The association between older age and receipt of care and outcomes in patients with acute coronary syndromes: A cohort study of the Myocardial Ischaemia National Audit Project (MINAP)

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Abstract

Aims

Older people increasingly constitute a large proportion of the acute coronary syndrome (ACS) population. We examined the relationship of age with receipt of more intensive management and secondary prevention medicine. Then, the comparative association of intensive management (reperfusion/angiography) over a conservative strategy on time to death was investigated by age.

Methods and Results

Using data from 155,818 patients in the national registry for ACS in England and Wales (the Myocardial Ischaemia National Audit Project (MINAP)), we found that older patients were incrementally less likely to receive secondary prevention medicines and intensive management for both ST-elevation myocardial infarction (STEMI) and non-ST elevation myocardial infarction (NSTEMI). In STEMI patients ≥85 years, 55% received reperfusion compared to 84% in those aged 18-<65 (odds ratio 0.22 (95% CI 0.21, 0.24)). Not receiving intensive management was associated with worse survival (mean follow-up 2.29 years (SD 1.42)) in all age groups (adjusted for sex, cardiovascular risk factors, co-morbidities, healthcare factors and case severity) but there was an incremental reduction in survival benefit from intensive management with increasing age. In STEMI patients aged 18-64, 65-74, 75-84 and ≥85, adjusted hazard ratios (HRs) for all-cause mortality comparing conservative treatment to intensive management were 1.98 (1.78,2.19), 1.65 (1.51,1.80), 1.62 (1.52,1.72) and 1.36 (1.27,1.47), respectively. In NSTEMI patients, the respective HRs were 4.37 (4.00, 4.78), 3.76 (3.54, 3.99), 2.79 (2.67, 2.91) and 1.90 (1.77, 2.04).

Conclusion

We found an incremental reduction in the use of evidence-based therapies with increasing age using a national ACS registry cohort. Whilst survival benefit from more intensive management reduced with older age, better survival was associated with intensive management at all ages highlighting the requirement to improve standard of care in older patients with ACS.

Keywords:

Acute Coronary Syndrome; Age; Elderly; Prognosis

Introduction

Clinical trials of therapies for acute coronary syndrome (ACS) such as coronary reperfusion and secondary prevention medicines such as statins have demonstrated effectiveness even in the oldest patients (1-2) - however this age group are less likely to receive both.(3-5) Such older patients may have increased co-morbidity (6) and higher risk of complications from more intensive management (7) and thus this under-treatment relative to younger patients may be appropriate. As the population ages and the older age group becomes an increasingly larger proportion of the population, it is important to understand what effect intensive management is having on outcomes in these older patients, and what other additional factors impact on outcomes.

Trial evidence on best practice in the older patient with ACS may not represent the real-world older ACS patient with multiple co-morbidities. The proportional representation in clinical trial populations of older patients is much lower (around 9%) than the real-world picture of the acute medical take,(8) where 35% patients are aged 75 or over.(9) There is a need for evidence from real-world data that more accurately depicts both receipt of treatment and outcomes in the older patient with ACS. Large clinical registries offer representative study populations with high generalisability, and importantly the statistical power to answer such questions.

Using the Myocardial Ischaemia National Audit Project (MINAP), a national registry which contains data from patients with an acute coronary syndrome admitted to all 230 National Health Service (NHS) hospital trusts in England and Wales,(10) we aimed to explore the relationship of age group with receipt of more intensive management and secondary prevention medicine. Then we aimed to compare the association of intensive management on time to death over a conservative strategy by age group, seeking to account for any differences in survival through adjustment for co-morbidities, standards of care and disease severity, and the interaction of age group with management strategy.

Methods

Study design

This was a cohort study of patients admitted to hospital with acute coronary syndrome and followed up for all-cause mortality. MINAP was set up in 1999 to examine the quality of management of acute myocardial infarction in England and Wales and to meet the audit requirements of the National Service Framework for Coronary Heart Disease.(11-12) By 2003, all 230 NHS hospital trusts in England and Wales were contributing data to MINAP. Each month, MINAP accrues over 7000 acute coronary syndrome events and records 113 data fields covering clinical and healthcare-related measures. (10) Data are collected by nurses and clinical audit staff and entered in a dedicated data application (either on-line or web based: http://web.nicor.org.uk) developed by the Central Cardiac Audit Database group

(13) which is part of the NHS Information Centre for Health and Social Care. MINAP is overseen by a multi-professional steering group representing the stakeholders and is based at the National Institute for Cardiovascular Outcomes Research (NICOR) at University College London. MINAP monitors the completeness of 20 key fields for patients with an admission diagnosis of a definite myocardial infarction and the data application contains data validation processes including range and consistency checks and also mechanisms to identify and remove duplicate records. The patients in MINAP are followed up for their date of all-cause death through linkage to the National Health Service Central Registry using a unique number. Data entry is subject to routine on-line error checking. MINAP has National Patient Information Advisory Group and Central Office for Research Ethics Committees approval for individual patient anonymous linkage for mortality. The current study obtained the ethical approval from the Faculty of Medicine & Health Sciences Research Ethics Committee, University of East Anglia.

Cohort profile

In this paper we used data pertaining to all patients from 2006 to 2010 (the most recent download of data with at least one-year follow-up for all-cause mortality). We analysed records of admissions between 1st January 2006 and 31st December 2010 for patients having a final diagnosis of ST-segment elevation myocardial infarction (STEMI) or of non-ST-segment elevation myocardial infarction (NSTEMI). The final diagnosis was formed from the history, clinical examination and results of in-patient investigations and was made by a senior member of the medical staff. Data were further extensively cleaned by us using *a priori* definitions and a data usage manual written. We further validated variables using cross-checks with other data fields – for instance, final diagnosis correlated well with elevated markers for STEMI and NSTEMI categories. The original dataset consisted of 363,098 participants with a final diagnosis of STEMI or NSTEMI (ACS with a positive troponin blood test). Of these, 11222 were dropped as one-year follow-up status was unknown as were 431 aged under 18 with missing or impossibly high values (>111) for age. A further 3729 exclusions included those for whom the census date (at which patients' one-year follow-up survival status was recorded) preceded the date of hospital admission and those in whom survival status was recorded before an entire year had passed since admission. Following these exclusions there remained 347,716 observations in the dataset, that is 96% of the original dataset. The dataset on which the analyses in this paper are based consists of 155,818 subjects on whom a complete set of explanatory variables was available. Previous published imputation analyses on the MINAP dataset by the lead author(14) have not significantly altered effect sizes and imply that missingness in MINAP is at random whilst work by others has also shown that the level of missingness of data in MINAP does not alter regional standardised mortality ratios.(15)

Study variables

We measured secondary prevention medicine therapy usage by examining receipt of aspirin, ACE inhibitor or statin on discharge. With regards to more intensive management, in

patients with STEMI this referred to receipt of reperfusion available locally at time of presentation (i.e., receipt of thrombolysis or primary percutaneous coronary intervention (PPCI)) - centres increasingly shifted to PPCI over the course of the cohort and thus the strongest determinant of receipt of either of these treatments was local availability not age). In patients with NSTEMI, we regarded more intensive management as receipt of angiography in hospital, as previous work in MINAP has shown that any disparity in revascularisation is driven primarily by less frequent referral for diagnostic angiogram.(16) The conservative group was defined as those who did not receive reperfusion in STEMI patients and those who did not receive angiography in NSTEMI patients. These group assignments of intensive management and conservative management were defined from the clinical management data as recorded by the MINAP clinical audit staff which outlined which treatment modalities each patient had undergone in hospital.

