International Journal of Cardiology 294 (2019) 6–12

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Mortality following first-time hospitalization with acute myocardial infarction in Norway, 2001–2014: Time trends, underlying causes and place of death

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ARTICLE INFO

Article history:
Received 18 March 2019
Received in revised form 19 July 2019
Accepted 28 July 2019
Available online 31 July 2019

Keywords:
Acute myocardial infarction
Norway
Epidemiology
Survival
Cause of death
Place of death

ABSTRACT

Background: Trends on cause-specific mortality following acute myocardial infarction (AMI) are poorly described and no studies have analyzed where do AMI patients die.
We analyzed trends in 28-day and one-year mortality following an incident AMI with focus on changes over time in the underlying cause and place of death.
Methods: We identified in the 'Cardiovascular Disease in Norway' Project all patients 25+ years, hospitalized with an incident AMI in Norway, 2001–2014. Information on date, underlying cause and place of death was obtained from the Cause of Death Registry.
Results: Of 144,473 patients included in the study, 11.4% died within first 28 days. The adjusted 28-day mortality declined by 5.2% per year ($p_{trend} < 0.001$).
Of 118,881 patients surviving first 28 days, 10.1% died within one year. The adjusted one-year CVD mortality declined by 6.2% per year ($p_{trend} < 0.001$) while non-CVD mortality increased by 1.4% per year ($p_{trend} < 0.001$), mainly influenced by increased risk of dying from neoplasms.
We observed a shift over time in the underlying cause of death toward more non-CVD deaths, and in the place of death toward more deaths occurring in nursing homes.
Conclusions: We observed a decline in 28-day mortality following an incident AMI hospitalization. One-year CVD mortality declined while one-year risk of dying from non-CVD conditions increased. The resulting shift toward more non-CVD deaths and deaths occurring outside a hospital need to be considered when formulating priorities in treating and preventing adverse events among AMI survivors.

1. Introduction

Coronary heart disease (CHD) is one of the leading causes of death, claiming nearly nine million deaths globally in 2015 [1]. Acute myocardial infarction (AMI) is a well-defined, life-threatening condition whose outcomes are influenced by many factors, including patient's age, severity of disease, co-existing medical conditions, burden of risk factors as well as treatment quality and secondary prevention measures. These factors typically change over time, and may influence AMI prognosis in different directions and to various extents.

Results from national [2–6] and regional [7–10] studies indicate a steady decline in short-term mortality following AMI. Analyses focusing on longer-term mortality on the other hand, have yielded mixed results. Declining mortality rates were observed in Denmark [4], Sweden [11], England and Wales [12] and Spain [13], while US studies reported stable [8], or even increasing [7] mortality rates following an AMI.

Most studies have focused on all-cause mortality and fewer have analyzed trends of CVD [2,7,11] and non-CVD mortality separately [2,7]. These studies suggested that the decline in CVD mortality, is partly offset by increased non-CVD mortality. However, data on mortality trends for various non-CVD conditions are lacking.

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https://doi.org/10.1016/j.ijcard.2019.07.084
0167-5273/

Many deaths involving AMI patients occur outside a hospital [14]. Out-of-hospital deaths (OHD) are related to disease severity, awareness of coronary signs and symptoms among patients and family members as well as time lap from symptoms' onset to accessing specialized care. To the best of our knowledge, no previous studies have analyzed trends in mortality following AMI by place of death.

The purpose of the present study was to i) examine trends in 28-day and one-year mortality among patients hospitalized with an incident AMI in Norway during 2001–2014 and ii) describe changes over time in the distribution of underlying cause of death and place of death, among 28-day survivors of an AMI.

2. Methods

2.1. Study design and setting

We conducted a population-based, nationwide observational study using data from the 'Cardiovascular Disease in Norway' (CVDNOR) Project. Detailed information on data collection and content is provided here [15] and at www.cvdnor.no. All hospital stays with a CVD-related diagnosis [International Classification of Diseases (ICD) 9 codes, 390–459 or ICD-10 codes, I00–I99] were retrieved from Patient Administrative Systems (PAS) in Norway for the period 1994–2009 [16]. The project was updated with new data through 2014 [17] from the Norwegian Patient Registry [18]. Data include patient's age, sex, admission and discharge dates, up to 20 diagnoses as well as diagnostic or treatment medical procedures performed at hospitals. Information on deaths (including date, underlying cause and place of death) was obtained from the Cause of Death Registry. Information on the highest attained education was obtained from the National Education Database. Different data sources were linked at the individual level, using a unique, project-specific identification code.

