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Risk of early recurrence and mortality in high-risk myocardial infarction patients: A population-based linked data study[☆]

Lee Nedkoff^{a,*}, Tom Briffa^a, Kevin Murray^a, James Gaw^b, Andrea Yates^b, Frank M. Sanfilippo^a, Stephen J. Nicholls^c

^a The University of Western Australia, M431, 35 Stirling Hwy, Crawley, WA, 6009, Australia

^b CSL Behring, 189 – 209 Camp Road, Broadmeadows, Victoria, 3047, Australia

^c Victorian Heart Institute, Monash University, Wellington Rd, Clayton, VIC, 3800, Australia

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ABSTRACT

Background: Survival during the early period following myocardial infarction (MI) has significantly improved although there are limited data on cardiovascular recurrence during this period.

Methods: We identified all emergency hospitalisations for MI from November 1, 2011 to October 31, 2016 in Western Australia from a linked hospitalisation/mortality dataset. Patients were included if they survived >3 days, had no acute kidney injury, and had ≥ 1 of: ≥ 65 years, prior MI, diabetes or peripheral arterial disease. Outcomes were major adverse cardiovascular events (MACE, a composite of CVD death, recurrent MI or stroke), cardiovascular disease (CVD) death, all-cause mortality, recurrent MI and stroke. Cumulative risks at 90-days and 1-year were estimated from Kaplan-Meier analyses and predictors of each outcome from multivariable Cox regression models.

Results: There were 8024 high-risk MI patients identified (males 61.8%). Median age was 73.7 years (IQR 66.3–82.2). Half of the risk of MACE occurred in the first 90-days post-MI (6.6% vs 12.6% at 1-year) and was underpinned by risk of recurrent MI. Risk was generally higher in women than men (MACE: 6.0% males, 7.7% females, $p = 0.0025$; CVD mortality: 1.7% males, 3.7% females; all-cause mortality: 2.8% males, 5.6% females, $p < 0.0001$). Independent predictors of 90-day MACE were increasing age, heart failure history, hypertension and prior stroke. Female sex was not associated with a higher rate of any of the outcomes after multivariable adjustment.

Conclusion: Half of cardiovascular events in the year following an MI occur within 90-days, demonstrating that reductions in MI burden could be achieved by further targeted intervention in the early period following an MI.

1. Introduction

Myocardial infarction (MI) is a leading cause of morbidity and mortality in high-income countries, despite sustained declines in coronary heart disease (CHD) mortality over the past four decades [1]. Significant advances in evidence-based therapies and systematic implementation of early revascularisation have contributed to reductions in case fatality after MI [2], even in some high-risk patient groups [3]. Early recurrent events are commonly the result of additional plaque rupture or erosion leading to thrombus formation within a coronary artery, and thus current treatment approaches place emphasis on antithrombotic agents and reduction of low-density lipoprotein (LDL)

cholesterol in the early phase following an MI [4]. Yet despite the use of these therapies, the risk of recurrent cardiovascular events remains high [5], particularly in the immediate weeks to months following the index event [6].

While longer-term mortality rates following MI have declined [7,8], the majority of recurrent events still occur in the early months after an MI [9]. The risk of major adverse cardiovascular events (MACE) in clinical trials ranges from 6% at 30-days in patients treated with a loading dose of atorvastatin prior to revascularisation [10] to 11.7% at 1-year following MI in those treated with clopidogrel [9]. A nationwide linked data study from Sweden reported a risk of MACE of 18.3% at 1 year in MI patients discharged alive following MI, with higher rates of adverse outcomes in patients deemed to be high-risk based on clinical

[☆] All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

* Corresponding author. School of Population and Global Health, The University of Western Australia, M431, 35 Stirling Hwy, Crawley, Western, 6009, Australia.

E-mail address: lee.nedkoff@uwa.edu.au (L. Nedkoff).

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Abbreviations

ACS	Acute coronary syndromes
AEGIS-II	ApoA-I Event Reducing in Ischemic Syndromes II
AM	Australian modification
CABG	Coronary artery bypass grafting
CHD	Coronary heart disease
CKD	Chronic kidney disease
CM	Clinical modification
COPD	Chronic obstructive pulmonary disease
CVD	Cardiovascular disease
HDL	High-density lipoprotein

HMDC	Hospital Morbidity Data Collection
ICD	International Classification of Diseases
LDL	Low-density lipoprotein
MACE	Major adverse cardiovascular events
MI	Myocardial infarction
NSTEMI	Non-ST-elevation myocardial infarction
PAD	Peripheral arterial disease
PCI	Percutaneous coronary intervention
SECURE-PCI	Statins Evaluation in Coronary Procedures and Revascularisation-PCI
STEMI	ST-elevation myocardial infarction
WA	Western Australia

trial criteria [6]. Higher mortality rates after MI have been reported in women than men, both during the in-hospital and post-discharge period [11], with differences extending to the longer-term, even after accounting for differences in clinical characteristics and lower rates of revascularisation [12]. While elevated cardiovascular risk extends beyond the initial in-hospital period, few population-level studies have reported the risk of cardiovascular event recurrence in the immediate months following MI.

