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DOI:
10.1177/2048872617710790

Document Version
Final published version

Published in:
European heart journal. Acute cardiovascular care

European Heart Journal
Acute Cardiovascular Care
ESC European Society of Cardiology

Original scientific paper

European Heart Journal: Acute Cardiovascular Care
2019, Vol. 8(1) 68–77

DOI: 10.1177/2048872617710790
journals.sagepub.com/home/acc
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Relative survival and excess mortality following primary percutaneous coronary intervention for ST-elevation myocardial infarction

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Abstract

Background: High survival rates are commonly reported following primary percutaneous coronary intervention for ST-elevation myocardial infarction, with most contemporary studies reporting overall survival.

Aims: The aim of this study was to describe survival following primary percutaneous coronary intervention for ST-elevation myocardial infarction corrected for non-cardiovascular deaths by reporting relative survival and investigate clinically significant factors associated with poor long-term outcomes.

Methods and Results: Using the prospective UK Percutaneous Coronary Intervention registry, primary percutaneous coronary intervention cases (*n*=88,188; 2005–2013) were matched to mortality data for the UK populace. Crude five-year relative survival was 87.1% for the patients undergoing primary percutaneous coronary intervention and 94.7% for patients <55 years. Increasing age was associated with excess mortality up to four years following primary percutaneous coronary intervention (56–65 years: excess mortality rate ratio 1.61, 95% confidence interval 1.46–1.79; 66-75 years: 2.49, 2.26–2.75; >75 years: 4.69, 4.27–5.16). After four years, there was no excess mortality for ages 56–65 years (excess mortality rate ratio 1.27, 0.95–1.70), but persisting excess mortality for older groups (66–75 years: excess mortality rate ratio 1.72, 1.30–2.27; >75 years: 1.66, 1.15–2.41). Excess mortality was associated with cardiogenic shock (excess mortality rate ratio 6.10, 5.72–6.50), renal failure (2.52, 2.27–2.81), left main stem stenosis (1.67, 1.54–1.81), diabetes (1.58, 1.47–1.69), previous myocardial infarction (1.52, 1.40–1.65) and female sex (1.33, 1.26–1.41); whereas stent deployment (0.46, 0.42–0.50) especially drug eluting stents (0.27, 0.45–0.55), radial access (0.70, 0.63–0.71) and previous percutaneous coronary intervention (0.67, 0.60–0.75) were protective.

Conclusions: Following primary percutaneous coronary intervention for ST-elevation myocardial infarction, long-term cardiovascular survival is excellent. Failure to account for non-cardiovascular death may result in an underestimation of the efficacy of primary percutaneous coronary intervention.

Keywords

Primary percutaneous coronary intervention, ST-elevation myocardial infarction, relative survival, excess mortality, cardiogenic shock, renal insufficiency, radial access, risk stratification

Date received: 2 January 2017; accepted: 30 April 2017

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Introduction

The development of specialist heart attack centres, evolving pharmacology, second and third generation stent technology and increasing expertise has resulted in a decline in short-term mortality following ST-elevation myocardial infarction (STEMI) treated by primary percutaneous coronary intervention (PPCI).[1,2] However, in the longer term non-cardiovascular death following PPCI is common and failure to account for this may underestimate the impact of PPCI on survival. Reported rates of death following PPCI are incongruent, with randomised studies suggesting three year mortality rates of 3–8% and observational cohorts reporting one-year mortality rates of around 10%.[3–6] Whilst variation in rates of death following PPCI may be due to unrepresentative cohorts, variable lengths of follow-up and different study designs, it has recently become apparent that the predominant cause of death following PCI may be non-cardiovascular and this may influence how mortality is attributed to PPCI.[1]

Conventionally, the majority of studies of PPCI report all-cause mortality as the primary outcome.[7] Whilst this establishes the overall survival advantage it fails to estimate or account for the underlying comorbidity in patients presenting with STEMI or to estimate the efficacy of treatment with PPCI on cardiovascular outcomes. In turn, this has potential repercussions for the design and study of new treatments as well as informing patients of the risks and benefits of the intervention. To overcome the limitations of all-cause mortality some studies report cause-specific mortality – addressing cardiac death rather than death due to any cause.[8] However, these data may be difficult to obtain, or adjudicate on, and are subject to bias by misclassification, for example, due to a lack of objectivity on death certificates or surmised cause of death without post-mortem studies.[9] An alternative method to estimate cause-specific outcomes is the technique of relative survival (RS), which compares outcomes between patients and an age and sex-matched comparator group of the overall population – this provides the advantage of being able to correct for non-cardiac death and enables quantification of factors associated with excess deaths.[10,11]

Using data from the UK PCI register (British Cardiovascular Intervention Society (BCIS) database), which includes all cases of PPCI in England and Wales; we aimed to estimate the relative survival of patients following PPCI and investigate factors associated with their excess mortality.