2.2. Eligible patients, study population and outcomes

We identified 147,030 patients, with an incident (first) AMI hospitalization (ICD-9 code 410 and ICD-10 codes I21 and I22) as primary discharge diagnosis. A hospitalization was defined as 'incident' after excluding the possibility of previous AMI hospitalizations for the same individual in the preceding seven years [16].

We excluded from the analyses patients i) younger than 25 years ($n = 112$) or older than 100 years ($n = 80$), ii) patients not matching with Population Registry data ($n = 1383$) and iii) patients with unusual length of stay (LOS) for the incident AMI (upper 99th percentile; $n = 1445$). The final study population comprised 144,473 patients; 90,884 (62.9%) men and 53,589 (37.1%) women.

The study endpoints were i) death within 28 days of incident AMI admission ('28-day mortality') and ii) death within one year of incident AMI admission, among patients surviving the first 28 days ('29–365 day mortality'). As previously done [4,11,19], we chose to analyze 28-day and 29–365 day mortality separately.

We categorized the underlying cause of death into ten categories; CVD and eight most frequent non-CVD causes. Less frequent non-CVD causes were grouped in a separate category named 'Other' (Supplemental Table 1).

Place of death was categorized into in-hospital deaths and out-of-hospital deaths (OHD). The latter category was further divided into three subcategories; deaths happening in nursing homes and care institutions, deaths happening at home and deaths happening in public places or during transportation to a hospital.

2.3. Data quality

The quality (including sensitivity, specificity and positive predictive value) of AMI diagnosis in administrative databases is high [20]. The most recent study analyzing the quality of data on deaths based on a six-dimension performance index, ranked the Norwegian Cause of Death Registry in the best group, assigning it a score of 87.6 out of 100 [21].

2.4. Statistical analyses

Continuous variables are presented as mean and standard deviation (SD) or median and interquartile range (IQR). Categorical variables are presented as proportions.

We constructed Nelson-Aalen cumulative hazard curves for 28-day and 29–365 day mortality across seven time periods and calculated the corresponding p values of log-rank tests for linear trend.

Cox proportional hazards models explored changes over time in 28-day and 29–365 day, all-cause mortality. The assumption of proportionality was graphically checked using *.stphplot* command in STATA and found it not to be violated.

Changes over time in 29–365 day mortality by underlying cause of death and place of death were analyzed using Fine and Grey competing risk regression [22].

We did not conduct cause and place-specific analyses for 28-day mortality as early deaths are related to the underlying coronary condition (CVD in nature) and occur mostly in a hospital (94.3% in our data).

The year of AMI hospitalization was introduced in the models as a continuous variable. Hazard ratios (HRs) and sub-hazard ratios (SHRs in competing risk analyses) estimated the average annual change in mortality risk over the study period.

We present here results from i) unadjusted analyses ('unadjusted model') and ii) analyses adjusted for age, relevant co-existing medical conditions (diabetes mellitus [DM], hypertension, chronic pulmonary obstructive disease, heart failure, stroke, renal failure, valvular heart disease, atrial fibrillation and neoplasms) and level of education ('adjusted analyses'). Results from analyses adjusted only for age were almost identical to fully adjusted analyses.

Finally, multinomial logistic regression analyses explored changes over time in relative probability of dying i) due individual non-CVD causes compared to CVD and ii) outside a hospital compared to dying in a hospital only among study participants experiencing the study endpoint. The results of these analyses are expressed as relative risk ratios and corresponding 95% CIs.

We analyzed time trends in men and women separately as well as in total, adjusting the later analyses for sex.

The study complies with the Declaration of Helsinki [23] and was approved by the Regional Committee for Medical and Health Research Ethics, Health Region West (2009/825).