An important focus for clinical trials is investigating therapies with the potential for early plaque regression and stabilisation including intensive LDL lowering, high-density lipoprotein (HDL) targeted therapy, and anti-inflammatory agents [13]. Robust contemporary population estimates of short-term cardiovascular recurrence rates are required to provide baseline estimates of disease burden, and to enable measurement of the economic benefit of implementing such therapies in the early phase following MI. Linked health data provide a pragmatic means of providing whole-population measures of short-term cardiovascular event rates in a high-risk MI patient cohort because of the ability to identify concurrent and prior medical history, comorbidities and complete capture of non-fatal and fatal outcomes. The aim of this study was to measure the baseline risk of cardiovascular recurrence and mortality at 90-days following MI in a contemporary, high-risk whole population patient cohort; to determine if there are differences by sex in these outcomes; and to identify independent predictors of risk for major cardiovascular outcomes.

2. Methods

2.1. Study setting and data source

The population of Western Australia (WA) in 2016 was 2.6 million, with 13.6% of the population aged ≥ 65 years [14]. Data for this study were obtained from the WA Department of Health Data Linkage Branch. The Hospital Morbidity Data Collection (HMDC) and Mortality register were used to extract a person-linked, de-identified dataset containing all cardiovascular disease (CVD) hospital admissions and deaths and all linked records from these datasets for these patients since 1985. The study dataset has been used extensively for studies investigating outcomes in patients with CVD [15–17]. Multiple records for an individual are linked by demographic identifiers, using probabilistic matching, for which there is a high level of accuracy [18]. Discharge diagnoses are coded in the HMDC in a principal diagnosis field and up to 20 additional (secondary) diagnosis fields, using the International Classification of Diseases (ICD) version current at the time (ICD-9 from 1979, ICD-9-Clinical Modification (CM) from 1988 including Australian versions from 1995, and ICD-10-Australian Modification (AM) since July 1, 1999).

2.2. Study cohort

All MI hospitalisations (ICD-10-AM I21) from November 1, 2011 to October 31, 2016 were identified from the study dataset. The first MI during the study period for each patient was considered for inclusion in the study. Inclusion and exclusion criteria were based on published definitions for identifying a high-risk patient cohort recruited to the ApoA-I Event Reducing in Ischemic Syndromes II (AEGIS-II) clinical trial and were derived from the linked study database [13]. Details of ICD codes, definitions and length of historical data used to define inclusion and exclusion criteria are outlined in [Supplementary Table 1](#). Patients were eligible for inclusion if the MI was an emergency admission coded in the principal diagnosis field, with no evidence of coding of acute kidney injury on the index admission, and with at least one of the following criteria present: age ≥ 65 years, prior history of MI, diabetes or peripheral arterial disease (PAD). Patients were excluded from the cohort if they had any of the following: haemodynamic instability, history of hepatobiliary disease, severe chronic kidney disease (CKD), coronary artery bypass grafting (CABG) occurring during or within 1 month following the index MI admission, history of allergies, pregnancy at the time of MI, alcohol, drug or medication abuse in the year prior to MI, current anti-cancer therapy, or transfer to a psychiatric hospital following the index MI hospitalisation. The definition of haemodynamic instability comprised the recording of heart failure and pulmonary oedema/cardiogenic shock, or hypotension, at the time of the MI admission, or two or more heart failure admissions in the previous year. Patients with heart failure and no other acute complications, or with a longer history of heart failure admissions, were not excluded from the cohort. To align with trial criteria, patients who died within 3 days of admission for the index MI were also excluded ([Supplementary Figure 1](#)).

2.3. Outcomes

The primary outcome of interest was MACE, a composite of CVD death, recurrent admission for MI, or stroke. Secondary outcomes identified were CVD death, all-cause mortality, and hospitalisation for MI and stroke. Recurrent MI and stroke were identified where recorded in the principal discharge diagnosis field in the hospitalisation data; CVD deaths were identified where the underlying cause of death was coded as coronary heart disease (including MI) (ICD-10-AM I20–I25), sudden cardiac death (I46.1), heart failure (I50), stroke (I60–I64), cardiovascular haemorrhage (I60–I62, I23.0, I31.2), pulmonary embolism (I26) or PAD (I70–I79). Follow-up data for all patients were available to 1-year following the index MI admission.

