim: To explore time-trends in the effect of aging on preventive drug treatment in community-dwelling elderly post-MI patients.
Design of study: Retrospective patient record study.
Setting: Eighteen general practices in the Netherlands.
Methods: At one time point in the years 2000, 2004 and 2007, respectively, complete prescription records about the preceding year were obtained for all post-MI patients aged ≥60 years. In three strata by age, the availability of antithrombotics, statins, beta-blockers and ACE-inhibitors for >50% of days in the preceding year was assessed.
Results: The prevalence of prior myocardial infarction in patients aged ≥60 years in the consecutive years was 234/3717 (6.3%), 266/4489 (5.9%) and 342/5995 (5.7%), respectively. Combination therapy with at least 3 out of 4 drugs increased over time, from 31% (CI 95% 26-37) of all patients in 2000 to 59% (CI 95% 53-64) of patients in 2007. This increase, particularly in treatment with statins, occurred in all age strata: from 38% to 70% (relative increase 1.8) in post-MI patients aged 60-69 years, from 31% to 54% (relative increase 1.7) in those aged 70-79, and from 19% to 48% (relative increase 2.5) in post-MI patients aged ≥80 years.
Conclusion: Preventive drug treatment in community-dwelling post-MI patients aged ≥60 years showed a steep increase over a recent seven-year period. Although in the oldest old (≥80 years) the greatest relative increase was observed, they still have most room for improvement.
Keywords: Age, Myocardial Infarction, Drug Therapy, Secondary Prevention, General Practice.

What is already known on this topic
- Although age restrictions have disappeared from current guidelines on secondary prevention following myocardial infarction, under treatment of elderly patients is commonplace

What this study adds
- Preventive drug treatment following myocardial infarction in community-dwelling patients aged ≥60 years showed a steep increase over a recent seven-year period
- In the oldest old (≥80 years) the greatest relative increase was observed, but they continue to have most room for improvement
- General practitioners should periodically review the preventive drug regimens of their elderly post-MI patients to ensure optimisation with current guidelines

Introduction

In the Netherlands, as in other industrialized societies, cardiovascular disease remains the leading cause of death, accounting for one third of all deaths in adults.[1] In old age, myocardial infarctions play a key role in cardiovascular mortality, not only due to a high incidence, but also due to an increased one-year mortality.[1-3]

With respect to secondary prevention following a myocardial infarction (MI), treatment with a combination of four preventive drugs is nowadays believed to result in a cumulative risk reduction of about 75% for recurrent cardiovascular events (cardiovascular death, strokes and myocardial infarctions).[4;5] Thus, following current guidelines, patients with a history of MI ('post-MI patients') should receive this combination therapy, namely antithrombotic drugs (antiplatelets and/or, if applicable, anticoagulants), statins, beta-blockers, and angiotensin-coverting-enzyme (ACE)-inhibitors.[6-10] No age restrictions apply, although legitimate reasons for non-prescribing in (very) old age may exist. In view of the high absolute risks of new cardiovascular (fatal and non-fatal) events with advancing age, the 'number needed to treat' actually becomes even lower with advancing age: the geriatric paradox.[11] Furthermore, a recent large cohort study in more than 5000 post-MI patients confirmed earlier reports that adequate combination therapy was independently associated with lower one-year mortality, and that this effect was as strong in those over 75 years of age as it was in younger patients.[5;12] Nevertheless, there is evidence to suggest that under treatment with preventive drugs in elderly post-MI patients is widespread.[13-16] To date however, time-trends in drug treatment in elderly post-MI patients, with respect to different age groups of elderly patients, have not been described.

Thus, to investigate time-trends (2000-2007) in preventive drug treatment in community-dwelling elderly with a history of myocardial infarction, and to study the effect of increasing age, we performed a population-based study in all post-MI patients aged ≥60 years in eighteen general practices in the Netherlands.