3. Results

A total of 144,473 patients hospitalized with an incident AMI were included in the study. Mean (SD) age was 70.8 (14.0) years. Compared to men, women were on average 8.7 years older ($p < 0.001$) (Table 1). The age-adjusted prevalence of hypertension, stroke, valvular heart disease and pulmonary edema were higher among women (all $p_{trend} < 0.001$) while men had a higher prevalence of renal failure and atrial fibrillation (both $p_{trend} < 0.001$) as well as rhythm (ventricular fibrillation -VF) and conduction (atrio-ventricular block -AVB) abnormalities (both $p_{trend} < 0.001$).

Over the study period, the proportion of men increased while the age on admission and length of AMI hospitalization shortened (Supplemental Table 2). Age and sex-adjusted prevalence of DM, hypertension, renal failure, valvular heart disease and AF increased while the prevalence of stroke, HF and neoplasms declined (Supplemental Table 2).

3.1. Time trends in mortality following acute myocardial infarction

3.1.1. 28-day mortality

Overall, 16,449 (11.4%) patients died during the first 28 days of follow up. The corresponding number of patients and proportions in men and women were 8575 (9.4%) and 7874 (14.7%), respectively. The adjusted 28-day mortality declined on average 5.7% per year (HR = 0.943; 95% CI, 0.938–0.949) in men and 4.5% per year (HR = 0.955; 95% CI, 0.949–0.961) in women (Table 2). The observed decline during 2001–2009 continued beyond 2009, and through 2014 (Supplemental Table 3).

3.1.2. 29–365 day mortality

Of 119,881 patients surviving the first 28 days, 12,124 (10.1%) died during days 29–365 of follow up. The corresponding number of patients and proportions in men and women were 6251 (8.1%) and 5873 (13.7%), respectively. The adjusted 29–365 day, all-cause mortality declined on average 3.6% per year (HR = 0.964; 95% CI, 0.950–0.970) in men and 3.2% per year (HR = 0.968; 95% CI, 0.961–0.975) in women (Table 2). The observed decline during 2001–2009 continued with a similar pace beyond 2009 and through 2014 (Supplemental Table 3).

3.2. Underlying cause of death

First, we analyzed trends in 29–365 day mortality by underlying cause of death among all AMI patients (Table 3). CVD mortality declined in both men (SHR = 0.934; 95% CI, 0.925–0.943) and women (SHR = 0.943; 95% CI, 0.934–0.952), On the contrary, non-CVD mortality increased in men (SHR = 1.013; 95% CI, 1.002–1.023) and women (SHR = 1.017; 95% CI, 1.005–1.029 in women), mainly contributed by increasing trends in mortality due to neoplasms and diseases grouped under the category 'Other' (Table 3). Overall trends were mainly influenced by trends observed during 2001–2009 (Supplemental Table 3).

Table 1
Baseline characteristics of patients admitted to hospital with an incident acute myocardial infarction, 2001–2014.

Patient's characteristics	Men ($n = 90,884$)	Women ($n = 53,589$)	Total ($n = 144,473$)
Age in years, mean (SD)	67.6 (13.6)	76.3 (12.8)	70.8 (14.0)
Length of hospitalization (days), median (IQR)	5 (4–9)	6 (4–10)	6 (4–9)
Co-existing medical conditions, *n* (%)			
Diabetes mellitus	12,749 (14.0)	7887 (14.7)	20,636 (14.3)
Hypertension	26,933 (29.6)	18,087 (33.8)	45,020 (31.2)
Renal failure	6806 (7.5)	3820 (7.1)	10,626 (7.4)
Chronic obstructive pulmonary disease	6557 (7.2)	4562 (8.5)	11,119 (7.7)
Valvular heart disease	5353 (5.9)	5444 (10.2)	10,797 (7.5)
Atrial fibrillation	13,214 (14.5)	9959 (18.6)	23,173 (16.0)
Stroke	1520 (1.7)	1341 (2.5)	2861 (2.0)
Heart failure	19,021 (20.9)	14,908 (27.8)	33,929 (23.5)
Neoplasms	4194 (4.6)	1934 (3.6)	6128 (4.2)
In-hospital AMI complications, *n* (%)			
Ventricular fibrillation	1745 (1.9)	598 (1.1)	2343 (1.6)
Pulmonary edema	660 (0.7)	694 (1.3)	1354 (0.9)
Cardiogenic shock	959 (1.1)	644 (1.2)	1603 (1.1)
Atrioventricular block (2nd or 3rd degree)	1279 (1.4)	809 (1.5)	2088 (1.4)
Invasive coronary procedures, *n* %			
Coronary angiography	47,312 (52.1)	17,999 (33.6)	65,311 (45.2)
Percutaneous coronary intervention	37,331 (41.1)	12,887 (24.1)	50,218 (34.8)
Coronary artery bypass graft	6517 (7.2)	1865 (3.5)	8382 (5.8)
Any type of revascularization	42,583 (46.9)	14,389 (26.9)	56,972 (39.4)

SD, standard deviation; IQR, interquartile range; AMI, acute myocardial infarction.