2.4. Covariates

Demographic and baseline data were identified from the hospitalisation dataset ([Supplementary Table 2](#)). Aboriginal and Torres Strait

Islander (hereafter termed Indigenous) status was identified where at least 25% of records in the dataset were coded as Indigenous, to account for known under-recording in administrative datasets [19]. MI type was identified from coding on the index admission, and stratified as ST-elevation MI (STEMI, I21.0-I21.3), non-ST-elevation MI (NSTEMI, I21.4) and unspecified MI (I21.9). Percutaneous coronary intervention (PCI) was also identified from the index MI admission. Comorbidities were identified using 25 years of hospitalisation history from the date of the index MI for each patient, from the principal or secondary diagnosis fields, including on the index MI admission. The exceptions were prior MI, acute coronary syndromes (ACS) and revascularisation procedures, which were only identified from prior admissions.

2.5. Statistical analyses

Cohort demographics and medical history are presented for the cohort overall, and separately for men and women. Comparisons by sex for each variable are from unadjusted logistic regression models (categorical variables) and Wilcoxon rank-sum tests (continuous variables). Unadjusted risk for each outcome was derived from Kaplan-Meier survival analyses, stratified by sex. Time to event was calculated as the time from day 3 following the index MI to the outcome event date. Those patients who did not experience the outcome of interest were censored at 90-days or 1-year for each of the relevant analyses. For recurrent MI and stroke, patients who died before the end of follow-up were censored at the date of death, and for CVD death, those who died of a non-cardiovascular cause were censored at the date of death. Time to event for MACE was time to the first event of recurrent MI, stroke or CVD death. Cases where the underlying cause of death was missing ($n = 6$) were excluded from the analyses of CVD death.

Multivariable Cox proportional hazards regression models were used to determine independent predictors of MACE and all secondary endpoints at 90-days following the index MI. Variables entered into the multivariable models were known cardiometabolic risk factors available in the dataset, and are listed in Table 1, and are reported as hazard ratios (HR, 95% confidence intervals). Indigenous status was also included in the model, although we are unable to report the hazard ratio separately due to ethics constraints. Because of the difference in the unadjusted risk of outcomes by sex, we also ran separate multivariable Cox models to test for differences in predictors by sex (by including an interaction term of sex by the covariate of interest). There were few significant interaction terms for each outcome and therefore the main effects multivariable model is presented for men and women combined. We also examined age as an effect modifier by including age by covariate interactions in separate multivariable models for each outcome. For those models with significant interaction terms, HRs (95% CI) are presented for ages 40, 60 and 80 years for the relevant covariate.

3. Results

A total of 18,058 emergency index admissions for MI coded in the principal discharge diagnosis field were identified during the study period. After application of inclusion and exclusion criteria, there were 8024 MI admissions eligible for inclusion in the study cohort (Supplementary Figure 1). Table 1 shows the baseline characteristics of the MI cohort. Males comprised 61.8% of the cohort and were younger than females (median age 71.0 vs 78.5 years). Around three-quarters of the cohort were NSTEMI patients (81.3% in women), with nearly half undergoing PCI during their hospital stay. A higher proportion of females than males had a history of heart failure (22.4 vs 14.4%), atrial fibrillation (22.2 vs 17.8%), hypertension (74.2 vs 65.3%), prior stroke (7.0 vs 5.1%), renal disease (8.1 vs 6.5%) and chronic obstructive pulmonary disease (COPD) (16.2 vs 11.5%) ($p < 0.05$). In contrast, a higher proportion of men had prior ACS (31.3 vs 23.9%), diabetes (37.0 vs 34.0%) and underwent PCI at baseline (55.4 vs 34.3%) ($p < 0.05$).

Table 1

Baseline characteristics of the study cohort of myocardial infarction patients.