Methods

Patients

We included all National Health Service (NHS) hospitals (n=111) in England and Wales which provided care for patients aged 18–100 years with STEMI and who received PPCI between 1 January 2005–30 June 2013 (n=88,188), (Figure 1). Patient-level data concerning demographics, cardiovascular risk factors, medical history and clinical and treatment characteristics at the time of hospitalisation were extracted from BCIS, whereby participation is mandated for all PCI operators and all NHS hospitals. Details of the BCIS registry have been described previously.[12] For multiple admissions, we used the earliest record, the diagnosis of STEMI was formulated by the attending clinician in line with the second (contemporary during the study period) universal definition of myocardial infarction (MI).[13]

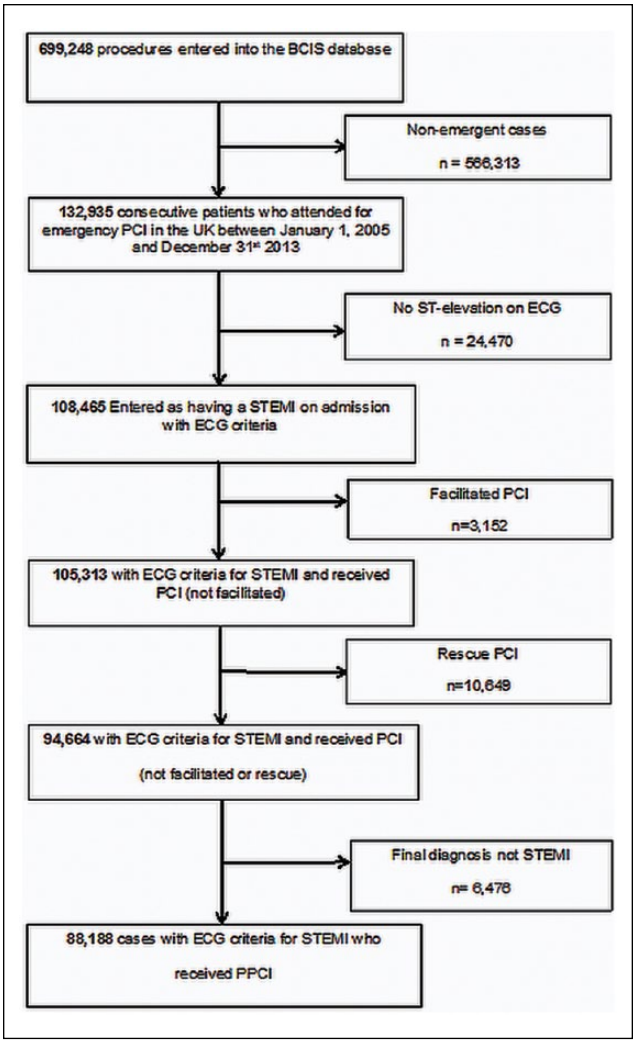

Figure 1. STROBE diagram. BCIS: British Cardiovascular Intervention Society; ECG: electrocardiogram; PCI: percutaneous coronary intervention; STEMI: ST-elevation myocardial infarction.

Mortality and follow-up

All-cause mortality data were extracted through linkage to the UK Office for National Statistics using each patient's unique anonymised NHS number. Patients were followed

for five years from date of PPCI, with censoring at the end of follow-up on 31 December 2013 (Appendix 1). Survival time was defined as the duration between the date of the procedure and the date of death or censoring.

Relative survival

Relative survival was defined as the observed survival of PPCI cases divided by the expected survival of the comparable UK populace, and expressed as a relative survival rate (RSR). Observed survival was estimated using the actuarial method which calculates the survival in time intervals from the effective number of patients at risk in that particular interval. The expected survival was estimated by the Ederer II method.[11] For expected survival, country-specific population mortality rates of the UK were based on life tables from the Office for National Statistics and matched to the cohort by age, sex and year of procedure. A relative survival rate of 100% implies that cases of PPCI have survival rates equal to that of the matched, disease-free background population.