Next, we analyzed changes over time in the structure of the underlying cause of deaths occurring during days 29–365 of follow up (Fig. 1, Supplemental Table 4). Overall, 58.1% of deaths in men and 63.7% in women were due to CVD. However, these proportions changed over time. In men, CVD deaths accounted for 71.3% of all deaths in 2001 and 54.9% of all deaths in 2013. In women, the proportion of CVD deaths (within all deaths) also declined from 75.7% in 2001 to 59.3% in 2013 (Supplemental Table 4).

After adjusting for patients' age, we observed an increase in the probability of dying from all individual non-CVD conditions compared to CVD (except for deaths due to endocrine, nutritional and metabolic diseases and digestive diseases in men and digestive diseases and those classified under the ICD-10 "R" chapter - symptoms, signs and ill-defined causes in women) (Supplemental Table 5).

3.3. Place of death

First, we analyzed trends in 29–365 day mortality by place of death. The risk of dying in a hospital declined 5.2% per year (SHR = 0.948; 95% CI, 0.940–0.959) in men and 5.0% per year (SHR = 0.950; 95% CI, 0.945–0.961) in women. The risk of dying outside a hospital also declined, though to a lesser degree (1.5% per year in men; SHR = 0.985, 95% CI; 0.975–0.995 and 1.7% per year; SHR = 0.983, 95% CI; 0.974–0.993 in women) compared to in-hospital deaths (Table 3).

Next, we explored changes over time in the distribution of deaths places occurring during days 29–365 of follow up (Fig. 1, Supplemental Table 6). Over the study period, 51.1% of men and 43.2% of women died in a hospital while 49.9% of men and 56.8% of women died outside a hospital. The majority of OHDs happened in nursing homes (Supplemental Table 6).

Over time, the proportion of in-hospital deaths (within all deaths) declined in men from 55.0% in 2001 to 51.6% in 2013. The proportion of deaths in nursing homes increased from 27.2% in 2001 to 40.2% in 2013. Similarly, the proportion of in-hospital deaths in women declined from 45.7% in 2001 to 39.7% in 2013 whilst the proportion of deaths in nursing homes increased from 43.4% in 2001 to 53.0% in 2013 (Supplemental Table 6).

When adjusting for patients' age, we observed an increase in the probability of dying outside a hospital (relative to in-hospital deaths), driven by trends in deaths happening in nursing homes (an increase of 3.0% per year in men and 2.7% per year in women) (Supplemental Table 7).

Table 2
Average annual changes in 28-day, 29–365 day and 0–365 day mortality among patients hospitalized with an incident acute myocardial infarction in Norway, 2001–2014.

Follow up	No. deaths/patients at risk	HR (95% CI)	
		Unadjusted model	Adjusted model [a]
Men			
28 days	8575/90,884	0.937 (0.932–0.942)	0.943 (0.938–0.949)
29–365 days	6251/76,919	0.962 (0.956–0.969)	0.964 (0.957–0.970)
0–365 days	14,462/85,130	0.947 (0.943–0.952)	0.952 (0.947–0.956)
Women			
28 days	7874/53,589	0.948 (0.943–0.953)	0.955 (0.949–0.961)
29–365 days	5873/42,962	0.967 (0.962–0.975)	0.968 (0.961–0.975)
0–365 days	13,464/50,553	0.958 (0.954–0.962)	0.961 (0.957–0.966)
Total			
28 days	16,449/144,473	0.941 (0.937–0.944)	0.948 (0.945–0.952)
29–365 days	12,124/119,881	0.964 (0.959–0.968)	0.965 (0.961–0.970)
0–365 days	27,926/135,683	0.951 (0.948–0.953)	0.956 (0.953–0.959)

HR, hazard ratio; CI, confidence interval.
[a] Adjusted for age, diabetes mellitus, hypertension, chronic pulmonary obstructive disease, heart failure, stroke, renal failure, valvular heart disease, atrial fibrillation, neoplasms and level of education.