For survival Cox regression analyses, the outcome was all-cause death. Markers of disease severity were collected as in-hospital clinical events of re-infarction, significant bleeding (any bleed as recorded by the clinician as well as retroperitoneal and intracranial haemorrhage), cardiac arrest and abnormal ECG (e.g. ST or T wave changes or left bundle branch block). Co-morbid conditions were chronic renal failure, cerebrovascular disease, peripheral vascular disease, chronic obstructive pulmonary disease and congestive cardiac failure whilst cardiovascular risk factors were smoking (ex or current), known diabetes mellitus and known hypertension (definitions for variables are pre-defined by MINAP and given in appendix 1). To account for potential regional differences in care, we used MINAP data on the patient's Strategic Health Authority, the regional body that oversees the provision of healthcare across a given region within the National Health Service of England and Wales.

Statistical analysis

We examined patient characteristics for the whole ACS cohort by age group (years) at presentation categorised as younger (18-<65), young–old (65-<75), old-old (75-< 85) and oldest old (≥85) in line with previous work.(17) We applied logistic regression analyses separately for STEMI and NSTEMI patients to compare the odds of receipt of treatments for ACS against not receiving them - in turn for intensive management, aspirin, ACE inhibitor or statin, and by age group using the youngest age group as the reference group on plots. We used the chi squared test to assess for trends by age.

To investigate whether the association of intensive management on time to death within a year of admission compared to the conservative group differed by age group, we constructed Cox proportional hazards regression models stratified by age group for STEMI and then NSTEMI, using intensive management as the reference group. Logistic regression of the whole cohort identified variables that independently contributed to mortality in order to build the Cox models. After crude estimates, we in turn adjusted for cardiovascular risk factors, co-morbidities, healthcare factors (receipt of secondary prevention and if under the care of a cardiologist rather than a generalist) and case severity variables (re-infarction, bleeding, cardiac arrest and abnormal ECG) including sex in all these models before building

a fully-adjusted combined model. Regression models included Hubert-White robust adjustment for intra-cluster correlation of outcomes within Strategic Health Authorities.

The interactions between the age and management strategy on time to death were evaluated separately for both STEMI and NSTEMI using a fully-adjusted model with an interaction terms between age group and management strategy. We also examined age-treatment interactions within the full model with age modelled as a continuous instead of an ordered categorical variable. Wald tests were used to test the significance of age-treatment interaction.

Analyses were performed using Stata SE, version 11 (Stata, College Station, Texas).

Results

The records of 155,818 patients with complete data were examined. Of these, 103,540 (66.5%) were men. The mean age of the cohort was 69 (SD 14). The mean follow-up was 2.29 years (SD 1.42). Our final dataset consisted of 68,025 STEMI and 87,793 NSTEMI patients. Patients' baseline characteristics by age group are shown in Table 1 for the whole ACS cohort. Younger patients were more likely to be men and smokers than older patients. Prevalence of hypertension rose with age though dyslipidaemia fell. Past history of coronary disease and co-morbidities rose with age, whilst receipt of previous coronary revascularisation decreased with older age and patients who were older were less likely to have been cared for by a cardiologist during their admission with an ACS.

Receipt of management in hospital

With older age, patients were less likely to receive secondary prevention medicines and intensive management for both STEMI (figure 1) and NSTEMI (figure 2). For STEMI, 55% of patients aged 85 or over received reperfusion compared to 84% of those patients aged 18-<65 (odds ratio (OR) 0.22 (95% CI 0.21,0.24). For NSTEMI, the odds of receiving coronary angiography were extremely low (OR 0.03 (0.03,0.04)) in the oldest old, with only 14% of those aged 85 or over undergoing angiography compared to 83% of those patients aged 18-<65. Regarding receipt of a statin, STEMI patients aged 85 or over were less likely to receive this at discharge compared to patients in the youngest age group (OR 0.31 (0.29,0.33)). There was an incremental reduction of receipt of treatment with older age for all these evidence-based treatments, for both STEMI and NSTEMI.

Association of older age on adjusted time to death by receipt of intensive management

The association of intensive management on time to death over conservative management was examined by age strata. In all age groups of patients with STEMI, not receiving reperfusion was associated with worse unadjusted survival (table 2). The benefit of this intensive management strategy was attenuated in older patients as the hazard ratios decrementally approached the reference category with older age groups. After adjusting for sex, further adjusting the hazard ratios in separate models (supplementary table 1) for cardiovascular risk factors and then for co-morbidities did not alter these results, though

when adjusting for healthcare factors (receipt of secondary prevention and care by a cardiologist), the adverse prognosis associated with not receiving reperfusion was attenuated markedly in the oldest age group (hazard ratio (HR) 1.34 (1.24, 1.44)). Adjusting for factors contributing to worse case severity (in-hospital cardiac arrest, in-hospital, re-infarction, abnormal ECG, in-hospital bleeding) did not alter these results in any age group. A fully-adjusted model (table 2) attenuated the worse prognosis in those who did not undergo reperfusion in all age groups, in particular for the oldest age group with the effect size changing from 1.64 to 1.36, though this is likely to be driven mostly by adjustment for healthcare factors. Further accounting for clustering by Strategic Health Authority within the fully-adjusted model did not change the point estimates (supplementary table 1).

In patients with NSTEMI, conservative management was associated with worse unadjusted survival (table 3) in all age groups, but again the benefit of an intensive management strategy was attenuated in older patients as the hazard ratios decrementally approached the reference category with older age groups. Adjustment for co-morbidities, healthcare factors and worse case severity (supplementary table 2) did not significantly alter the results for any age group, nor did accounting for clustering by Strategic Health Authority within the fully-adjusted model.

The interaction of age and receipt of intensive investigation

For both STEMI and NSTEMI, the fully-adjusted Cox model showed an interaction between age group and receipt of intensive investigation (P<0.001 for both). In NSTEMI, there was a reduced benefit from receiving intensive management with older age groups (final column of table 3), with those undergoing a conservative management strategy aged 85 or over having a HR of 1.90 (1.77, 2.04) when compared to those undergoing intensive management, with the comparable risk of death from a conservative approach being much higher (HR 4.37 (4.00, 4.78) in those aged 18-<65. This pattern replicated with STEMI to a lesser extent (final column of table 2).