	Males (n = 4956)	Females (n = 3068)	Total (n = 8024)
Median age, years (IQR)	71.0 (65.1–79.1)	78.5 (69.8–85.8)	73.7 (66.3–82.2) ^b
Age ≥ 75 years, n (%)	1830 (36.9)	1862 (60.7)	3692 (46.0) ^b
Length of stay, days, median (IQR)	4.0 (3.0–5.0)	4.0 (3.0–7.0)	4.0 (3.0–6.0) ^b
Indigenous status, n (%)	192 (3.9)	149 (4.9)	341 (4.2) ^b
MI type, n (%)			
ST-elevation MI	1244 (25.1)	485 (15.8)	1729 (21.5) ^b
Non-ST-elevation MI	3580 (72.2)	2495 (81.3)	6075 (75.7)
Unspecified MI	132 (2.7)	188 (2.8)	220 (2.7)
Percutaneous coronary intervention	2747 (55.4)	1051 (34.3)	3798 (47.3) ^b
Comorbidities and prior history, n (%)			
Prior MI	1137 (22.9)	485 (15.8)	1622 (20.2) ^b
Prior ACS	1550 (31.3)	732 (23.9)	2282 (28.4) ^b
Heart failure	712 (14.4)	687 (22.4)	1399 (17.4) ^b
Atrial fibrillation	880 (17.8)	680 (22.2)	1560 (19.4) ^b
Hypertension	3238 (65.3)	2276 (74.2)	5514 (68.7) ^b
Prior stroke	255 (5.1)	216 (7.0)	471 (5.9) ^b
Renal disease ^a	322 (6.5)	250 (8.1)	572 (7.1) ^b
Diabetes	1833 (37.0)	1044 (34.0)	2877 (35.8) ^b
Peripheral arterial disease	536 (10.8)	290 (9.4)	826 (10.3)
Chronic obstructive pulmonary disease	569 (11.5)	497 (16.2)	1066 (13.3) ^b
Cancer	2025 (40.9)	1334 (43.5)	3359 (41.9) ^b
Prior percutaneous coronary intervention	1036 (20.9)	362 (11.8)	1398 (17.4) ^b
Prior coronary artery bypass grafting	488 (9.8)	136 (4.4)	624 (7.8) ^b

IQR, interquartile range; MI, myocardial infarction; ACS, acute coronary syndromes.

^a Renal disease excludes anyone with a history of renal dialysis or chronic renal failure.

^b $p < 0.05$ for comparison by sex from unadjusted logistic regression models (categorical variables) or Wilcoxon rank-sum test (continuous variables).

3.1. Cardiovascular recurrence and mortality

The cumulative risk of the primary composite outcome of MACE at 90 days was 6.0% in males and 7.7% in females (log-rank p -value = 0.0025; Table 2, Fig. 1). The risk for CVD death and all-cause mortality at 90-days following MI was higher in females than males (3.7 vs 1.7%, log-rank p -value < 0.0001 ; 5.6 vs 2.8%, log-rank p -value < 0.0001 respectively). The risk of recurrent MI at 90-days was 4.0%, with no significant difference by sex, and marginally higher in females for stroke hospitalisation (0.7 vs 0.3%, log-rank p -value = 0.0066).

The risk of MACE at 1-year following MI was double that seen at 90-days (12.6% overall; 11.4% males, 14.6% females, log-rank p -value < 0.0001). There was a similar magnitude of increase for all other outcomes compared with risk at 90-days, with significantly higher risk in females than males for all outcomes except recurrent MI.

The majority of covariates were significantly associated with each outcome in univariate models (Table 3). The exception was diabetes, which was not significant at the univariate level with MACE at 90-days. Following multivariable adjustment, independent predictors of MACE at 90-days were increasing age, heart failure, hypertension and prior stroke, while there was a 48% lower hazard of MACE associated with PCI at baseline (HR 0.48, 95% CI 0.39, 0.60). Patients with STEMI or where the MI type was unspecified also had significantly higher multivariable risk of MACE compared to NSTEMI patients (HR 1.52, 95% CI 1.20, 1.93; HR 2.28, 95% CI 1.59, 3.25, respectively). There were generally similar independent predictors for CVD and all-cause mortality within 90-days, although with a greater effect size than for MACE. The exception was that the association with hypertension became non-significant after multivariable adjustment. Additionally, atrial fibrillation became an independent predictor for both outcomes, and PAD an independent

Table 2

Kaplan-Meier risk estimates for cardiovascular outcomes and all-cause mortality at 90 days and 1-year post myocardial infarction.