Table 3
Average annual change in 29–365 day mortality by underlying cause of death and place of death among patients hospitalized with an incident acute myocardial infarction in Norway, 2001–2013.

	No. deaths	SHR (95% CI)	
		Unadjusted model	Adjusted model [a]
Men			
I. Underlying cause of death [b]			
Cardiovascular conditions	3599	0.935 (0.927–0.944)	0.934 (0.925–0.943)
Non-cardiovascular conditions (all)	4225	1.001 (0.931–1.011)	1.013 (1.002–1.023)
Neoplasms	1075	0.991 (0.976–1.007)	1.012 (0.995–1.029)
Diseases of the respiratory system	543	1.002 (0.980–1.024)	1.015 (0.992–1.039)
Diseases of the genitourinary system	184	1.021 (0.986–1.056)	0.984 (0.949–1.024)
Endocrine, nutritional and metabolic diseases	165	0.972 (0.935–1.011)	0.958 (0.918–0.998)
External causes	137	1.022 (0.981–1.065)	1.032 (0.987–1.080)
Diseases of the digestive system	118	0.982 (0.937–1.028)	0.979 (0.933–1.028)
Infectious and parasitic diseases	122	1.024 (0.980–1.070)	1.025 (0.979–1.075)
Symptoms, signs, ill-defined causes	87	1.021 (0.970–1.075)	1.027 (0.972–1.085)
Other [c]	169	1.041 (1.001–1.084)	1.057 (1.021–1.095)
II. Place of death [d]			
In a hospital	3151	0.953 (0.944–0.962)	0.948 (0.940–0.959)
Outside a hospital	3010	0.975 (0.966–0.984)	0.985 (0.975–0.995)
Women			
I. Underlying cause of death [b]			
Cardiovascular conditions	3715	0.944 (0.936–0.953)	0.943 (0.934–0.952)
Non-cardiovascular conditions (all)	3577	1.012 (1.001–1.023)	1.017 (1.005–1.029)
Neoplasms	648	1.019 (0.999–1.039)	1.038 (1.016–1.061)
Diseases of the respiratory system	400	1.012 (0.987–1.038)	1.009 (0.982–1.037)
Diseases of the genitourinary system	164	1.011 (0.974–1.051)	0.985 (0.944–1.026)
Endocrine, nutritional and metabolic diseases	196	0.976 (0.942–1.011)	0.974 (0.937–1.013)
External causes	141	1.007 (0.968–1.049)	1.010 (0.946–1.057)
Diseases of the digestive system	146	0.987 (0.946–1.029)	0.991 (0.954–1.036)
Infectious and parasitic diseases	120	1.032 (0.988–1.077)	1.028 (0.980–1.079)
Symptoms, signs, ill-defined causes	105	0.986 (0.937–1.037)	0.964 (0.911–1.020)
Other [c]	199	1.047 (1.013–1.083)	1.055 (1.013–1.099)
II. Place of death [d]			
In a hospital	2505	0.952 (0.942–0.962)	0.950 (0.939–0.960)
Outside a hospital	3292	0.982 (0.973–0.991)	0.983 (0.974–0.993)
Total			
I. Underlying cause of death [b]			
Cardiovascular conditions	7314	0.936 (0.933–0.944)	0.938 (0.932–0.945)
Non-cardiovascular conditions (all)	4719	1.005 (0.997–1.012)	1.010 (1.002–1.018)
Neoplasms	1723	1.001 (0.989–1.014)	1.022 (1.008–1.035)
Diseases of the respiratory system	943	1.005 (0.989–1.022)	1.013 (0.995–1.031)
Diseases of the genitourinary system	348	1.015 (0.989–1.041)	0.985 (0.957–1.013)
Endocrine, nutritional and metabolic diseases	361	0.972 (0.947–0.998)	0.967 (0.939–0.994)
External causes	278	1.013 (0.984–1.042)	1.022 (0.991–1.055)
Diseases of the digestive system	264	0.982 (0.952–1.013)	0.986 (0.954–1.018)
Infectious and parasitic diseases	242	1.025 (0.995–1.058)	1.026 (0.992–1.061)
Symptoms, signs, ill-defined causes	192	0.999 (0.964–1.036)	0.994 (0.955–1.035)
Other [c]	368	1.042 (1.016–1.070)	1.055 (1.027–1.084)
II. Place of death [d]			
In a hospital	5656	0.951 (0.945–0.958)	0.949 (0.942–0.956)
Outside a hospital	6302	0.977 (0.970–0.983)	0.984 (0.978–0.991)