Excess mortality

Excess mortality provides a measure of the additional hazard associated with a procedure or treatment and is expressed as a rate ratio (excess mortality rate ratio (EMRR)). For example, an EMRR of 1.5 for men/women indicates that men experience 50% higher excess mortality than women after accounting for the matched background rates of death. A multivariable model was built based on the following covariates: previous MI, diabetes, chronic renal impairment (creatinine >2.26 mg/dl or 200 micromol/l), pre-procedural cardiogenic shock, flow in the infarct-related artery, use of mechanical ventilation, number of stents deployed, number of vessels attempted, previous PCI and family history of coronary artery disease. The statistical model used collapsed life table data and generalised linear regression with a Poisson error structure. We checked for time-dependency and non-proportional hazards by fitting interaction terms between short-term follow-up periods (<4 years and ≥4 years respectively) with age, which were significant (likelihood ratio test p=0.005). There was no evidence for non-proportional hazards for sex and calendar year by follow-up. Missing data were addressed using multiple imputation by chained equations to create 20 imputed datasets and model estimates pooled over each imputation. All tests were two-tailed with 5% significance level and performed using Stata IC version 13.1 (StataCorp, Texas, USA).

Results

The PPCI cohort comprised 73.9% men, mean age 63.4 (standard deviation (SD) 13.1) years; 41.1% were smokers and 13.4% had diabetes. Over half (56.1%) of cases were completed via radial access route, 7.4% presented with cardiogenic shock, 9.3% received more than three stents, 4.5% had >50% left main stem disease and 0.9% had a history of renal disease (Table 1).

Relative survival

Over 216,846 person-years follow-up (median follow up 2.5 years), in total 12,178 (13.8%) patients died. Overall (crude) relative survival was 92.8% (95% confidence interval (CI), 92.6–93.0%) at three months, 92.5% (92.3–92.7%) at six months, 92.3% (92.1–92.5%) at one year and 87.1% (86.6–87.7%) at five years. One-year relative survival declined with increasing age such that survival estimates for patients aged <55, 56–65, 66–75 and >75 years were 97.3%, 95.3%, 91.8% and 83.1% respectively (Figure 2). The corresponding five-year estimates were 95.4%, 92.8%, 88.3% and 79.0%.

Excess mortality

Up to four years following PPCI, compared with those less than 55 years old there was excess mortality among patients aged 55–65 years (EMRR 1.61, 95% CI 1.46–1.79), 66–75 years (2.49, 2.26–2.75) and >75 years (4.69, 4.27–5.16). After four years, there was no excess mortality for ages 56–65 years (EMRR 1.27, 0.95–1.70), but ongoing excess mortality for ages 66–75 years (1.72, 1.30–2.27) and >75 years (1.66, 1.15–2.41) (Figure 3). Excess mortality was a third higher amongst females than males (EMRR 1.33, 1.26–1.41).

Clinical factors significantly associated with increased excess mortality were diabetes (EMRR 1.58, 95% CI 1.47–1.69), renal failure (2.52, 2.27–2.81), pre-procedural ventilation (3.82, 3.56–4.12), pre-procedural cardiogenic shock (6.10, 5.72–6.50), left main stem stenosis >50% (1.67, 1.54–1.81) and previous MI (1.52, 1.40–1.65). This contrasted with previous PCI (EMRR 0.67, 0.60–0.75), a family history of coronary artery disease (0.75, 0.69–0.81), the use of stents over balloon angioplasty (0.38, 0.34–0.41) and radial artery access (0.70, 0.63–0.71). The use of radial vs femoral access was associated with lower excess mortality in the elderly <75years (EMRR 0.70, 0.65–0.76) and ≥75 years (0.64, 0.59–0.69) (Figure 3). The use of the bare metal stent (BMS) was associated with lower excess mortality compared to balloon angioplasty alone (EMRR 0.49, 0.45–0.55) and the drug eluting stent (DES) was superior to balloon angioplasty (0.27, 0.24–0.29).

Discussion

This study of nearly 90,000 patients over five years of follow-up addresses a key limitation of real-world survival data for PPCI. For the first time in the literature, we report

Table 1. Primary percutaneous coronary intervention (PPCI) cohort baseline characteristics.