Modelling age as a continuous variable, the adjusted hazards ratios for age-treatment interaction were 0.989 (0.985-0.992, P<0.001) for STEMI and 0.969 (0.967-0.972, P<0.001) for NSTEMI for each extra year of age – thus the increased hazard ratios associated with conservative management were reduced by 0.989 and 0.969 respectively for STEMI and NSTEMI for each extra year of age.

Discussion

We found an incremental reduction in the use of evidence-based therapies - both medicine-based and intensive - with increasing age using a national ACS registry cohort that reflects real-world clinical practice in England and Wales and that enabled categorisation of ACS patients into STEMI and NSTEMI. We also found that improved survival was associated with intensive management at all ages though the difference in survival benefit between it and a conservative strategy reduced incrementally with older age. Furthermore, we

show that receipt of secondary prevention and care by a cardiologist might be of significant benefit in older patients with STEMI in reducing death within one year.

Our work correlates with the 2009 UK Department of Health commissioned report carried out by the Centre for Policy on Ageing which revealed clear and widespread evidence of age discrimination in hospital-based acute investigation and treatment of heart disease and in the subsequent instigation of secondary prevention regimes to be carried forward to the community following discharge.(18) Despite international guidelines(19) reminding clinicians that intensive management in the older patients with ACS is as effective as in their younger counterparts, we in line with other studies(17, 20) show that older patients are less likely to receive them. We add to this literature by using outcomes out to one year and thus presenting a population in which the sickest (who often die in hospital) are less influential in the data and which allows clinicians more scope to influence prognosis. We also distinguish between the two very different phenotypes that are STEMI and NSTEMI, undertake full adjustment for a wide range of prognostic factors within clinically relevant models and use a large nationwide registry cohort study highly representative of the real-world ACS population. Then importantly, we sought to demonstrate which factors might influence longer-term mortality in different age groups in order to facilitate clinical decision-making in management. We suggest that an increasing usage of secondary prevention medicine therapy and specialist cardiologist input could account for the better outcomes increasingly seen in older patients with ACS - previous work in MINAP has revealed incremental reductions in short-term (in-hospital) mortality from 2003 to 2010 across all age groups including the oldest old. (17) Our work here also confirms ideas from others that improvements in hospital care for older patients would reduce mortality rates and that this might be achieved through the application of evidence-based ACS therapies to patients regardless of age.(21-22)

The relative under-treatment of older patients with ACS may be down to a perception on the part of the clinician of a higher risk in older patients from intensive management, previous analyses in a subset of MINAP (using only those hospitals with interventional facilities) have shown that although co-morbidities are associated with higher mortality, the presence of co-morbidities do not significantly diminish the impact of intensive management on long-term mortality.(16) Though bleeding was more common with older age, the prevalence of such side effects in our work was low even in those aged 85 and over (2.9% had a significant in-hospital bleed and in those undergoing reperfusion only 0.84% of this oldest age group had an intracranial bleed compared to 0.2% of those aged 18-64 (data not shown)). A single-centre study from a hospital with interventional facilities also suggested that the lesser treatment in older patients cannot be explained by the nature of the healthcare facility they are admitted to.(23) On reviewing the literature on clinical trials of an intensive strategy in the older patient, these trial patients remain highly selected(24) and there remains a general dearth of clinical trial data in older patients.(25)

The reduced benefits with older age of intensive management may be due to the higher risk of dying from ACS afforded by older age alone (as observed by around a half of patients aged 85 years and over in the conservative groups dying within a year),(26) whilst

those youngest patients who do not undergo intensive management must have good reason not to - such as life-threatening clinical presentations or serious co-morbidity - thus widening the relative benefit between intervening intensively or not. Our separate models adjusting for potential confounding factors attempted to control for this but were unable to fully explain the survival differences between conservative and intensive management strategies. We included patients who died in hospital for these analyses to render this paper applicable to clinicians who have to make management decisions at the front door. Analysing only those that survived to discharge attenuated point estimates (e.g. 2.04 to 1.74 for the fully-adjusted model in those NSTEMI patients aged 85 and above, data not shown) but not the overall patterns of the results. We found that in the oldest STEMI patients who did not undergo reperfusion that receipt of secondary prevention medication and being under the care of a cardiologist reduced the relative risk of dying compared to those who did undergo reperfusion, suggesting a role for optimised and carefully supervised specialist medicine therapy even in those aged 85 and above.

What we cannot conclude from this paper is the appropriateness for intensive management in the older patient with ACS. It is likely that clinicians are already applying clinical judgement in selecting patients for an intensive management strategy, and appropriately not intensively managing those patients that are frail, or have extensive co-morbidity. To a degree thus, the under-management we see in the older age groups here may be entirely reasonable but without a randomised controlled clinical trial design in all-comer older patients with ACS, criteria for selection for an intensive management strategy will remain unclear. Certainly data from other registries suggests that older patients potentially stand to gain the most from an intensive management strategy due to their overall highest risk, consistent with the substantial impact of age on risk in scores such as the GRACE score.(20) However, selection of older patients for an intensive management strategy in the real world remains highly variable and they tend to be sicker and have more co-morbidities than those recruited in a trial.(27) Even if a trial were planned, it would be unethical to randomise all older patients to either strategy as - from clinical trial evidence on highly-selected older patients - we know that an intensive strategy does work in those selected groups, and thus no such trial exists to this day. Any trial in this area would hence need to recruit and randomise those older patients in whom there was reasonable doubt as to the benefit of an intensive strategy in light of possible harm from such a strategy. What constitutes 'reasonable doubt' is however itself far from clear. Teasing out biological age from chronological age is perhaps key to this through the judicious use of a wider range of prognostic measures to guide the clinician as to the appropriateness of intensive management following presentation with ACS. Frailty is estimated to be present in more than 25% in those aged 85 and older(28) and some single-item measures (e.g. gait speed measured as 15-foot walk time with usual assistive device during the walk) are independently associated with mortality risk over follow-up as short as six months in an older population with coronary disease(29) - such measures are feasible in older patients in a clinical trial context(30) and may provide supplemental and useful information for clinical discussions about treatment risks and benefits.

