Temporal Trends in Identification, Management, and Clinical Outcomes After Out-of-Hospital Cardiac Arrest

Insights From the Myocardial Ischaemia National Audit Project Database

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***Background*—**There is wide variation in survival rates from out-of-hospital cardiac arrest (OHCA) and overall survival remains poor. There is an expert consensus that early reperfusion therapy in ST-elevation reduces mortality. The management of patients without ST-elevation, however, is controversial.

***Methods and Results*—**The Myocardial Ischaemia National Audit Project database is a national registry of all hospital admissions in England and Wales treated as an acute coronary syndrome (ACS). We examined temporal trends, over a 5-year period, of OHCAs identified by Myocardial Ischaemia National Audit Project, admitted to hospital and treated as ACS, the interventional management of these patients and clinical outcomes. Four hundred ten thousand four hundred sixty-two patients were admitted to hospital in England and Wales with ACS. Of these, 9421 presented with OHCA (2.30%). There was an increase in OHCA cases as a proportion of ACS between 2009 and 2013 (1.79% in 2009 versus 2.74% in 2013; $P_{trend}<0.001$). The rate of coronary angiography+percutaneous coronary intervention increased in ACS patients presenting with OHCA (54.9% in 2009 [876/1595] versus 66.3% in 2013 [884/1334]; $P_{trend}<0.001$). Cox proportional hazards model with time-varying exposure to coronary angiography demonstrated a significant reduction in mortality in both the ST-elevation (hazard ratio, 0.30; 95% confidence interval, 0.28–0.32; $P<0.05$) and non–ST-elevation cohort (hazard ratio, 0.44; 95% confidence interval, 0.42–0.46; $P<0.001$). Predictors of favorable outcome were synonymous with the selection criteria for patients undergoing coronary angiography±percutaneous coronary intervention.

***Conclusions*—**This observational study showed that selection for coronary angiography±percutaneous coronary intervention was associated with reduced mortality in OHCA patients diagnosed with ACS. These data support the need for a randomized controlled trial. **(*Circ Cardiovasc Interv*. 2018;11:e005346. DOI: 10.1161/CIRCINTERVENTIONS.117.005346.)**

Key Words: acute coronary syndrome ■ coronary angiography ■ coronary artery disease ■ out-of-hospital cardiac arrest ■ percutaneous coronary intervention

Out-of-hospital cardiac arrest (OHCA) is a global public health issue. Each year there are ≈28 000 emergency medical services–treated OHCA in England and ≈330 000 emergency medical services-attended OHCA in the United States.[1,2] There is wide variation in survival rates from OHCA and overall survival remains poor, with a reported average of 7%.[1] The adoption of systematic approaches to cardiopulmonary resuscitation may improve long-term survival from OHCA.[3,4] Postresuscitation care in-hospital including targeted temperature management and treatment of the underlying cause through coronary reperfusion is thought to further improve this survival in patients with acute coronary syndromes (ACS).[5] It is difficult to conclude which of the components of postarrest care is essential, given the observational nature of studies. Coronary artery disease is responsible for >70% of OHCA of presumed cardiac cause, with an acute occlusion demonstrated in 50% of consecutive patients taken immediately to coronary angiography (CA).[6] There is an expert consensus that early reperfusion therapy in ST-elevation (STE)

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WHAT IS KNOWN

- There is wide variation in survival rates from out-of-hospital cardiac arrest and overall survival remains poor.
- There is an expert consensus that early reperfusion therapy in ST-elevation reduces mortality.
- The management of patients without ST-elevation, however, is controversial.

WHAT THE STUDY ADDS

- We demonstrate that over a 5-year period the rate of coronary angiogram+percutaneous coronary intervention increased after out-of-hospital cardiac arrest and was associated with favorable outcome in patients with and without ST-elevation; however, predictors of favorable outcome were synonymous with the selection criteria for patients undergoing coronary angiogram±percutaneous coronary intervention.
- These data support the need for a randomized controlled trial.

reduces mortality.[7,8] The management of patients without STE, however, is controversial, with an emphasis placed on prior rule out of noncoronary causes.[8] Randomized data are lacking and the benefit of early reperfusion therapy remains debated. This has led to a variable uptake of such a strategy among the interventional cardiology community. The Myocardial Ischaemia National Audit Project (MINAP) database is a noncommercially funded national registry of all hospital admissions treated as ACS in England and Wales, established to examine the quality of management of hospitals providing acute cardiac care.[9] The strengths of this registry include its size and national reach. This database selectively captures OHCAs that are admitted to hospital with a final diagnosis of ACS and does not encompass all OHCA admissions to hospital. Therefore, the aim of this study was to examine the temporal trends, over a 5-year period, of OHCAs identified by the MINAP registry, admitted to hospital and treated as ACS, the interventional management of these patients and clinical outcomes.