		STEMI *n*=88,188	Missing (%)
Demographics			
Mean age, years (SD)		63.4 (13.1)	76 (0.1)
Male (%)		65,178 (73.9)	285 (0.32)
IMD score, mean (SD)		21.2 (17.1)	2422 (2.7)
Medical history			
Current smoker (%)		32,874 (41.1)	8198 (9.3)
Previous smoker (%)		20,996 (23.8)	
Never smoked (%)		26,120 (29.6)	
Diabetes mellitus (%)		11,839 (13.4)	3675 (4.2)
Hyperlipidaemia (%)		33,849 (38.4)	2366 (2.7)
Hypertension (%)		34,608 (39.2)	2366 (2.7)
Family history of CAD (%)		28,547 (32.4)	12,135 (13.8)
History of renal disease (%)		821 (0.9)	365 (0.4)
Previous MI (%)		11,048 (12.5)	3562 (4.0)
Previous PCI (%)		7747 (8.8)	1679 (1.9)
Previous CABG (%)		2405 (2.7)	2089 (2.4)
Pre-procedural medications			
Aspirin (%)		72,035 (85.6)	4057 (4.6)
2nd Antiplatelet agent[a] (%)		66,917 (75.9)	4057 (4.6)
Procedural details			
Bivalirudin at procedure (%)		11,250 (12.8)	4057 (4.6)
Radial access route (%)		49,452 (56.1)	1522 (1.7)
Femoral access route (%)		37,090 (42.1)	
Others – brachial and unspecified (%)		124 (0.1)	
Cardiogenic shock (%)		6496 (7.4)	645 (0.7)
LMS stenosis	No or <50% (%)	71,384 (80.9)	12,860 (14.6)
	≥50% (%)	3944 (4.5)	
Flow in IRA pre-procedure	TIMI 0 (%)	56,729 (64.3)	8451 (9.6)
	TIMI 1 (%)	6510 (7.4)	
	TIMI 2 (%)	7645 (8.7)	
	TIMI 3 (%)	8853 (10.0)	
Vessels attempted	None (%)	397 (0.5)	561 (0.6)
	Single (%)	78,229 (88.7)	
	Multiple (%)	9001 (10.2)	
Post-procedure LMS stenosis	None or <50%	73,344 (83.2)	12,455 (14.1)
	≥50% (%)	2389 (2.7)	
Flow in IRA post-procedure	TIMI 0 (%)	4549 (5.2)	8691(9.8)
	TIMI 1 (%)	1059 (1.2)	
	TIMI 2 (%)	4079 (4.6)	
	TIMI 3 (%)	69,810 (79.2)	
Number of stents used	0 (%)	6691 (7.6)	642 (0.7)
	1 (%)	51,633 (58.5)	
	2 (%)	21,058 (23.9)	
	≥3 (%)	8164 (9.3)	

CABG: coronary artery bypass grafting; CAD: coronary artery disease; IMD: Index of Multiple Deprivation; IRA: infarct-related artery; LMS: left main stem coronary artery; MI: myocardial infarction; PCI: percutaneous coronary intervention; SD: standard deviation; STEMI: ST-elevation myocardial infarction; TIMI: Thrombolysis In Myocardial Infarction flow score.

[a]Clopidogrel, ticlopidine, prasugrel or ticagrelor.