Strengths and Limitations

The strength of MINAP is its large size, representativeness and that it contains extensive data on clinical management and characterisation. MINAP importantly allowed us to take into account the heterogeneity of ACS, as considerable differences exist in the pathology and subsequent management of a STEMI compared to a NSTEMI. Though it collects data from all 230 hospitals in England and Wales, MINAP cannot collect data on every patient with an ACS and it is possible that patients entered into the MINAP database differ from those not recorded, and that there may be differences in missingness by age. However, older and frailer patients with non-specific symptoms may be less likely to be included in registry data and therefore the magnitude of the relationships we observed may represent an underestimation. Regarding missing data, some fields were more problematic in this regards - in particular clopidrogrel usage was missing in around half of patients and thus could not be used- and which reflects the fact that MINAP is an on-going audit-driven dataset that describes evolving healthcare. As iterated above in this paper, missingness is not thought to be a major concern in the validity of analyses within MINAP. Future work using MINAP in England may be strengthened through the linkage of electronic health records available in the Clinical Practice Research Datalink (www.cprd.com) and data on hospital admissions from Hospital Episode Statistics.(31) MINAP also lacks data on more detailed clinical measures (e.g. acute angiographic findings, presence of acute heart failure (thus not allowing us a calculation of a GRACE score(32)), echocardiographic or angiographic measurement of ventricular function etc.), the actual time of the angiogram and cause of death. It also did not have data on cognition, extreme frailty nor patient choice and its co-morbidity data were limited (e.g. no data on cancer) - thus we were unable to explore in greater detail reasons underlying the differences in receipt of care by age group, and on survival.

We also were unable to assess accurately the impact of older age on time from onset of symptoms to arrival within MINAP, and the relationship between in-hospital death and receipt of either management strategy - however, less than 5% of patients with ACS were considered to have had a delay in getting to hospital and of these less than 1% were delays associated with transfer, and less than 3% of patients (and less than 5% of patients aged 75-84) died in hospital. Finally, as an ongoing audit-driven dataset, MINAP spans evolving healthcare trends and our data covered the period in which reperfusion was moving from thrombolysis to PPCI. We combined these fields as if we were to exclude patients that had fibrinolysis, this exclusion would have been driven not by their appropriateness for fibrinolysis over PPCI but simply because at the time of their admission, their hospital could not offer PPCI. Equally, splitting the STEMI group into fibrinolysis and PPCI would not provide a meaningful analysis as the selection would simply be driven by the institution at which they were admitted to rather than being a clinically meaningful grouping. That fibrinolysis and PPCI are different treatments is less important when compared to the fact that they are both tools for reperfusion. By clearly splitting all the cohort analyses into STEMI (in whom the decision to reperfuse is made immediately) and NSTEMI (in whom patients are

considered for an intensive strategy sometime later in the hospital), we have kept these two different ACS phenotypes and their specific management pathways separate.

Conclusions

We found an incremental reduction in the use of evidence-based therapies for ACS with older age in the national registry cohort for England and Wales and that better survival was associated with intensive management at all ages, though this benefit was attenuated the older the patient. Whether the optimal benefit could be achievable by a multidisciplinary care model with active involvement of cardiologists in the oldest old requires further evaluation in a clinical trial setting.

Ethical approval

The National Institute for Cardiovascular Research (NICOR) which includes the Myocardial Ischaemia National Audit Project (MINAP) (Ref: NIGB: ECC 1-06 (d)/2011) has support under section 251 of the National Health Service (NHS) Act 2006. The current study obtained the ethical approval from the Faculty of Medicine & Health Sciences Research Ethics Committee, University of East Anglia.

Funding

This work was supported by the Sir Halley Stewart Trust. MINAP is funded by the Health Quality Improvement Partnership (HQIP).

Conflicts of interest: none declared.

Acknowledgements

The extract from the MINAP database was provided through the MINAP Academic Group following peer review of our research proposal. We acknowledge all the hospitals in England and Wales for their contribution of data to MINAP. We gratefully acknowledge the funder of this research work, the Sir Halley Stewart Trust. There are no competing interests and the authors have nothing to declare.

Disclaimer

This work was undertaken by the research team led by Dr Zaman and Dr Myint and funded by the Sir Halley Stewart Trust. The views expressed within this paper are those of authors' and not necessarily those of the Trust.

Table 1 Baseline characteristics of whole MINAP cohort

	<65	65-74	75-84	>85	p-trend
N	59,994	37,014	38,637	20,173	
SOCIODEMOGRAPHICS					
Age, yrs (mean, SD)	54.4 (7.6)	70.0(2.9)	79.8(2.9)	88.9(3.3)	-
Men (%)	47,713(79.5)	25,102(67.8)	21,853(56.6)	8,872 (44.0)	p<0.001
Current smoker (%)	30,784(51.3)	9,175(24.8)	4,778(12.4)	1,033(5.1)	p<0.001
PAST MEDICAL HISTORY					
Diabetic (%)	8,587(14.3)	8,397(22.7)	9,070(23.5)	3,527(17.5)	p<0.001
Hypertensive(%)	22,643(37.7)	19.506(52.7)	22,760(58.9)	11,435(56.7)	p<0.001
Dyslipidaemia (%)	20,144(33.6)	14,282(38.6)	13,283(34.4)	4,975(24.7)	p<0.001
Ischaemic heart disease (%)	9,513 (15.9)	9,340(25.2)	12,368(32.0)	6,941(34.4)	p<0.001
Heart failure(%)	817 (1.4)	1,594(4.3)	3,173(8.21)	2,485(12.3)	p<0.001
Chronic renal failure (%)	1,057(1.8)	1,613(4.4)	3,103(8.0)	2,020(10.0)	p<0.001
Cerebrovascular disease (%)	1,884(3.1)	3,064(8.3)	4,724(12.2)	2,906(14.4)	p<0.001
Peripheral vascular disease	1,556(2.6)	2,031(5.5)	2,457(6.4)	964(4.8)	p<0.001
Chronic obstructive	6,164(10.3)	6,326(17.1)	7,094(18.4)	2,929(14.5)	p<0.001

pulmonary disease (%)					
PREVIOUS REVASCULARISARION	7,001(11.7)	6,156(16.6)	5,724(14.8)	1,287(6.4)	p<0.001
Percutaneous Coronary Intervention	5,683(9.5)	4,070(11.0)	3,368(8.7)	779(3.9)	p<0.001
Coronary bypass surgery	2,010(3.4)	3,035(8.2)	3,168(8.2)	652(3.2)	p<0.001
Under Cardiologist care	35,440(59.1)	19,406(52.4)	16,863(43.6)	6,648(33.0)	p<0.001
DISCHARGE MEDICATIONS					
Aspirin	52,054(86.8)	30,738(83.0)	30,309(78.5)	15,192(75.3)	p<0.001
Statin	52,155(86.9)	31,323(84.6)	31,196(80.7)	14,603(72.4)	p<0.001