Methods

To gain more insight in changes over the last decade in drug treatment following myocardial infarction, three points in time were chosen with an approximately 4-year interval (August 2000, July 2004 and January 2008). At these time points, from here referred to as years 2000, 2004 and 2007, all patients 60 years and over with the diagnosis 'myocardial infarction' confirmed in their medical records (code K75 according to the International Classification of Primary Care[17]) were selected from the Registration Network of General Practices associated with Leiden University (RNUH-LEO), a longitudinal central database of electronic medical records of all patients listed in eighteen

ordinary general practices in the western part of the Netherlands.[18] From these records, data were extracted about each patient's age, date of MI-diagnosis and complete records of drug prescriptions during the year preceding the abovementioned three time points. Patients could reappear in consecutive samples.

Four categories of preventive cardiovascular drugs were selected by Anatomical Therapeutic Chemical classification (ATC)-code, namely antithrombotics (anticoagulants or antiplatelets; ATC-codes B01AA* or B01AC*), statins (C10AA*), beta-blockers (C07*) and ACE-inhibitors (C09A* or C09B*). Availability of antithrombotics, statins, beta-blockers and ACE-inhibitors (in days) in the preceding year was calculated by dividing the total number of prescribed pills in a year by the prescribed daily dose. If this resulted in ≥183 days per year of pill availability (corresponding to >50% of the year), preventive treatment with this specific drug was arbitrarily considered adequate. For anticoagulants availability was set at 100%, regardless of the amount prescribed in the preceding year, since the daily dosage of antithrombotics usually varies. Per patient, adequate treatment with various combinations of the four classes of drugs was assessed and categorized as '0 drugs', '1-2 drugs' and '3-4 drugs'. Lacking a generally accepted definition of 'adequate combination therapy', this was defined as 'adequate treatment with at least three out of four categories of preventive drugs'.

Data analysis

In three cross-sectional datasets (years 2000, 2004 and 2007) and within strata by age (60-69, 70-79 and ≥80 years), we calculated the proportion of patients who were adequately treated with various combinations of preventive drugs ('0', '1-2' or '3-4' drugs), including 95% confidence intervals. Within the same age strata, proportions and 95% confidence intervals were calculated for adequate treatment with each specific drug category: antithrombotics, statins, beta-blockers and ACE-inhibitors. Within age groups, at the three time points, we also determined the proportion of patients in the category 'time since (last) MI > 5 years'. Since time and age trends are intertwined in all analyses, no additional significance testing was feasible.

All analyses were performed using SPSS 14.0 for Windows (SPSS inc., Chicago, IL, USA). Confidence intervals were calculated using a Spreadsheet for the Analysis of Epidemiologic Data (Episheet, version of September 17, 2003) in Microsoft Excel.[19]

Results

The total population under observation (all patients aged ≥60 years) in 2000 was 3717, in 2004 the population was 4489, and in 2007 it was 5995. The proportions of post-MI patients were 6.3% (234/3717) in 2000, 5.9% (266/4489) in 2004 and 5.7% (342/5995) in 2007.

Table 1. Characteristics and preventive drug treatment in patients aged ≥60 years with a history of myocardial infarction (total n=842), at three time points, in percentages (95% confidence intervals).

	2000 (n=234)	2004 (n=266)	2007 (n=342)
Male gender	70 (64-76)	74 (69-79)	71 (66-76)
Age group			
60-69 yrs	43 (37-50)	44 (39-50)	41 (36-46)
70-79 yrs	34 (28-40)	34 (29-40)	34 (29-39)
≥80 yrs	23 (18-28)	21 (17-27)	25 (21-30)
Time since last myocardial infarction			
0-5 yrs	41 (35-47)	34 (28-40)	32 (28-38)
>5 yrs	59 (53-65)	66 (60-72)	68 (62-72)
Adequate treatment with preventive drugs*			
Antithrombotics	81 (75-85)	85 (80-89)	87 (83-91)
Statins	43 (37-49)	65 (59-71)	70 (65-74)
Beta-blockers	38 (32-45)	51 (45-57)	57 (52-62)
ACE-inhibitors	30 (24-36)	35 (30-41)	44 (39-50)
Numbers of preventive drugs*			
0	11 (7.7-16)	9.0 (6.1-13)	7.9 (5.5-11)
1-2	58 (51-64)	41 (35-47)	33 (29-38)
3-4	31 (26-37)	50 (44-56)	59 (53-64)