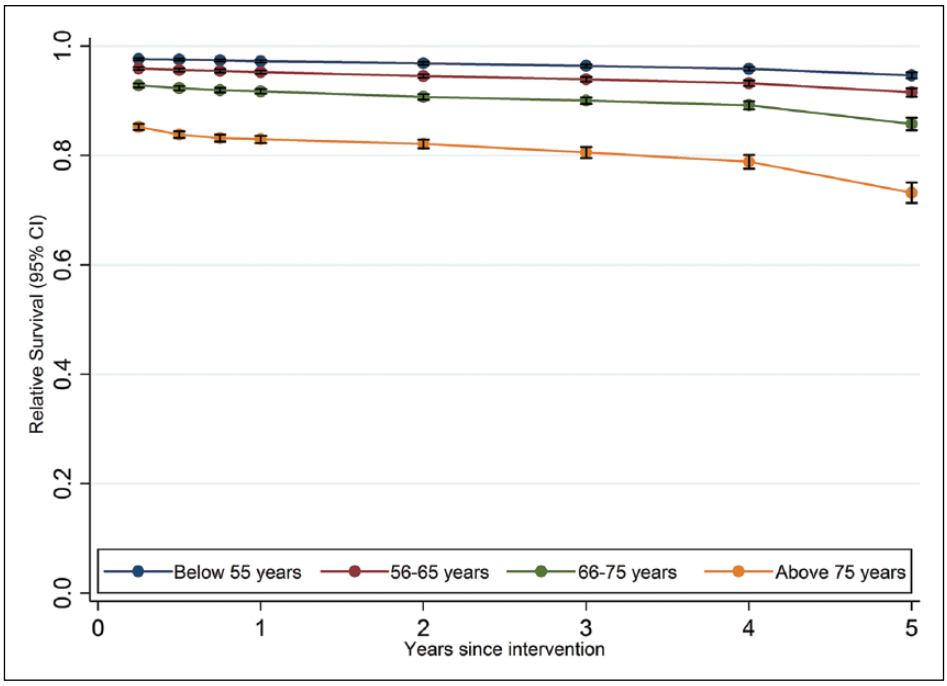

Figure 2. Five-year relative survival following primary percutaneous coronary intervention (PPCI) for ST-elevation myocardial infarction (STEMI), stratified by age. CI: confidence interval.