[a] Adjusted for age, diabetes mellitus, hypertension, chronic pulmonary obstructive disease, heart failure, stroke, renal failure, valvular heart disease, atrial fibrillation, neoplasms and level of education.
[b] Missing information for 91 individuals; 52 men and 39 women.
[c] Includes diseases of blood and blood-forming organs (D50-D89; $n = 41$; 16 men and 25 women), mental and behavioral conditions (F01-F99; $n = 143$; 68 men and 75 women), diseases of the nervous system (G00-G99; $n = 115$; 58 men and 57 women), diseases of skin and subcutaneous tissue (L00-L99; $n = 22$; 9 men and 13 women) and those of musculoskeletal system (M00-K95; $n = 47$; 20 men and 27 women).
[d] Missing information for 166 individuals; 90 men and 76 women.

4. Discussion

Using a nationwide cohort of patients hospitalized with an incident AMI, we demonstrated a steady and continuous decline in 28-day mortality, at a similar pace in both men and women. One-year mortality also declined, though to a lesser extent compared to 28-day mortality. Over the study period, the risk of dying in a hospital declined more rapidly than that of dying outside a hospital. The positive changes in short-term mortality, reported previously in Norway [2] until 2009, extended throughout 2014. During 2009–2013, one-year CVD mortality rates continued to decline, though to a slower pace compared to 2001–2009. The previously observed increase in non-CVD mortality rates seems to have haltered beyond 2009.

Our findings are in line with international studies showing reductions in short-term mortality following AMI in the US (1986–2007) [7], the Netherlands (2003–2007) [3], Sweden (1987–2006) [11], Denmark (1984–2008) [4] and more recently in Taiwan (1997–2011) [24].

Longer-term mortality following AMI declined in Denmark (1984–2008) [4], Sweden (1987–2006) [11] and Spain (1978–2007) [13]. However, they remained stable [8] or even increased [7] in the US (1986–2007). When disentangling all-cause mortality into CVD and non-CVD, it becomes apparent that trends of the two components were divergent; CVD mortality declined over time while non-CVD mortality increased [2,7], attenuating the magnitude of decline for all-cause mortality in our study or even stopping or reversing it in other studies [7,8].