* Pills available for more than 50% of days in preceding year

The characteristics of all post-MI patients at the three time points are summarized in Table 1. The majority of patients were men, and approximately every fourth patient was 80 years or over. The median time since the last myocardial infarction was 7.8 years (IQR 2.9-13.5) in 2000, 9.3 years (IQR 4.7-14.5) in 2004 and 9.7 years (IQR 4.4-14.9) in 2007. The time since the last myocardial infarction was >5 years in 59%, 66% and 68% of all post-MI patients at the consecutive time points. In general, more than 80% of all post-MI patients were treated with antithrombotics, with a small increase over time. The treatment with beta-blockers and ACE-inhibitors showed an increase over time, with 57% of all post-MI patients on beta-blockers in 2007 and 44% of patients on ACE-inhibitors. Treatment with statins almost doubled over time, from 43% of all patients in 2000 to 70% of patients in 2007. Adequate combination therapy also showed a marked increase over time, with 31% of post-MI patients receiving at least three out of four drugs in 2000, almost doubling to 59% of patients receiving this therapy in 2007. At all three time

points, some 10% of all patients were not prescribed any of the four recommended drugs.

Table 2 presents preventive combination therapy in different age groups at the three time points. In all age groups adequate combination therapy increased over time, and was highest (70% of patients) in 2007 for patients aged 60-69 years. The relative increase from 2000 to 2007 was 1.8 in patients aged 60-69 years, 1.7 in patients aged 70-79 years, and 2.5 in patients aged ≥80 years. At all time points, the proportion of patients aged ≥80 years who were treated with at least three out of four drugs was less compared to the younger counterparts. In 2007 fewer than half of oldest old patients were on adequate combination therapy (48% of patients) (Figure 1).

Table 2. Preventive combination therapy* in patients aged ≥60 years with a history of myocardial infarction, depending on age group, at three time points, in percentages (95% confidence intervals).

	2000 (total n=234)	2004 (total n=266)	2007 (total n=342)
60-69 yrs	n=101	n=118	n=139
0 drugs	13 (7.7-21)	9.3 (5.3-16)	4.3 (2.0-9.1)
1-2 drugs	50 (41-59)	33 (25-42)	26 (19-39)
3-4 drugs	38 (29-47)	58 (49-66)	70 (62-77)
70-79 yrs	n=80	n=91	n=117
0 drugs	7.5 (3.5-15)	11 (6.1-19)	10 (6.0-17)
1-2 drugs	61 (50-71)	42 (32-52)	36 (28-45)
3-4 drugs	31 (22-42)	47 (37-57)	54 (45-63)
≥80 yrs	n=53	n=57	n=86
0 drugs	13 (6.5-25)	5.3 (1.8-14)	11 (5.6-19)
1-2 drugs	68 (55-79)	54 (42-67)	42 (32-52)
3-4 drugs	19 (11-31)	40 (29-53)	48 (37-58)

* Pills available for more than 50% of days in preceding year

Table 3 shows a specification of preventive drug treatment in post-MI patients in different age groups at the three time points. Treatment with antithrombotics was high in all age groups, already in 2000. In 2007 78% of post-MI patients aged 60-69 years were treated with statins, increasing from 55% of patients in that age group in 2000. In contrast, 55% of post-MI patients aged ≥80 years were on statins in 2007, but this was an increase from just 17% of patients in 2000. For beta-blockers and ACE-inhibitors moderate increases of treatment were observed in all age groups between 2000 and 2007. However,

treatment with these classes of drugs remained relatively low at all ages compared to treatment with antithrombotics and statins.

Table 3. Specification of preventive drug treatment* in patients aged ≥60 years with a history of myocardial infarction, depending on age group, at three time points, in percentages (95% confidence intervals).