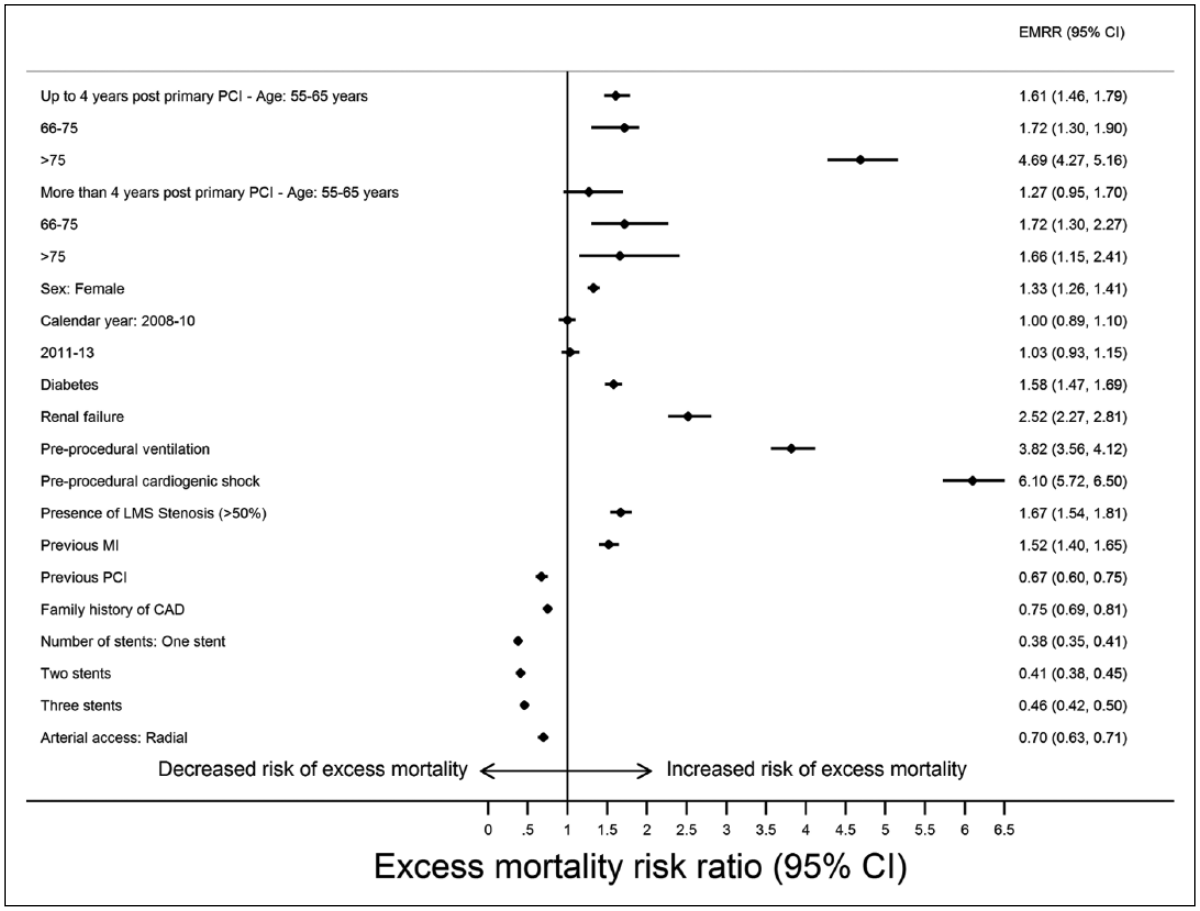

Figure 3. Factors associated with excess mortality following primary percutaneous coronary intervention (PPCI) for ST-elevation myocardial infarction (STEMI). CAD: coronary artery disease; CI: confidence interval; LMS: left main stem coronary artery; MI: myocardial infarction; PCI: percutaneous coronary intervention.

the long-term relative survival for PPCI and investigate factors attributable to death from index STEMI and its treatment with PPCI.

The methods employed here are relevant in the current era of high cardiovascular survival when the majority of deaths are remote from the date of intervention, not cardiovascular in origin and relate to the background risk of the population.[8] In particular, when studying the efficacy of an intervention amongst older age groups, lack of adjustment for increasing mortality amongst the general population can lead to underestimation of the intervention's efficacy. This study provides evidence for very high rates of five-year relative survival – between 2005 and 2013 survival was 90% for the cohort and approached 96% for patients aged <55 years. After adjustment for baseline clinical characteristics and death with the matched general population, evidence for excess mortality was associated with increasing age, renal failure, pre-procedural cardiogenic shock, mechanical ventilation, presence of left main stem disease, previous MI and femoral access.

Overall, relative survival rates were lower early after PPCI, after which the hazards then decreased, this effect was most notably in the elderly. The survival for those younger than 65 years old, four years after PPCI was the same as that of the age, sex, year and country matched background population. Previous studies report worse outcomes for the elderly at one (13.9% mortality), three (43.0%) and five years (53.6%) with increasing age being an independent risk factor.[14–16] In our study, we found that the five-year survival rate among patients over 75 years was 53%, and 79% when adjusted for the age, sex, year and country-specific background rates of death. These data suggest that despite the survival advantage conferred with PPCI for STEMI, the elderly fail to reach rates of survival comparable with their matched counterparts in the general population. We speculate that this may be due to a greater evidence-to-practice gap in secondary preventative care after hospital discharge among the elderly compared with the young.[2,17,18] The database does not record recognised measures of co-morbidity such as the Charlson score, adherence or other determinants such as participation in cardiac rehabilitation or post-discharge management.[19]

We found that females had a third higher risk of excess mortality, consistent with other studies that have also shown that the femoral approach is associated with early mortality in this group.[20–22] Females also had an ongoing disadvantage, suggesting that although femoral access may be unfavourable in the short–term, other sex-specific factors including multimorbidity, mode of presentation and medications prescribed may influence longer-term outcome.

Other factors associated with excess mortality were major pre-existing medical conditions such as diabetes and renal failure as well as the presence of acute STEMI-related scenarios including cardiogenic shock and mechanical ventilation.[23] Cardiogenic shock conferred a six-fold increased risk of death relative to the general population which persisted up to five years from the date of the procedure. This is likely related to the degree of acute myocardial necrosis which persists even after successful revascularisation and its long term counterpart – chronic left ventricular dysfunction.[24] Our study cohort included those who had PPCI for STEMI but did not include those having facilitated or rescue PCI.

Previous MI was associated with a 50% increase excess mortality. It is probable that this is a marker of infarction-mediated left ventricular dysfunction and/or pre-existent multi vessel coronary artery disease – each is known to impact upon survival.[25] We found that a family history of coronary artery disease and previous PCI were each associated with improved outcomes. Whilst we cannot fully explain this, it may represent a healthy user bias – with those with a family history of cardiovascular disease and previous PCI being targeted for pharmacotherapeutic intervention or having healthier behaviour.[26]

To date, there are a number of trials which have reported long-term mortality after PPCI.[27–29] Even though these studies demonstrate favourable outcomes, their interpretation is challenging because none have accounted for non-cardiovascular deaths or the greater background mortality rates among older patients.[1,7] So far, studies which have reported short- and medium-term outcomes are limited because they are historic,[28,30,31] from small cohorts[32] or have been derived from trials which may not be generalisable.[27] Furthermore, cohort studies may have underestimated the benefits of PPCI through not considering the impact of an ageing and increasingly co-morbid population. We respond to this by analysing national registry data within a relative survival framework to provide an alternative, objective and up-to-date measure of the proportion of patients dying following PPCI for STEMI.