	Males	Females	Total	Log-rank p-value ^a
Number at risk, n	4956	3068	8024	
MACE				
Outcomes at 90 days, n	294	234	528	0.0025
90-day risk, %	6.0	7.7	6.6	
Outcomes at 365 days, n	559	439	998	<0.0001
365-day risk, %	11.4	14.6	12.6	
Cardiovascular disease mortality				
Outcomes at 90 days, n	84	114	198	<0.0001
90-day risk, %	1.7	3.7	2.5	
Outcomes at 365 days, n	177	186	363	<0.0001
365-day risk, %	3.6	6.2	4.6	
All-cause mortality				
Outcomes at 90 days, n	140	171	311	<0.0001
90-day risk, %	2.8	5.6	3.9	
Outcomes at 365 days, n	357	352	709	<0.0001
365-day risk, %	7.2	11.5	8.8	
Myocardial infarction				
Outcomes at 90 days, n	211	105	316	0.0830
90-day risk, %	4.3	3.5	4.0	
Outcomes at 365 days, n	386	231	617	0.8889
365-day risk, %	8.0	8.0	8.0	
Stroke				
Outcomes at 90 days, n	15	22	37	0.0066
90-day risk, %	0.3	0.7	0.5	
Outcomes at 365 days, n	57	57	114	0.0055
365-day risk, %	1.2	2.0	1.5	

^a Log-rank p-value for difference by sex, from Kaplan-Meier survival analyses. MACE, major adverse cardiovascular event.

predictor for 90-day CVD mortality (HR 1.46, 95% CI 1.01, 2.12).

Hypertension was associated with a 42% increase in the risk of recurrent MI at 90-days (HR 1.42, 95% CI 1.07, 1.88), while female sex was associated with a 33% reduction in the hazard of MI (HR 0.67, 95% CI 0.52, 0.86) (Supplementary Table 3). Prior stroke and history of atrial fibrillation were the strongest independent predictors of stroke onset in the 90-days following index MI.

The association of diabetes with 90-day MACE was greater in younger than older patients (age 40 years HR 3.84 95% CI 2.09, 7.05; age 60 years HR 1.89, 95% CI 1.36, 2.64; age 80 years HR 0.93, 95% CI 0.76, 1.15, diabetes by age interaction $p < 0.0001$), with a similar pattern seen for CVD death and all-cause mortality (Supplementary Table 4). A similar age-related pattern was also seen for renal disease (CVD death) and chronic obstructive pulmonary disease (all-cause mortality). In contrast, the effect of heart failure on MACE was greater in older compared to younger patients (interaction $p = 0.007$). There was a marginally greater association of hypertension with recurrent MI in older versus younger patients ($p = 0.04$), and no significant interactions with age for stroke outcomes.

4. Discussion

This contemporary population-based study of over 8000 patients with MI demonstrates high levels of residual cardiovascular risk in the early post-MI phase. Risks of the composite outcome of MACE were 6.0% in men and 7.7% in women at 90-days, primarily driven by a high risk of MI recurrence. Unadjusted absolute risks of most outcomes, particularly all-cause and CVD mortality, were higher in women than men, however this difference was attenuated by the older age of the female patients. Despite these differences in absolute risk between men and women, there was limited difference in independent predictors of primary and secondary outcomes in males and females. Increasing age, MI type, and history of heart failure, hypertension and prior stroke were the strongest predictors of MACE occurring during the 90 days following MI, with history of atrial fibrillation contributing significantly to risk of stroke post MI.

4.1. Comparison of level of risk against other studies

In recent decades, rates of short-term death in people hospitalised with MI have declined significantly [20,21], primarily due to the application of evidence-based management in this patient population. However, studies demonstrate that ongoing risk persists in this patient group particularly in the early period following MI. Risk of MACE at 30-days have been reported from the Statins Evaluation in Coronary Procedures and Revascularisation (SECURE)-PCI trial at 6.2% and 7.1% in treatment and placebo groups respectively [10]. A contemporary Australian registry study reported rates of MACE of 6% and all-cause mortality of 3% at 6 months following ACS [22]. This is considerably lower than the risk of MACE at 90-days in our study, likely due to the older age and higher risk profile of our study cohort. We have previously shown that declines in 30-day deaths have extended to high-risk patient groups such as those with diabetes, with hospitalised 30-day case fatality in people with diabetes now similar to that of non-diabetics [3]. Similarly, an Australian cohort study demonstrated a significant decline in 30-day mortality after MI in people with chronic heart failure, declining from 23.2% to 9.2% between 1999 and 2007 [23].

Our findings support previous reports that the risk of recurrent events and mortality in the year following an MI is high in the early phase [9,24]. Our study shows that at least 50% of cardiovascular events in the first year following MI occur within the first 90 days, highlighting the high risk nature of this period and need for more effective treatment strategies and close monitoring of patients following hospital discharge. A further important finding in our study is the high contribution of recurrent MI events to risk in the short-term following MI. Recurrent MI underpinned the high levels of MACE in our study, concordant with 6-month MACE rates in a Swedish linked data study of high-risk MI patients [6]. Studies have previously shown that CVD mortality and recurrent MI had similar proportional contributions to MACE [10], while the contemporary results likely reflecting more recent improvements in survival.