Methods

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure without prior approval for release of patient-identifiable data from the National Institute of Clinical Outcomes Research.

The MINAP registry consists of 123 core data points, including cardiovascular risk factors, occurrence of cardiac arrest, postresuscitation therapies including CA and percutaneous coronary intervention (PCI), and outcomes including in-hospital mortality and neurological outcome; these data points have been published previously.[10] Of the 123 separate fields, 49 data sets were extracted and examined (Tables I through V in the Data Supplement). These clinical audit data are a valuable resource and missing values are inevitable when large volumes of data are collected and have the potential to bias or reduce the efficiency of statistical estimators if they are not treated appropriately. Thus, we performed multiple imputations to deal with these missing data. Patients are identified at the individual hospital level and data entry, performed by trained personnel, undergoes annual validation through reaudit. MINAP has approval from the Patient Information Advisory Group to use patient-identifiable information without individual patient consent. MINAP approved this current registry-based project and data analyses were performed at King's College London, St Thomas' Hospital, United Kingdom with the support of London School of Hygiene and Tropical Medicine Clinical Trials Unit, United Kingdom.

Study Population and Outcomes Reported

For the purposes of this study, fully anonymized data were retrospectively extracted from the MINAP data set of hospitals in England and Wales accepting admissions between January 2009 and July 2013. ACS was categorized as ST-segment–elevation myocardial infarction or non–ST-segment–elevation myocardial infarction based on biomarker and electrocardiographic criteria. OHCA was defined as cardiac arrest before arrival at the hospital. Procedural intervention was classed as no coronary angiogram, coronary angiogram alone, and coronary angiogram+PCI. In-hospital mortality is defined as patient death in-hospital. Life status is tracked by MINAP through linkage with the Office of National Statistics using the unique National Health Service identifier (number), thus represents in-hospital mortality and subsequent mortality after discharge.

Statistical Analysis

Categorical data were presented as counts and percentages, and comparison between groups performed using χ^2 test; numeric data were presented as mean±SD, and analysis performed using 1-way ANOVA. The temporal trends in identification of OHCA, followed by distribution of baseline characteristics (male gender, presence of STE, previous MI, previous angina, hypertension, hypercholesterolemia, peripheral vascular disease, cerebrovascular disease, chronic renal failure, heart failure, smoking history, diabetes mellitus, previous PCI, previous coronary artery bypass graft surgery, family history, presenting rhythm of pulseless ventricular tachycardia/ventricular fibrillation [VT/VF] and age >75), the rate of procedural intervention, in-hospital mortality, and good neurological outcome (defined as cerebral performance category 1 or 2 at discharge) of the ACS cohort presenting with OHCA were examined. For trend analysis, year-on-year we used the Cochran–Armitage test for trend to test for linear relationships between categorical variables. To determine independent predictors for in-hospital mortality and the odds of undergoing procedural intervention (CA±PCI), multivariable-adjusted logistic regression models were used to generate odds ratios (ORs). To limit the number of variables for the final multivariable models, stepwise regression was performed using the above covariates (entry criteria $P<0.05$, exit criteria $P>0.1$); significant variables were used in the final model. Final model selection was performed using multiple imputations (fully conditional specification, SPSS v24.0 [IBM Corp]) to impute missing data on baseline covariates by chained equations to create 5 multiply imputed data sets to maximize statistical power (missing values and multiple imputation methodology is reported in Methods in the Data Supplement). The variables used in the final model of the odds of undergoing CA±PCI were gender, STE, previous MI, previous angina, hypertension, hypercholesterolemia, peripheral vascular disease, cerebrovascular disease, chronic renal failure, heart failure, smoking history, diabetes mellitus, previous PCI, previous coronary artery bypass graft surgery, family history, VT/VF, and age>75. The variables used in the final model for in-hospital mortality were as for the previous model with the addition of CA±PCI. No significant collinearity was demonstrated. Because of the large proportion of missing data, complete case analysis was performed in parallel, these results were compared with those of multiply imputed data to increase the robustness of our conclusions (Methods in the Data Supplement). Time to event analysis was performed using

Kaplan–Meier curves, Cox proportional hazard analyses model was performed to generate (1) time-varying hazard ratio (HR) for <30 days and >30 days and (2) time-varying exposure to CA (to account for survival bias) using time-varying covariate of transition time to coronary angiogram. All P values were 2-sided with a significance threshold P<0.05. Statistical analysis was performed using SPSS v24.0 (IBM Corp).