Strengths and limitations

The strengths of this study include a national dataset with consecutive cases, the depth of detail, robust mortality tracking and the ability to match cases to the background national population by age, sex, and year of procedure. Survival analysis using relative survival and excess mortality are novel concepts in cardiovascular outcome evaluation and provide additional insight compared to the conventional Cox model or Kaplan Meier analysis.[33] However, biased estimates could be produced if the condition of interest is common and therefore mortality from the condition will also be represented in the background population. If the condition of interest is common this may affect the relative survival analysis, however, bias is negligible when assessing EMRR.[10] Rates of STEMI are around 100–400 per 100,000 population, our sensitivity analyses demonstrated that the estimates derived from standard survival techniques were aligned with those from the relative survival modelling, except among the elderly where the

relative survival estimates were attenuated reflecting the background population rates of death associated with ageing (Appendix 2).

A lack of information in the national life tables about co-morbidities directly related to PPCI may have introduced bias to the estimates because we could only match cases by age, sex, year of procedure and country. The BCIS dataset comprises data at intervention and does not include validated measures of frailty such as the Charlson model, likewise it does not record post-discharge management or adherence to therapy. Whilst there were missing data we mitigated against potential bias using multiple imputation.

Conclusion

This nationwide study of survival following PPCI for STEMI standardised mortality to matched background population death data found that five-year relative survival was very high. Among the elderly, however, there was evidence for significant persisting excess mortality which contrasted with younger age groups where survival rates approached those of the background population. Cardiogenic shock, pre-procedural ventilation, renal failure and the femoral vascular access route were associated with the highest long-term excess mortality after PPCI for STEMI.

Impact on daily practice

Primary PCI for STEMI is an effective treatment and most patients have excellent long-term outcomes. High-risk groups have persisting excess mortality and require appropriate secondary prevention therapy and a targeted approach to reducing their risk of STEMI-related death. Further studies are required to elucidate the underlying mechanism of ongoing risk.

Acknowledgements

The extract from the British Cardiovascular Intervention Society (BCIS) registry was provided through the BCIS/National Institute for Cardiovascular Outcomes Research (NICOR). The authors gratefully acknowledge all the hospitals in England and Wales for their contribution of data to BCIS.

Conflict of interest

RAB, OA, MH, SA, TBD, MM, PDB, PB, MdB, and PFL have no conflicts of interest. CPG has received consultancy and speaker bureau fees from AstraZeneca and Novartis. NC has received unrestricted research grants from Medtronic, Haemonetics, Boston Scientific, St Jude Medical, Heartflow; honoraria from St Jude Medical, Heartflow; unrestricted education grant from Volcano.

Funding

TBD and MH are funded by the British Heart Foundation as a research assistant and research fellow, respectively (Project Grant PG/13/81/30474).

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Appendix 1

Life table

Population mortality estimates derived from life tables for England and Wales were used to calculate expected survival. The latest published life table data available were for 2012; therefore 2012 population data were matched to 2013 patient data without extrapolation (Table 2).

Table 2. Calendar year of procedure and years of follow-up included in the calculations of five-year relative survival for the years 2005–2013.

Year of procedure	Year of follow-up								
	2005	2006	2007	2008	2009	2010	2011	2012	2013
2005	1	1/2	2/3	3/4	4/5	5/6	6/7	7/8	8/9
2006		1	1/2	2/3	3/4	4/5	5/6	6/7	7/8
2007			1	1/2	2/3	3/4	4/5	5/6	6/7
2008				1	1/2	2/3	3/4	4/5	5/6
2009					1	1/2	2/3	3/4	4/5
2010						1	1/2	2/3	3/4
2011							1	1/2	2/3
2012								1	1/2
2013									1

The numbers within the cells indicate the number of years following procedure.

Appendix 2

Sensitivity analysis

We matched cases by age, sex, year of procedure and country, and not comorbidity. The latter was not matched because there is a lack of information concerning comorbidities in the general population as recorded in the UK life tables. Not matching to these additinoal factors may have introduced bias to the estimates. This was addressed this by running a baseline model which included covariates available both in the cohort and general population groups (Table 3). Poisson regression found no difference in estimates between the relative survival technique (excess mortality rate ratio (EMRR) and observed all-cause mortality (mortality rate ratio (MRR)) (Table 4).