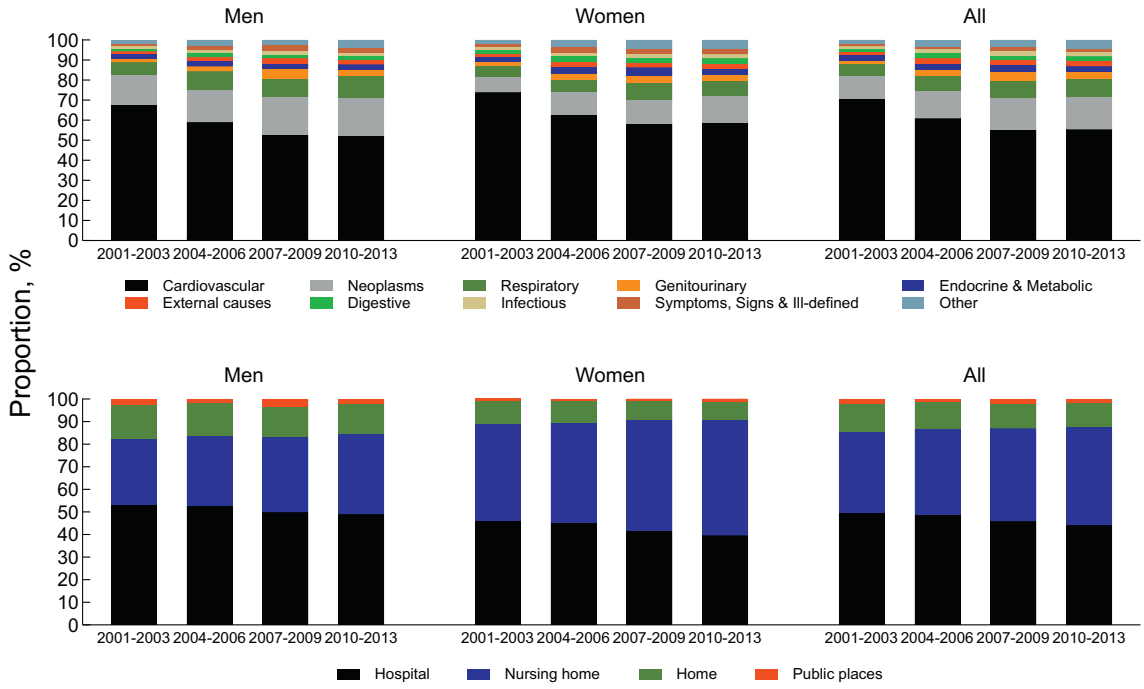

Fig. 1. Distribution of the most common underlying causes of death (upper panel) and places of death (lower panel) in patients dying during days 29–365 of follow up.

4.1. Underlying cause of death

We observed a decline in one-year CVD mortality. The non-CVD mortality increased, due to increases in the risk of dying due to neoplasms and stagnations in trends of other individuals non-CVD causes. We could identify only one study, by Kostis et al. [7] reporting a similar increase in mortality due to neoplasms, respiratory conditions, renal failure, septicemia and Alzheimer disease among AMI patients in the US (1986–2007) [7]. The results of both studies may point to a universal pattern in recent mortality trends following AMI.

The opposite trends observed between most non-CVD conditions and CVD, led to a shift in the causes of death over time; the specific weight of CVD deaths in our study decreased relative to non-CVD deaths. This finding is in line with a report from the US, where the specific weight of CVD deaths decreased from 62% during 1987–1991 to 50% during 2002–2006 [8]. This shift may reflect the increase in the burden of comorbidities among hospitalized AMI patients and the effect of significant reductions in CVD mortality, 'exposing' AMI patients to non-CVD conditions.

4.2. Place of death

We observed a greater reduction in 29–365 day mortality for deaths happening in a hospital compared to OHDs. This difference led to a shift over time from in-hospital toward out-of-hospital deaths, mainly happening in nursing homes.

The reduction in the length of stay (LOS) for the incident AMI (LOS) may have influenced the observed shift in the place of death. The average reduction of 1.8 days in the LOS over the study period was associated with an increase in the proportion of early OHDs (from 43.6% in 2000 to 55.6% in 2013) within all early deaths (i.e. within 28 days from incident AMI discharge), suggesting a direct link between them. Of note, increases in the proportion of OHDs (within all deaths) were also observed for deaths occurring later during follow up, suggesting other potential mechanisms involved. In this context, a previous study showed that shortening of LOS was associated with increased risk of heart failure among AMI survivors [25]. Although we cannot establish a direct causal relationship between LOS and AMI outcomes, it seems that advances in reducing in-hospital mortality, shortening LOS and improving treatment during the acute phase of the disease [26] may have an impact on later outcomes.

While OHDs, happening at home or in public places can be regarded as a missed opportunity to hospitalize high-risk patients, deaths occurring in nursing homes require further consideration. Nursing homes in Norway host up to 12–13% of individuals age 80+ years. Over the study period, the number of individuals age 80+ years increased by nearly 24,000 but these changes were not followed by a similar increase in the number of beds in nursing homes and other care institutions. Our group has previously shown that the proportion of elderly surviving an AMI episode is increasing over time [2]. A recent publication from Denmark showed that the risk of being admitted to a nursing home after surviving an incident AMI is twice as high compared to general population of the same age [27]. Further, as the threshold for admittance to nursing homes has increased, their population is becoming more physically and cognitively frail [28]. Taken together, these findings suggest an increase over time in the proportion of nursing home residents with underlying cardiac and other medical conditions. These residents are susceptible to acute complications while residing in nursing homes. In these occasions, the decision to hospitalize them is not always an easy and purely medical-related decision. Other factors, such as staffing, location and size of the nursing home and potential influence of family members are also to play a role [29]. There are claims that hospitalizations from nursing homes may not be beneficiary [30]. However, these findings are confined to nursing home residents experiencing an infectious episode and cannot be generalized to AMI survivors experiencing acute complications.