	2000 (total n=234)	2004 (total n=266)	2007 (total n=342)
60-69 yrs	n=101	n=118	n=139
Antithrombotics	76 (67-83)	82 (74-88)	90 (84-94)
Statins	55 (45-64)	75 (67-82)	78 (70-83)
Beta-blockers	41 (32-50)	53 (44-62)	63 (55-71)
ACE-inhibitors	28 (20-37)	36 (28-45)	52 (41-62)
70-79 yrs	n=80	n=91	n=117
Antithrombotics	85 (76-91)	86 (77-91)	85 (77-90)
Statins	45 (35-56)	66 (56-75)	71 (62-79)
Beta-blockers	34 (24-45)	48 (38-58)	57 (48-66)
ACE-inhibitors	34 (24-45)	29 (20-39)	39 (30-48)
≥80 yrs	n=53	n=57	n=86
Antithrombotics	83 (71-91)	90 (79-95)	87 (79-93)
Statins	17 (9.2-29)	42 (30-55)	55 (44-65)
Beta-blockers	42 (29-55)	51 (38-63)	48 (37-58)
ACE-inhibitors	26 (16-40)	42 (30-55)	41 (31-51)

* Pills available for more than 50% of days in preceding year

As indicated above, the overall proportion of relatively 'old' myocardial infarctions (>5 years) slowly increased over time, but this proportion showed no consistent trend over time when stratified by age: the proportions of patients with a time since last MI of > 5 years in age group 60-69 years were 55% (95% CI 46-65) in 2000, 59% (95% CI 49-67) in 2004 and 64% (95% CI 56-72) in 2007; in age group 70-79 years the proportions were 66% (95% CI 55-76), 77% (95% CI 67-84) and 71% (95% CI 62-78), respectively; and in patients aged ≥80 years the proportions were 57% (95% CI 43-69), 66% (95% CI 52-76) and 68% (95% CI 58-77), respectively. The observed differences in drug treatment between age groups at each time point are therefore most likely not explained by differences in time since last MI.

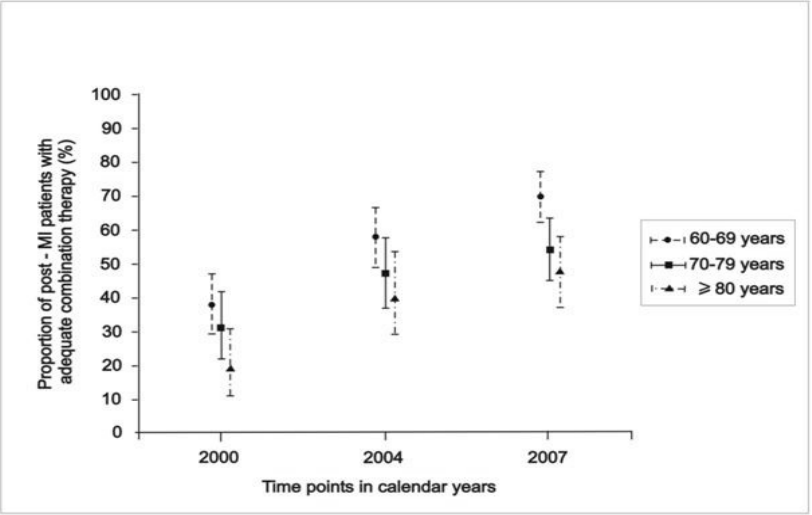

Figure 1. Proportion of post-MI patients on adequate combination therapy (at least three out of four categories of preventive drugs) at three points in time, according to age group.

Discussion

Summary of main findings

This study shows that adequate combination therapy for the prevention of recurrent cardiovascular events in patients aged 60 years and over with a history of myocardial infarction doubled over a recent seven-year period: from 31% of patients receiving adequate combination therapy in 2000 to 59% of patients in 2007. In all age groups considerable improvements were observed, with the greatest relative increase in patients aged ≥80 years. However, absolute differences in treatment between age groups were equally clear: in 2007 more than two-thirds of all patients aged 60-69 years were on adequate combination therapy, as opposed to less than half of the patients aged ≥80 years. The oldest old patients therefore still have most room for improvement, as treatment with statins, beta-blockers and ACE-inhibitors lagged behind the treatment with these drugs in their younger counterparts.