4.2. Sex differences

There is well-documented evidence of sex differences in outcomes following an MI. Worse outcomes in women are attributed to higher levels of comorbidities, older age and disparities in receipt of evidence-based medications and early revascularisation. Our results agree with Australian registry data showing that the higher risk levels and comorbidities in women than men contribute to higher rates of adverse cardiovascular outcomes in women [22]. However, in a study restricted to STEMI patients, higher rates of MACE and all-cause mortality at 6 months after MI persisted, even after adjustment for risk levels [12]. Rates of reperfusion and revascularisation therapies are often lower in women, with disparities in ongoing secondary prevention following MI also reported [22]. Higher early mortality risk and treatment disparities in women are primarily seen at younger ages [25,26], and given the significantly older age in women in our cohort, the effect of such disparities may be attenuated. Females are also more likely to present with non-obstructive coronary artery disease (CAD) at the time of MI, however in those with obstructive CAD, there is limited evidence of a difference by sex in mortality immediately following MI in these patients [27].

4.3. Predictors of risk

Major cardiometabolic comorbidities are strong predictors of short-term MACE and CVD mortality in high-risk MI patients. In our study, hypertension and heart failure were associated with between 20% and 50% greater risk of MACE. The risk associated with heart failure is present in both higher risk heart failure patients such as those with concomitant shock, as well as those without added complications [27]. Our findings similarly show that even when patients with higher risk