Table 3. Excess mortality and observed mortality using imputed data (baseline model).

Full model	EMRR	MRR
Age by follow-up interaction		
≤55 years (reference)	1.00	1.00
Up to 4 years post primary PCI		
Age 56–65	1.71 (1.54–1.90)[a]	1.81 (1.66–1.99)[a]
Age 66–75	3.01 (2.74–3.32)[a]	3.39 (3.10–3.69)[a]
Age >75	6.40 (5.84–7.01)[a]	8.26 (7.62–8.96)[a]
More than 4 years post primary PCI		
Age 56–65	1.40 (1.07–1.83)[a]	2.03 (1.77–2.32)[a]
Age 66–75	1.90 (1.43–2.52)[a]	4.02 (3.55–4.55)[a]
Age>75	2.60 (1.86–3.65)[a]	11.56 (10.29–12.99)[a]
Sex		
Male (reference)	1.00	1.00
Female	1.29 (1.22–1.36)[a]	1.11 (1.07–1.15)[a]
Calendar year		
2005–2007 (reference)	1.00	1.00
2008–2010	0.91 (0.82–1.01)	0.95 (0.89–1.02)
2011–2013	0.98 (0.88–1.08)	1.04 (0.97–1.11)

EMRR: excess mortality rate ratio; MRR: mortality rate ratio; PCI: percutaneous coronary intervention.
[a]Significance at 5% level.

Table 4. Excess mortality and observed all-cause mortality using imputed data (full model).

Full model	EMRR	MRR
Age by follow-up interaction		
≤55 years (reference)	1.00	1.00
Up to 4 years post primary PCI		
Age 56–65	1.61 (1.46–1.79)[a]	1.73 (1.57–1.90)[a]
Age 66–75	2.49 (2.26–2.75)[a]	2.96 (2.71–3.23)[a]
Age >75	4.69 (4.27–5.16)[a]	6.63 (6.11–7.20)[a]
More than 4 years post primary PCI		
Age 56–65	1.27 (0.95–1.70)	1.95 (1.71–2.24)[a]
Age 66–75	1.72 (1.30–2.27)[a]	3.60 (3.18–4.08)[a]
Age>75	1.66 (1.15–2.41)[a]	9.73 (8.65–10.94)[a]
Sex		
Male (reference)	1.00	1.00
Female	1.33 (1.26–1.41)[a]	1.16 (1.12–1.21)[a]
Calendar year		
2005–2007 (reference)	1.00	1.00
2008–2010	1.00 (0.89–1.10)	1.02 (0.96–1.10)
2011–2013	1.03 (0.93–1.15)	1.11 (1.03–1.19)
Medical history		
Diabetes	1.58 (1.47–1.69)[a]	1.45 (1.38–1.52)[a]
Renal Failure	2.52 (2.27–2.81)[a]	2.25 (2.07–2.45)[a]
Pre procedural ventilation	3.82 (3.56–4.12)[a]	3.36 (3.15–3.58)[a]
Pre procedural cardiogenic shock	6.10 (5.72–6.50)[a]	3.73 (3.55–3.91)[a]
Presence of LMS stenosis (>50%)	1.67 (1.54–1.81)[a]	0.50 (0.47–0.52)[a]
Previous MI	1.52 (1.40–1.65)[a]	1.50 (1.42–1.58)[a]
Previous PCI	0.67 (0.60–0.75)[a]	0.75 (0.70–0.81)[a]
Family history of CAD	0.75 (0.69–0.81)[a]	0.78 (0.74–0.816)[a]
Number of stents		
No stents (reference)	1.00	1.00
1	0.38 (0.35–0.41)[a]	0.50 (0.47–0.52)[a]
2	0.41 (0.38–0.45)[a]	0.51 (0.48–0.54)[a]
3	0.46 (0.42–0.50)[a]	0.56 (0.52–0.60)[a]
Arterial access		
Femoral (reference)	1.00	1.00
Radial	0.70 (0.63–0.71)[a]	0.78 (0.75–0.82)[a]

CAD: coronary artery disease; EMRR: excess mortality rate ratio; LMS: left main stem; MI: myocardial infarction; MRR: mortality rate ratio; PCI: percutaneous coronary intervention.
[a]Significance at 5% level.