B-blocker	47,054(78.4)	26,087(70.5)	24,920(64.5)	11,774(58.4)	p<0.001
ACE inhibitor	48,232(80.4)	28,338(76.6)	27,001(69.9)	11,879(58.9)	p<0.001
MARKERS OF DISEASE SEVERITY					
Abnormal ECG	53,920(89.9)	33,826(91.4)	35,695(92.4)	18,757(92.9)	p<0.001
In-patient re-infarction	1,111(1.9)	740(2.0)	799(2.1)	426(2.1)	p=0.005
In-patient cardiac arrest	2,764(4.6)	1,680(4.5)	1,604(4.2)	717(3.6)	p<0.001
In-patient bleeding	778(1.3)	789(2.1)	1,087(2.8)	580(2.9)	p<0.001
DISCHARGE DIAGNOSIS					
STEMI	33,603(56.0)	16,283(44.0)	12,914(33.4)	5,225(25.9)	p<0.001
NSTEMI	26,391(44.0)	20,731(56.0)	25,723(66.6)	14,948 (74.1)	p<0.001

Table 2 Effect of a conservative management strategy compared to receipt of reperfusion on risk of all-cause death by age group for STEMI patients

Age	Cases, n	Deaths, n (%)	HR (95%CI)[1]	p	HR (95%CI)[2]	p	HR (95%CI)[3]	p
18-<65								
Conservative	5234	494 (9.4)	2.22 (2.00,2.46)	<0.001	1.96 (1.76,2.18)	<0.001	1.98 (1.78,2.19)	<0.001
Reperfusion	28369	1374 (4.8)	1.00		1.00		1.00	
65 to 74								
Conservative	3307	737 (22.2)	1.96 (1.80,2.14)	<0.001	1.62 (1.48,1.78)	<0.001	1.65 (1.51,1.80)	<0.001
Reperfusion	12976	1766 (13.6)	1.00		1.00		1.00	
75 to 84								
Conservative	3816	1618 (42.4)	1.91 (1.79,2.03)	<0.001	1.63 (1.53,1.74)	<0.001	1.62 (1.52,1.72)	<0.001
Reperfusion	9098	2577 (28.3)	1.00		1.00		1.00	
≥85 years								
Conservative	2367	1530 (64.6)	1.64(1.53,1.77)	<0.001	1.35 (1.25,1.46)	<0.001	1.36 (1.27,1.47)	<0.001
Reperfusion	2858	1466 (51.3)	1.00		1.00		1.00	

1 Crude

2 Full model - Adjusted HR for age, sex, diabetes, hypertension and smoking, previous chronic renal failure, cerebrovascular disease, peripheral vascular disease, chronic obstructive pulmonary disease and congestive cardiac failure, receipt of ACE inhibitor, statin, aspirin, b-blocker and care by a cardiologist, in-hospital cardiac arrest, in-hospital re-infarction, abnormal ECG and in-hospital bleeding. Each age stratum had a separate model.
3 Full model with all patients and interaction term between age and management strategy

Table 3 Effect of a conservative management strategy compared to receipt of angiography on risk of all-cause death by age group for NSTEMI patients

Age	Cases, n	Deaths, n (%)	HR (95%CI)[1]	p	HR (95%CI)[2]	p	HR (95%CI)[3]	p
18-<65								
Conservative	4473	909 (20.3)	4.38 (4.00,4.78)	<0.001	3.38 (3.07,3.71)	<0.001	4.37 (4.00,4.78)	<0.001
Angiography	21918	1032 (4.7)	1.00		1.00		1.00	
65 to 74								
Conservative	6364	2739 (43.0)	3.98 (3.75,4.23)	<0.001	3.43 (3.22,3.65)	<0.001	3.76 (3.54,3.99)	<0.001
Angiography	14367	1797 (12.5)	1.00		1.00		1.00	
75 to 84								
Conservative	14381	7994 (55.6)	2.75 (2.64,2.87)	<0.001	2.82 (2.69,2.95)	<0.001	2.79 (2.67,2.91)	<0.001
Angiography	11342	2724 (24.0)	1.00		1.00		1.00	
≥85 years								
Conservative	12816	8486 (66.2)	1.92 (1.79,2.06)	<0.001	2.04 (1.90,2.19)	<0.001	1.90 (1.77,2.04)	<0.001

Angiography	2132	869 (40.8)	1.00		1.00		1.00	

1 Crude

2 Full model - Adjusted HR for age, sex, diabetes, hypertension and smoking, previous chronic renal failure, cerebrovascular disease, peripheral vascular disease, chronic obstructive pulmonary disease and congestive cardiac failure, receipt of ACE inhibitor, statin, aspirin, b-blocker and care by a cardiologist, in-hospital cardiac arrest, in-hospital re-infarction, abnormal ECG and in-hospital bleeding. Each age stratum had a separate model.