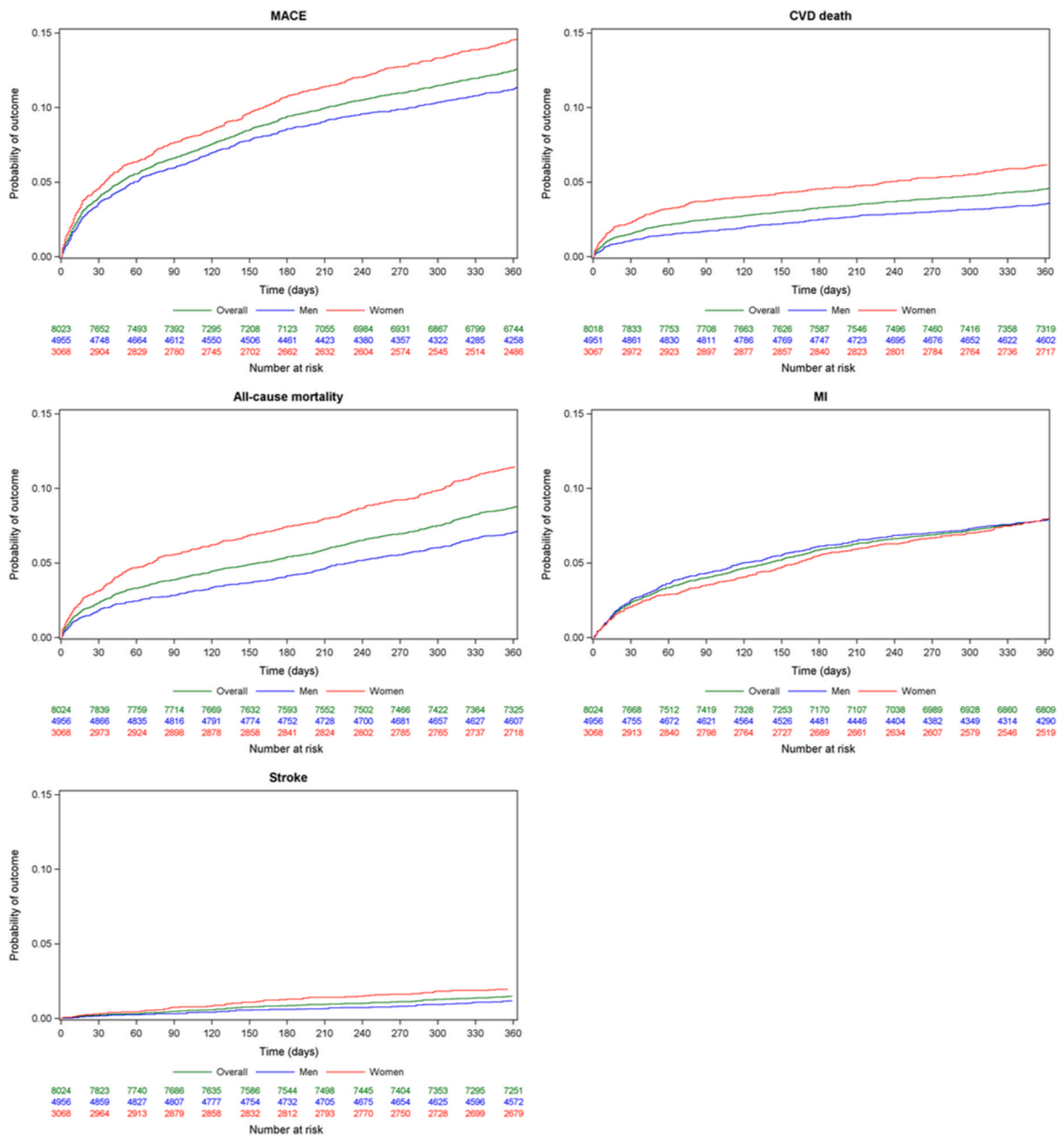


Fig. 1. Kaplan-Meier survival curves for major cardiovascular outcomes and all-cause mortality following myocardial infarction in men and women.

heart failure presentations are excluded, heart failure remains a strong indicator of poor outcomes. Prior stroke is also a strong predictor of short-term MACE, and this association also holds for CVD mortality. Diabetes was not significantly associated with adverse outcomes at 90-days, and this may be a more recent phenomena [3,28]. However the effect of diabetes differed by age, with a higher risk in younger adults, possibly associated with survivor bias in the very elderly and the overwhelming impact of diabetes when it occurs at a young age. While sex was not associated with MACE or mortality outcomes, there was a lower risk of recurrent MI in females in multivariable models, which occurred because of adjustment for the higher levels of comorbidities in females.

4.4. Strengths and limitations

The statutory reporting requirements in WA mean that all patients hospitalised with MI are included in the study dataset, thus minimising selection bias. The criteria used to select patients into the cohort rely on

coding in administrative hospitalisation datasets. Comorbidities and medical history, such as anti-cancer therapy and history of allergies, are not always recorded in hospitalisation data, however the very long history available in the dataset (25 years) ensured that we were able to maximise capture of these conditions. Some conditions did not have exact matches between clinical classification and ICD codes, therefore proxy measures were developed, based on known coding, published definitions and sensitivity analyses. Back-mapping from ICD-10-AM to ICD-9-CM and ICD-9 was undertaken manually and with the guidance of mapping tables to ensure specific one-to-one matches. Our risk estimates are consistent with those from published clinical trial populations [9], indicating a likely high concordance between clinical and linked data definitions. While we were unable to match some trial criteria, such as presence of multi-vessel CAD and identifying diabetic patients on pharmacotherapy, the application of the clinical trial eligibility criteria mean that this is a high-risk population of MI patients. It is possible that some patients with single-vessel CAD may be included in the cohort,

Table 3

Cox proportional hazard models for major adverse cardiovascular event (MACE), cardiovascular disease death and all-cause mortality at 90-days following index admission for myocardial infarction.