Results

Trends in Incidence of ACS Presenting As OHCA

Figure 1 details case identification. From January 2009 to July 2013, we identified 410 462 patients admitted to hospital in England and Wales with a final discharge diagnosis of troponin positive ACS. Over the 5-year period, 385 509 did not experience cardiac arrest and 24 953 experienced cardiac arrest. Of the 24 953 cardiac arrest patients, 9421 of these patients were identified as OHCA. The overall proportion of ACS patients presenting with OHCA (9421) relative to the overall cohort of patients diagnosed with ACS (410 462) was 2.3%. This proportion increased yearly from 2009 to 2013 (1.8% [1595/89 380] in 2009, 2.0% [1835/91 087] in 2010, 2.4% [2142/90 559] in 2011, 2.8% [2515/90 705] in 2012 to 2.7% [1334/48 731] in 2013; P_{trend}<0.001; Figures in the Data Supplement).

Baseline Characteristics of Identified Cases of OHCA

Table 1 depicts the changes in baseline demographics from 2009 to 2013 of the study cohort under question of patients identified in-hospital with a discharge diagnosis of ACS who presented with OHCA (n=9 421; Figure 1). In the overall cohort of ACS patients presenting with OHCA, the prevalence of known underlying ischemic heart disease (previous angina [20.4% (326/1595) in 2009 versus 15.8% (211/1334) in 2013; P_{trend}<0.001], previous acute myocardial infarction [21.8% (348/1595) in 2009 versus 17.4% (232/1334) in 2013; P_{trend}<0.05], and previous coronary artery bypass graft surgery [7.3% (116/1595) in 2009 versus 5.5% (73/1334) in 2013; P_{trend}<0.05] and risk factors for coronary artery disease (hypercholesterolemia [28.8% (459/1595) in 2009 versus 25.0% (333/1334) in 2013; P_{trend}<0.05], smoking history [64.5% (1028/1595) in 2009 versus 60.6% (809/1334) in 2013; P_{trend}<0.05], and positive family history [25.5% (407/1595) in 2009 versus 23.1% (308/1334) in 2013; P_{trend}<0.001]) significantly decreased. There was no significant change in patients presenting with pulseless VT/VF (88.9% [1418/1595] in 2009 versus 86.9% [1159/1334] in 2013; P_{trend}=0.06; Methods in the Data Supplement). An increase in male gender (74.8% [1193/1595] in 2009 versus 77.7% [1037/1334] in 2013; P_{trend}<0.05) and STE on the postresuscitation ECG (62.6% [999/1595] versus in 2009 versus 65.4% [872/1334] in 2013; P_{trend}<0.05) was seen. In this overall cohort of 9421 OHCA patients identified in-hospital with a discharge diagnosis of ACS, male gender (75.9%, 7148/9421) with presenting rhythm of VT/VF (88.2%, 8313/9421) and STE on the postresuscitation ECG (65.0%, 6124/9421) predominated.

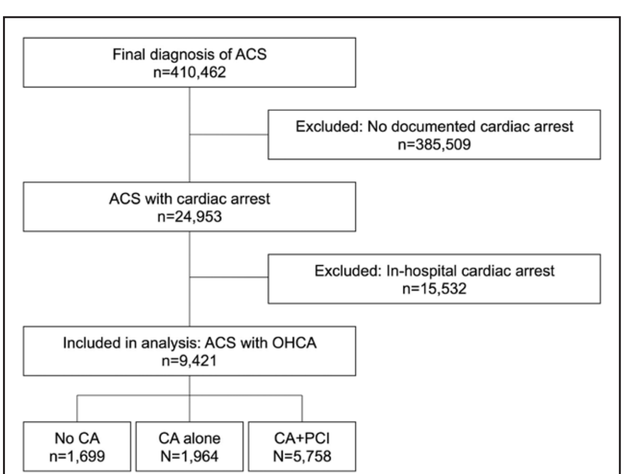

Figure 1. Patient flow diagram and study design. Data were extracted for the time period January 2009 to July 2013. Patients were identified in-hospital. All patients with a final discharge diagnosis of the acute coronary syndrome (ACS) complicated by out-of-hospital cardiac arrest (OHCA) were included in the final analysis. CA indicates coronary angiogram; and PCI, percutaneous coronary intervention.