Comparison with existing literature

Our data are in line with those from the DIN-LINK database in the UK, in which time-trends between 1994 and 2005 in treatment with preventive drugs were studied.[16] By 2005 only 27% of all patients aged ≥85 years with ischemic heart disease received adequate combination treatment. The authors concluded that "it is apparent that the treatment gap is greatest in older subjects where

the event rate is also highest and thus the greatest mortality benefits may be gained".[16] A similar conclusion was drawn from another UK study of older patients using medical record data from 2003.[14] Our study concurs with these earlier findings but also goes further to describe age specific cross-sectional data at three different time points in the same (dynamic) source-population, thus allowing time-trends within specific age strata of elderly patients to be assessed.

Clarification of findings

The increase over time in treatment with preventive drugs in elderly patients following myocardial infarction can partly be explained by changes in medical guidelines. For years only antithrombotics were advised, with recommendations expanding to include beta-blockers[20] and statins[21] in the last two decades. Ultimately ACE-inhibitors were added to the list of preventive drugs for post-MI patients, irrespective of left ventricular function.[22;23] Furthermore there has been gradual disappearance of upper age limits for preventive drug therapy, as evidence grew that such drugs were also, even particularly, effective in older age, at least up to the age of 80 years. [6;9;24] Together these changes to recommendations may in part underlie the overall increase of combination therapy and may, at the same time, explain the continual lagging behind of combination therapy in the oldest old.

Another explanation for less preventive drug therapy in the oldest old may relate to a higher prevalence of co-morbidities, and a concomitant higher risk of adverse events, contra-indications or potential interactions with other medication, as well as occasionally conflicting priorities. However in our study, adequate combination therapy in patients aged ≥80 years in 2004 was already at a higher level than it was in patients aged 60-69 years in 2000 (Figure 1). Therefore, it appears that the gap observed between these age groups in 2000 was more likely attributable to 'ageism' than strictly medical considerations at that time. Furthermore, if strictly medical considerations were involved, we expected that this would be particularly apparent in the observed treatment with antithrombotics, which occupy a key position on consensus-based lists of potentially inappropriate drug treatments in the elderly.[25] In our study, however, treatment with antithrombotics in the oldest old was as high as in their younger counterparts at all time points. This observation also suggests that 'very old age' *per* se is an independent factor in the under treatment of post-MI patients aged ≥80 years. More qualitative research into the motives of prescribing doctors is needed to confirm this hypothesis.

Strengths and limitations of this study

Since the doctors from the registration network (RNUH-LEO) are all trained in the systematic registration process, we are confident that all post-MI patients were correctly identified. Furthermore, accurate data from the electronic records of prescriptions of all drugs, irrespective of the prescribing doctor, increases the internal validity of our study. In contrast to this, one may argue that, because the general practitioners involved in our study worked in health

care centres and, in a few instances, in an academic institution, implementation of guidelines may have been more than usual, thus hampering the generalization of our findings. However, if this were true, we would expect the treatment gaps that we observed to be bigger nationwide, thus strengthening rather than weakening our conclusions. Another possible limitation of our study is the definition of 'adequate treatment' (availability >50% of the days in the previous year), which may be considered a low threshold and does not take patients' adherence to treatment into account. However, there is no general consensus in the research community about such a definition and in fact, all studies use different ones.[14;16]

Implications for future research and clinical practice
Our findings suggest that, although over the last seven years the oldest old post-MI patients are catching up with their younger counterparts, they still have most room for improvement. On referring these patients back to primary care, the medical specialist should therefore recommend that the general practitioner periodically review the patients' preventive drug regimens to ensure optimisation with the latest guidelines. Accurate patient registration systems, doctors' collaboration with pharmacists ('vigilance') and regular pharmacotherapeutic meetings with relevant parties may be helpful to achieve adequate combination therapy in patients with a history of myocardial infarction. In addition, transparent guidelines for both cardiologists and general practitioners are necessary, as well as optimal levels of communication between them.

In conclusion, over a recent seven-year period an impressive doubling was observed in adequate combination therapy for prevention of cardiovascular events in the population of post-MI patients ≥60 years. Although in the oldest old (≥80 years) the greatest relative increase was observed, they still have most room for improvement: in 2007 still less than 50% of these patients were on adequate combination therapy according to current guidelines. Increases were predominantly seen for statins, followed by beta-blockers and ACE-inhibitors.

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