3 Full model with all patients and interaction term between age and management strategy

Figure legends

Figure 1 Receipt of treatment by age group in patients with STEMI

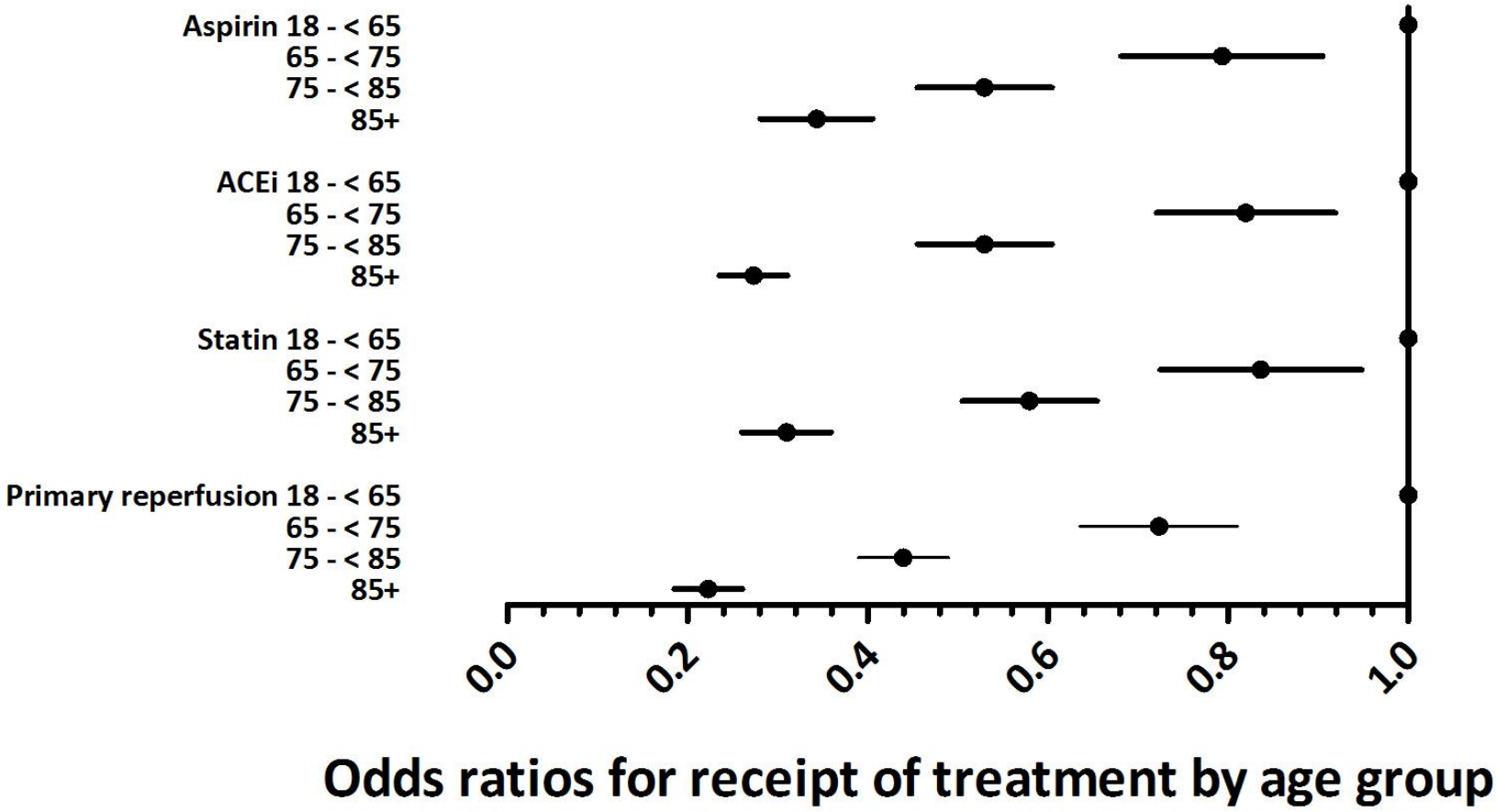
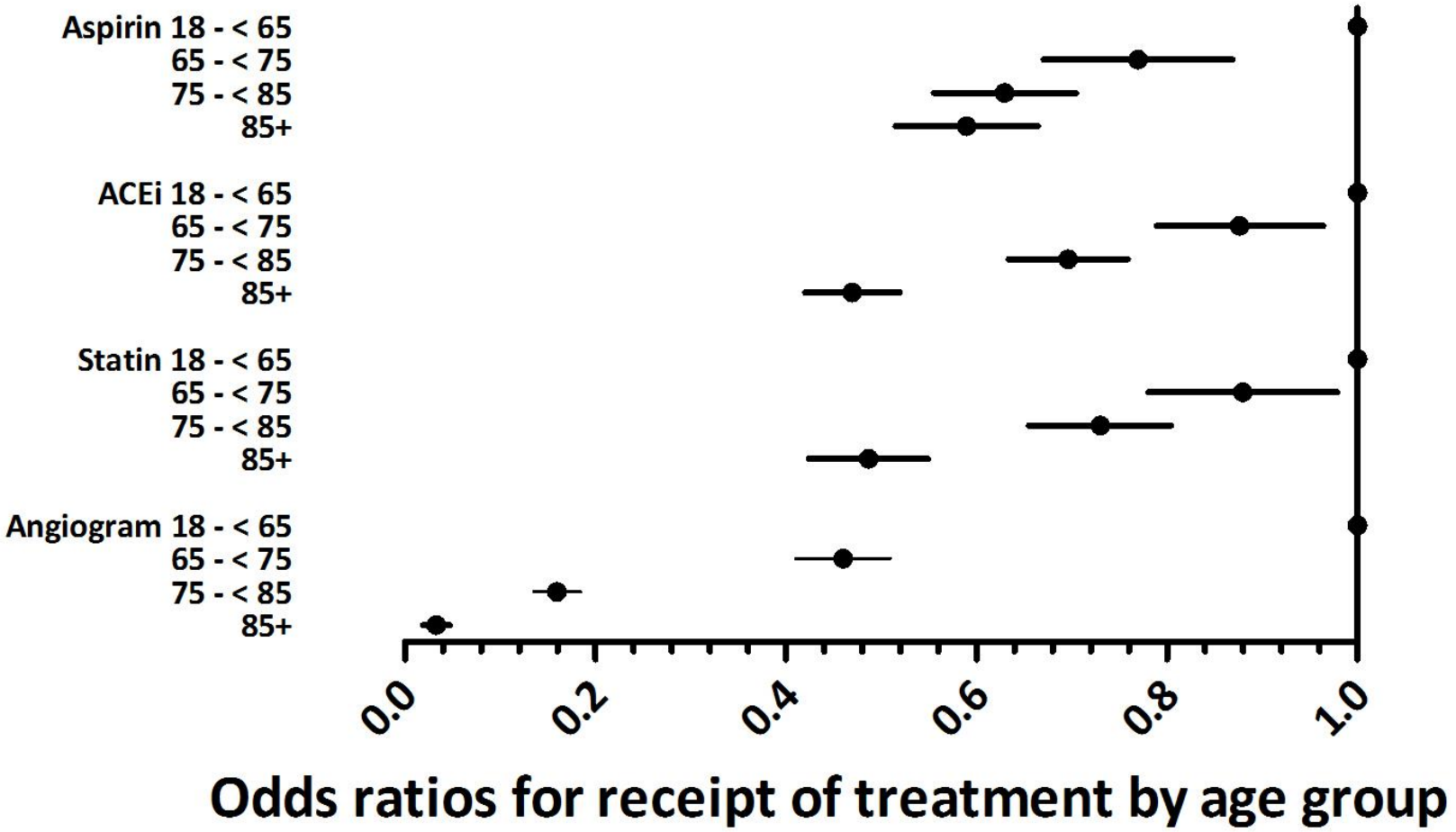


Figure 2 Receipt of treatment by age group in patients with NSTEMI



Supplementary tables

Table S1 Effect of a conservative management strategy compared to receipt of reperfusion on risk of all-cause death by age group for STEMI patients

Age	Cases, n	Deaths, n (%)	HR (95%CI)[1]	HR (95%CI)[2]	HR (95%CI)[3]	HR (95%CI)[4]	HR (95%CI)[5]
18-<65							
Conservative	5234	494 (9.4)	2.14 (1.93,2.38)	2.11 (1.90,2.34)	1.96 (1.76,2.18)	2.37 (2.13,2.63)	1.96 (1.68,2.29)
Reperfusion	28369	1374 (4.8)	1.00	1.00	1.00	1.00	1.00
65 to 74							
Conservative	3307	737 (22.2)	1.88 (1.73,2.06)	1.78 (1.63,1.95)	1.70 (1.56,1.86)	2.05 (1.88,2.24)	1.62 (1.47,1.80)
Reperfusion	12976	1766 (13.6)	1.00	1.00	1.00	1.00	1.00
75 to 84							
Conservative	3816	1618 (42.4)	1.88 (1.76,2.00)	1.76 (1.66,1.88)	1.67 (1.57,1.78)	2.04 (1.91,2.17)	1.63 (1.48,1.80)
Reperfusion	9098	2577 (28.3)	1.00	1.00	1.00	1.00	1.00
≥85 years							
Conservative	2367	1530 (64.6)	1.64 (1.52,1.76)	1.58 (1.47,1.70)	1.34 (1.24,1.44)	1.76 (1.63,1.89)	1.35 (1.20,1.51)