We believe our study has several implications. First, the continuous decline in short-term mortality following AMI, leads to more survivors being at risk of acute and chronic complications at a later stage. More studies are needed to explore the nature of these complications, quality of treatment received and related outcomes. Second, the decline in CVD-related mortality among AMI survivors, coupled with aging of the population and a seemingly increase in the burden of comorbidities may change the death structure among AMI survivors. In this context, optimal treatment of these comorbidities and control of risk factors

would help minimizing the frequency of acute non-cardiac complications. Lastly, we observed that more AMI survivors are dying in nursing homes. Therefore, further research aiming at assessing the quality of care in such institutions, as well as routines and protocols for hospitalizing their residents in case of severe complications may help preventing or at least postponing death.

4.3. Strength and limitations

Our study represents the most recent nationwide analysis without restrictions with regard to age, gender, socioeconomic status, disease severity or other factors that may jeopardize the generalizability of our findings. It covers a period of relatively established AMI diagnostic criteria, as troponin was included in AMI diagnostic algorithm in Norway around 1998–2000. Further, a complete follow-up of patients was possible through individual-level linkages of different data sources. To the best of our knowledge, this is the first study exploring trends in mortality by underlying cause and place of death. By including only incident cases, we avoided the potential role of case-mixture (i.e. mixing incident and prevalent AMI hospitalizations) on trends in survival.

Our study used patient administrative data. Consequently, information on AMI type (i.e. ST-elevation myocardial infarction-STEMI versus non-ST elevation myocardial infarction-NSTEMI) is not available. As such distinction based on ICD-10 codes only is not accurate, we did not conduct stratified analyses on AMI type. International studies have shown differences between the two AMI types with regard to the direction and/or magnitude of trends over time [9,31]. The lack of data on prescribed medication and adherence to treatment as well as participation in rehabilitation programs upon discharge - both proven to influence survival - may be regarded as another limitation. We did not have information on lifestyle-related risk factors including smoking and obesity.

Although the quality of death data in the Norwegian Cause of Death Registry is deemed to be very good [21], they are concerns about the accuracy of information in death certificates [32], especially in population subgroups, including elderly and those whose death was not followed by a medical autopsy [33]. In Norway, the proportion of deceased who undergo a medical autopsy is generally low [34] and even lower among individuals who die outside a hospital [35].

Death certificates in Norway are filled out by the doctor who confirms the patient's death and may not always have a complete overview of patient's medical history. This, coupled with existence of multiple medical conditions among elderly and nursing home residents, challenge the accuracy of information on the death certificate.

Lastly, while mortality rates in our study were comparable to those reported from other international studies [4,8,12], the prevalence of relevant comorbidities registered during the hospitalization for the incident AMI was lower. Whether this indicate a healthier study population or not is difficult to establish as comorbidities in our study are registered during the index AMI hospitalization and may therefore underestimate the true prevalence of these comorbidities among AMI patients.

4.4. Conclusions

Our study delineates a continuous decline in short-term mortality following incident AMI. The reduction in one-year CVD mortality was associated with an increase in the risk of dying due to non-CVD causes, attenuating the magnitude of reduction in overall mortality and shifting the death structure toward more non-CVD deaths.

The reduction in one-year in-hospital mortality was greater than that of one-year out-of-hospital mortality, resulting in a shift of death place from hospitals toward nursing homes.

Disclaimers

Data from the Norwegian Patient Registry have been used in this publication. The interpretation and reporting of these data are the sole responsibility of the authors, and no endorsement by the Norwegian Patient Registry is intended, nor should be inferred. This study used data from the Norwegian Cause of Death Registry. The interpretation and reporting of these data are the sole responsibility of the authors, and no endorsement by the Norwegian Cause of Death Registry is intended, nor should be inferred.

Acknowledgement

The authors thank Tomislav Dimoski at The Norwegian Institute of Public Health, Norway for his contribution by developing the software necessary for obtaining data from Norwegian hospitals, conducting the data collection and quality assurance of data in this project.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

Financial support

This study has not received financial support.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2019.07.084.

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