	Hazard ratios (95% confidence intervals)					
	90-day MACE ^a		90-day cardiovascular disease mortality		90-day all-cause mortality	
	Univariate	Multivariable ^b	Univariate	Multivariable ^b	Univariate	Multivariable ^b
Age	1.04 (1.03, 1.05)	1.03 (1.02, 1.04)	1.11 (1.09, 1.13)	1.08 (1.06, 1.10)	1.11 (1.09, 1.12)	1.07 (1.06, 1.09)
Sex, female	1.30 (1.10, 1.55)	0.91 (0.77, 1.11)	2.22 (1.67, 2.94)	1.20 (0.88, 1.62)	2.00 (1.60, 2.50)	1.04 (0.82, 1.32)
PCI ^c	0.37 (0.31, 0.45)	0.48 (0.39, 0.60)	0.17 (0.11, 0.26)	0.37 (0.23, 0.59)	0.16 (0.12, 0.23)	0.33 (0.23, 0.48)
MI type						
NSTEMI	Reference	Reference	Reference	Reference	Reference	Reference
STEMI	0.88 (0.70, 1.10)	1.52 (1.20, 1.93)	1.04 (0.73, 1.48)	2.53 (1.74, 3.69)	0.88 (0.66, 1.18)	2.17 (1.59, 2.96)
Unspecified MI	2.47 (1.73, 3.52)	2.28 (1.59, 3.25)	4.73 (3.02, 7.42)	4.19 (2.65, 6.60)	3.35 (2.23, 5.02)	2.91 (1.94, 4.39)
Comorbidities						
Prior MI	1.31 (1.07, 1.59)	1.11 (0.88, 1.39)	1.33 (0.97, 1.84)	1.01 (0.71, 1.45)	1.34 (1.04, 1.74)	1.08 (0.81, 1.43)
Heart failure	2.38 (1.98, 2.85)	1.50 (1.23, 1.84)	4.94 (3.74, 6.52)	2.06 (1.52, 2.81)	4.78 (3.82, 5.97)	2.04 (1.60, 2.61)
Hypertension	1.68 (1.36, 2.06)	1.27 (1.02, 1.58)	1.87 (1.32, 2.66)	1.12 (0.76, 1.60)	1.88 (1.42, 2.49)	1.13 (0.85, 1.53)
Atrial fibrillation	1.56 (1.29, 1.89)	0.99 (0.81, 1.22)	3.00 (2.26, 3.97)	1.45 (1.08, 1.95)	2.73 (2.18, 3.43)	1.32 (1.04, 1.67)
Diabetes	0.95 (0.80, 1.14)	1.04 (0.86, 1.26)	0.58 (0.42, 0.81)	0.81 (0.58, 1.13)	0.71 (0.56, 0.91)	1.00 (0.77, 1.30)
Peripheral arterial disease	1.58 (1.24, 2.00)	1.21 (0.94, 1.54)	2.09 (1.47, 2.98)	1.46 (1.01, 2.12)	1.85 (1.38, 2.48)	1.30 (0.96, 1.76)
Prior stroke	2.39 (1.85, 3.10)	1.61 (1.24, 2.11)	4.27 (3.02, 6.05)	2.51 (1.75, 3.60)	3.55 (2.65, 4.76)	2.05 (1.51, 2.78)
COPD	1.65 (1.33, 2.04)	1.17 (0.94, 1.46)	2.08 (1.50, 2.88)	1.24 (0.88, 1.73)	2.15 (1.66, 2.79)	1.30 (1.00, 1.70)
Renal disease	1.63 (1.24, 2.14)	1.17 (0.88, 1.55)	1.39 (0.86, 2.23)	0.85 (0.52, 1.38)	1.55 (1.08, 2.23)	0.95 (0.66, 1.38)
Prior PCI	1.00 (0.79, 1.25)	0.95 (0.73, 1.22)	0.81 (0.55, 1.20)	0.92 (0.60, 1.42)	0.80 (0.58, 1.09)	0.89 (0.63, 1.25)
Prior CABG	1.21 (0.90, 1.62)	0.92 (0.67, 1.25)	1.11 (0.67, 1.82)	0.84 (0.50, 1.42)	0.90 (0.58, 1.38)	0.67 (0.43, 1.06)

MACE, major adverse cardiovascular event; MI, myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting.

^a MACE comprises CVD death, recurrent myocardial infarction or stroke.

^b Multivariable models include all variables shown in the table, as well as Indigenous status. We are unable to report the hazard ratio for Indigenous status in this study due to ethics constraints.

^c PCI undertaken during hospitalisation for the index myocardial infarction.

meaning that our risk estimates could be an underestimate compared to a true multi-vessel disease cohort. In addition, this is an Australian study and the results may not be generalizable to other populations. We did not have available data on clinical parameters such as systolic blood pressure and drug treatment during and post-hospital stay, therefore there may be some residual confounding in our analysis of independent predictors which is not accounted for.

5. Conclusions

This large scale study has used linked hospitalisation and mortality data to uniquely identify a contemporary cohort of MI patients at high risk of mortality and cardiovascular events in the early months post-MI. Despite known improvements in short-term mortality after MI in recent years, our findings demonstrate ongoing residual cardiovascular risk in these patients in the first year following MI with at least half of that burden occurring in the first 90 days, highlighting the need to target treatment and prevention efforts during this period. Specific focus on women post-MI are required as our study indicates that the high level of comorbidities and older age make them a particularly high risk group. Given the elevated risk in the first 3 months post discharge, it is important for general practitioners to closely monitor this period in their patients with MI.

Author contributions

LN: Conceptualisation, Funding acquisition, Methodology, Formal analysis, Writing – original draft preparation; TB: Funding acquisition, Methodology, Writing – reviewing and editing; KM: Methodology, Writing – reviewing and editing; AY: Conceptualisation, Methodology, Writing – reviewing and editing; JG: Conceptualisation, Methodology, Writing – reviewing and editing; FMS: Data curation, Writing – reviewing and editing; SJN: Writing – reviewing and editing. All authors have had substantial contribution to conception, Formal analysis, drafting or critical revision of the article, and approval of the final version for submission.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijcrp.2023.200185>

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