Reperfusion	2858	1466 (51.3)	1.00	1.00	1.00	1.00	1.00

HR for all-cause death

1 Adjusted HR for sex, diabetes, hypertension and smoking

2 Adjusted HR for sex, previous chronic renal failure, cerebrovascular disease, peripheral vascular disease, chronic obstructive pulmonary disease and congestive cardiac failure

3 Adjusted HR for sex, receipt of ACE inhibitor, statin, aspirin, b-blocker and care by a cardiologist

4 Adjusted HR for sex, in-hospital cardiac arrest, in-hospital re-infarction, abnormal ECG and in-hospital bleeding

5 Fully adjusted model accounted for clustering by Strategic Health Authority (adjusted HR for sex, diabetes, hypertension and smoking, previous chronic renal failure, cerebrovascular disease, peripheral vascular disease, chronic obstructive pulmonary disease and congestive cardiac failure, receipt of ACE inhibitor, statin, aspirin, b-blocker and care by a cardiologist, in-hospital cardiac arrest, in-hospital re-infarction, abnormal ECG and in-hospital bleeding)

Table S2 Effect of a conservative management strategy compared to receipt of angiography on risk of all-cause death by age group for NSTEMI patients

Age	Cases, n	Deaths, n (%)	HR (95%CI)[1]	HR (95%CI)[2]	HR (95%CI)[3]	HR (95%CI)[4]	HR (95%CI)[5]
<65							
Conservative	5234	909 (20.3)	3.92 (3.58,4.29)	3.34 (3.04,3.66)	4.63 (4.22,5.07)	4.42 (4.04,4.83)	3.38 (2.88,3.95)
Angiography	28369	1032 (4.7)	1.00	1.00	1.00	1.00	1.00
65 to 74							
Conservative	3307	2739 (43.0)	3.71 (3.50,3.94)	3.38 (3.18,3.59)	4.18 (3.94,4.45)	3.99 (3.76,4.24)	3.43 (3.04,3.87)
Angiography	12976	1797 (12.5)	1.00	1.00	1.00	1.00	1.00
75 to 84							
Conservative	3816	7994 (55.6)	2.75 (2.63,2.87)	2.57 (2.46,2.69)	3.06 (2.92,3.20)	2.83 (2.71,2.96)	2.82 (2.50,3.17)
Angiography	9098	2724 (24.0)	1.00	1.00	1.00	1.00	1.00
≥85 years							
Conservative	2367	8486 (66.2)	1.96 (1.83,2.10)	1.92 (1.79,2.06)	2.07 (1.93,2.23)	1.99 (1.85,2.13)	2.04 (1.83,2.28)
Angiography	2858	869 (40.8)	1.00	1.00	1.00	1.00	1.00

HR for all-cause death
1 Adjusted HR for sex, diabetes, hypertension and smoking
2 Adjusted HR for sex, previous chronic renal failure, cerebrovascular disease, peripheral vascular disease, chronic obstructive pulmonary disease and congestive cardiac failure
3 Adjusted HR for sex, receipt of ACE inhibitor, statin, aspirin, b-blocker and care by a cardiologist
4 Adjusted HR for sex, in-hospital cardiac arrest, in-hospital re-infarction, abnormal ECG and in-hospital bleeding
5 Fully adjusted model accounted for clustering by Strategic Health Authority (adjusted HR for sex, diabetes, hypertension and smoking, previous chronic renal failure, cerebrovascular disease, peripheral vascular disease, chronic obstructive pulmonary disease and congestive cardiac failure, receipt of ACE inhibitor, statin, aspirin, b-blocker and care by a cardiologist, in-hospital cardiac arrest, in-hospital re-infarction, abnormal ECG and in-hospital bleeding)

References

1. Hoenig MR, Aroney CN, Scott IA. Early invasive versus conservative strategies for unstable angina and non-ST elevation myocardial infarction in the stent era. Cochrane Database Syst Rev. 2010(3):CD004815.
2. Afilalo J, Duque G, Steele R, Jukema JW, de Craen AJ, Eisenberg MJ. Statins for secondary prevention in elderly patients: a hierarchical bayesian meta-analysis. J Am Coll Cardiol. 2008 Jan 1;51(1):37-45.
3. Avezum A, Makdisse M, Spencer F, Gore JM, Fox KA, Montalescot G, Eagle KA, White K, Mehta RH, Knobel E, Collet JP. Impact of age on management and outcome of acute coronary syndrome: observations from the Global Registry of Acute Coronary Events (GRACE). Am Heart J. 2005 Jan;149(1):67-73.
4. Ramsay SE, Morris RW, Papacosta O, Lennon LT, Thomas MC, Whincup PH. Secondary prevention of coronary heart disease in older British men: extent of inequalities before and after implementation of the National Service Framework. J Public Health (Oxf). 2005 Dec;27(4):338-43.
5. Collinson J, Bakhai A, Flather MD, Fox KA. The management and investigation of elderly patients with acute coronary syndromes without ST elevation: an evidence-based approach? Results of the Prospective Registry of Acute Ischaemic Syndromes in the United Kingdom (PRAIS-UK). Age and ageing. 2005 Jan;34(1):61-6.
6. Taneva E, Bogdanova V, Shtereva N. Acute coronary syndrome, comorbidity, and mortality in geriatric patients. Annals of the New York Academy of Sciences. 2004 Jun;1019:106-10.
7. Leoncini M, Maioli M, Bellandi F, Galvani M, Ottani F, Toso A, Di Vincenzo E, Gallopin M, Dabizzi RP. Therapeutic strategies, immediate and mid-term outcomes in non-ST-segment elevation acute coronary syndromes with respect to age: a single-center registry of 488 consecutive patients. Clinical cardiology. 2004 Aug;27(8):475-9.
8. Lee PY, Alexander KP, Hammill BG, Pasquali SK, Peterson ED. Representation of elderly persons and women in published randomized trials of acute coronary syndromes. JAMA. 2001 Aug 8;286(6):708-13.
9. Alexander KP, Roe MT, Chen AY, Lytle BL, Pollack CV, Jr., Foody JM, Boden WE, Smith SC, Jr., Gibler WB, Ohman EM, Peterson ED. Evolution in cardiovascular care for elderly patients with non-ST-segment elevation acute coronary syndromes: results from the CRUSADE National Quality Improvement Initiative. J Am Coll Cardiol. 2005 Oct 18;46(8):1479-87.
10. Birkhead JS, Weston C, Lowe D, National Audit of Myocardial Infarction Project (MINAP) Steering Group. Impact of specialty of admitting physician and type of hospital on care and outcome for myocardial infarction in England and Wales during 2004-5: observational study. BMJ. 2006 June 3, 2006;332(7553):1306-11.
11. Birkhead J, Walker L. National audit of myocardial infarction (MINAP): a project in evolution. Hosp Med. 2004 Aug;65(8):452-3.
12. Herrett E, Smeeth L, Walker L, Weston C. The Myocardial Ischaemia National Audit Project (MINAP). Heart. 2010 Aug;96(16):1264-7.
13. Rickards A, Cunningham D. From quantity to quality: the central cardiac audit database project. Heart. 1999 October 1, 1999;82(90002):18ii-22.