Trends in CA in Identified Cases of OHCA

Of the 9421 patients identified in-hospital with a discharge diagnosis of ACS that presented with OHCA: 18.0% (1699/9421) did not undergo a coronary procedure; 20.8% (1964/9421) underwent CA alone and 61.1% (5758/9421) underwent CA+PCI. Within this OHCA cohort of ACS patients, over the 5-year period, CA+PCI increased from 54.9% (876/1595) in 2009 to 66.3% (884/1334) in 2013 (P_{trend}<0.001); conversely, CA alone decreased from 22.0% (351/1595) in 2009 to 20.0% (267/1334) in 2013 (P_{trend}<0.001) and the proportion of patients who did not undergo coronary procedure also decreased from 23.1% (368/1595) in 2009 to 13.7% (183/1344) in 2013 (P_{trend}<0.001; annual trends are available in Tables I through V in the Data Supplement). The median number of days to angiogram was 0.3 days (interquartile range, 0–1.3 days) and the maximum time to angiogram was 365 days. Of the overall cohort of ACS patients presenting with OHCA, 9.4% (882/9421) of patients died before CA.

We then examined the temporal trends in baseline characteristics of patients selected to undergo CA±PCI within the OHCA subgroup of ACS patients (CA±PCI; 7722/9421) over the 5-year period (Table 2). From 2009 to 2013, in the cohort of patients documented as having undergone CA±PCI, there was a significant increase in the proportion of male patients (76.0% [933/1227] in 2009 versus 79.1% in 2013 [910/1151]; P_{trend}<0.05) undergoing CA±PCI. There was a significant decrease in the prevalence of cardiovascular risk factors in this cohort including a family history of cardiovascular disease (27.8% in 2009 [341/1227] versus 24.7% in 2013 [284/1151]; P_{trend}<0.001); previous myocardial infarction (19.7% [242/1227] in 2009 versus 16.0% [184/1151] in 2013; P_{trend}<0.05); history of angina (18.6% [228/1227] in 2009 versus 14.7% [169/1151] in 2013; P_{trend}<0.05); hypercholesterolemia (29.3% [360/1227] in 2009 versus 25.1% [289/1151] in 2013; P_{trend}<0.05); and smoking history (65.4% (803/1,227) in 2009 versus 61.6% (709/1,151) in 2013; P_{trend}<0.05). The proportion of patients undergoing CA±PCI with VT/VF as the presenting rhythm also decreased (91.2% [1119/1227] in 2009 versus 89.5% [1030/1151] in 2013; P_{trend}<0.05). From

Table 1. Temporal Trends in Baseline Characteristics of the Overall MINAP OHCA Cohort