14. Zaman MJ, Philipson P, Chen R, Farag A, Shipley M, Marmot MG, Timmis AD, Hemingway H. South Asians and coronary disease: is there discordance between effects on incidence and prognosis? Heart. 2013 Feb 13.
15. Gale CP, Cattle BA, Moore J, Dawe H, Greenwood DC, West RM. Impact of missing data on standardised mortality ratios for acute myocardial infarction: evidence from the Myocardial Ischaemia National Audit Project (MINAP) 2004-7. Heart. 2011 Dec;97(23):1926-31.
16. Birkhead JS, Weston CF, Chen R. Determinants and outcomes of coronary angiography after non-ST-segment elevation myocardial infarction. A cohort study of the Myocardial Ischaemia National Audit Project (MINAP). Heart. 2009 Oct;95(19):1593-9.
17. Gale CP, Cattle BA, Woolston A, Baxter PD, West TH, Simms AD, Blaxill J, Greenwood DC, Fox KA, West RM. Resolving inequalities in care? Reduced mortality in the elderly after acute coronary syndromes. The Myocardial Ischaemia National Audit Project 2003-2010. Eur Heart J. 2012 Mar;33(5):630-9.
18. Lievesley N. Ageism and age discrimination in secondary health care in the United Kingdom. A review from the literature carried out on behalf of the Department of Health: Centre for Policy on Ageing2009.
19. Steg PG, James SK, Atar D, Badano LP, Blomstrom-Lundqvist C, Borger MA, Di Mario C, Dickstein K, Ducrocq G, Fernandez-Aviles F, Gershlick AH, Giannuzzi P, Halvorsen S, Huber K, Juni P, Kastrati A, Knuuti J, Lenzen MJ, Mahaffey KW, Valgimigli M, van 't Hof A, Widimsky P, Zahger D. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J. 2012 Oct;33(20):2569-619.
20. Malkin CJ, Prakash R, Chew DP. The impact of increased age on outcome from a strategy of early invasive management and revascularisation in patients with acute coronary syndromes: retrospective analysis study from the ACACIA registry. BMJ Open. 2012;2(1):e000540.
21. Rosengren A, Wallentin L, Simoons M, Gitt AK, Behar S, Battler A, Hasdai D. Age, clinical presentation, and outcome of acute coronary syndromes in the Euroheart acute coronary syndrome survey. Eur Heart J. 2006 Apr;27(7):789-95.
22. Smith LG, Herlitz J, Karlsson T, Berger AK, Luepker RV. International comparison of treatment and long-term outcomes for acute myocardial infarction in the elderly: Minneapolis/St. Paul, MN, USA and Goteborg, Sweden. Eur Heart J. 2013 Nov;34(41):3191-7.
23. Timoteo AT, Ramos R, Toste A, Lousinha A, Oliveira JA, Ferreira ML, Cruz Ferreira R. [Impact of age on treatment and outcomes after acute myocardial infarction, particularly in very elderly patients]. Rev Port Cardiol. 2011 Dec;30(12):897-903.
24. Shanmugasundaram M. Percutaneous coronary intervention in elderly patients: is it beneficial? Tex Heart Inst J. 2011;38(4):398-403.
25. Lindley RI. Drug trials for older people. J Gerontol A Biol Sci Med Sci. 2012 Feb;67(2):152-7.
26. Jernberg T, Johanson P, Held C, Svennblad B, Lindback J, Wallentin L. Association between adoption of evidence-based treatment and survival for patients with ST-elevation myocardial infarction. JAMA. 2011 Apr 27;305(16):1677-84.
27. Steg PG, Lopez-Sendon J, Lopez de Sa E, Goodman SG, Gore JM, Anderson FA, Jr., Himbert D, Allegrone J, Van de Werf F. External validity of clinical trials in acute myocardial infarction. Arch Intern Med. 2007 Jan 8;167(1):68-73.

28. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001 Mar;56(3):M146-56.
29. Purser JL, Kuchibhatla MN, Fillenbaum GG, Harding T, Peterson ED, Alexander KP. Identifying frailty in hospitalized older adults with significant coronary artery disease. J Am Geriatr Soc. 2006 Nov;54(11):1674-81.
30. Ridda I, Lindley R, MacIntyre RC. The challenges of clinical trials in the exclusion zone: the case of the frail elderly. Australas J Ageing. 2008 Jun;27(2):61-6.
31. Herrett E, Shah AD, Boggon R, Denaxas S, Smeeth L, van Staa T, Timmis A, Hemingway H. Completeness and diagnostic validity of recording acute myocardial infarction events in primary care, hospital care, disease registry, and national mortality records: cohort study. BMJ. 2013;346:f2350.
32. Fox KA, Dabbous OH, Goldberg RJ, Pieper KS, Eagle KA, Van de Werf F, Avezum A, Goodman SG, Flather MD, Anderson FA, Jr., Granger CB. Prediction of risk of death and myocardial infarction in the six months after presentation with acute coronary syndrome: prospective multinational observational study (GRACE). BMJ. 2006 Nov 25;333(7578):1091.

All Table and Figure legends

Table 1 Baseline characteristics of whole MINAP cohort

Figure 1 Receipt of treatment by age group in patients with STEMI

Figure 2 Receipt of treatment by age group in patients with NSTEMI

Table 2 Effect of a conservative management strategy compared to receipt of reperfusion on risk of all-cause death by age group for STEMI patients

Table 3 Effect of a conservative management strategy compared to receipt of angiography on risk of all-cause death by age group for NSTEMI patients

Supplementary tables

Table S1 Effect of a conservative management strategy compared to receipt of reperfusion on risk of all-cause death by age group for STEMI patients

Table S2 Effect of a conservative management strategy compared to receipt of angiography on risk of all-cause death by age group for NSTEMI patients