Baseline Characteristic	Year of Admission										*P* Value
	2009		2010		2011		2012		2013*		
Age >75	391/1595	24.5%	422/1835	23.0%	524/2142	24.5%	625/2515	24.9%	304/1334	22.8%	0.880
Sex (male)	1193/1595	74.8%	1369/1835	74.6%	1596/2142	74.5%	1952/2515	77.6%	1037/1334	77.7%	<0.05†
ST-elevation	999/1595	62.6%	1205/1835	65.7%	1352/2142	63.1%	1696/2515	67.4%	872/1334	65.4%	<0.05†
Previous AMI	348/1595	21.8%	364/1835	19.8%	436/2142	20.4%	483/2515	19.2%	232/1334	17.4%	<0.05†
Previous angina	326/1595	20.4%	365/1835	19.9%	392/2142	18.3%	394/2515	15.7%	211/1334	15.8%	<0.001†
Hypertension	661/1595	41.4%	768/1835	41.9%	891/2142	41.6%	1046/2515	41.6%	542/1334	40.6%	0.820
Hypercholesterolemia	459/1595	28.8%	531/1835	28.9%	584/2142	27.3%	670/2515	26.6%	333/1334	25.0%	<0.05†
Peripheral vascular disease	46/1595	2.9%	59/1835	3.2%	97/2142	4.5%	94/2515	3.7%	51/1334	3.8%	0.180
Cerebrovascular disease	111/1595	7.0%	129/1835	7.0%	152/2142	7.1%	208/2515	8.3%	86/1334	6.4%	0.729
Chronic renal failure	65/1595	4.1%	74/1835	4.0%	87/2142	4.1%	114/2515	4.5%	62/1334	4.6%	0.638
Heart failure	92/1595	5.8%	92/1835	5.0%	122/2142	5.7%	144/2515	5.7%	66/1334	4.9%	0.756
Smoker	1028/1595	64.5%	1160/1835	63.2%	1350/2142	63.0%	1563/2515	62.1%	809/1334	60.6%	<0.05†
Diabetes mellitus	188/1595	11.8%	260/1835	14.2%	306/2142	14.3%	382/2515	15.2%	172/1334	12.9%	0.234
Previous PCI	134/1595	8.4%	143/1835	7.8%	161/2142	7.5%	201/2515	8.0%	99/1334	7.4%	0.339
Previous CABG	116/1595	7.3%	103/1835	5.6%	112/2142	5.2%	140/2515	5.6%	73/1334	5.5%	<0.05†
Family history	407/1595	25.5%	460/1835	25.1%	548/2142	25.6%	544/2515	21.6%	308/1334	23.1%	<0.001†
Pulseless VT/VF	1418/1595	88.9%	1656/1835	90.2%	1861/2142	86.9%	2218/2515	88.2%	1159/1334	86.9%	0.061

Baseline characteristics, including the cardiovascular risk factors, of the 9421 patients with troponin positive acute coronary syndrome (ACS) presenting as out-of-hospital cardiac arrest (OHCA) over the 5-year period. Data are displayed per year, as counts n/N and percentages (%), where n is the number of patients documented as having the presence of a baseline characteristic, N is the total number of ACS patients in that year documented as OHCA and % is the proportion (2009, N=1595; 2010, N=1835; 2011, N=2142; 2012, N=2515; 2013, N=1334). AMI indicates acute myocardial infarction; CABG, coronary artery bypass graft surgery; MINAP, Myocardial Ischaemia National Audit Project; PCI, percutaneous coronary intervention; and VT/VF, pulseless ventricular tachycardia/ventricular fibrillation.

*Numeric data only available from January to July 2013.

†Unadjusted $P<0.05$.

the 5-year cohort of ACS patients presenting with OHCA (9421), an overall comparison of baseline characteristics was made between the groups of patients selected to undergo CA alone (1964/9421), CA+PCI (5758/9421) and patients who did not undergo a coronary angiogram (1699/9421); these are presented in Table 3.

Multivariable logistic regression analysis of the patients identified in-hospital with a discharge diagnosis of ACS who presented with OHCA (n=9421) was performed to determine the odds of undergoing (1) CA±PCI and (2) CA+PCI in this cohort (Table 4). If STE was present, there was an 8-fold increased probability of receiving CA+PCI (adjusted OR, 8.34; 95% confidence interval [CI], 7.00–9.94; $P<0.05$). A presenting rhythm of VT/VF (adjusted OR, 2.16; 95% CI, 1.29–3.63; $P<0.05$) or previous PCI (adjusted OR, 1.88; 95% CI, 1.24–2.85; $P<0.05$) was associated with a 2-fold increased probability of receiving CA+PCI. Patients had a significantly higher probability of receiving CA+PCI in the presence of cardiovascular risk factors including hypercholesterolemia (adjusted OR, 1.31; 95% CI, 1.04–1.66; $P<0.05$) and smoking history (adjusted OR, 1.45; 95% CI, 1.20–1.76; $P<0.05$). Conversely, those with previous coronary artery bypass grafting (adjusted OR, 0.46; 95% CI, 0.35–0.61; $P<0.05$) and heart failure (adjusted OR, 0.69; 95% CI, 0.49–0.98; $P<0.05$) were less likely to undergo a coronary procedure (Table 4).

Trends in Clinical Outcomes

Length of stay was also examined in the overall cohort of ACS patients presenting with OHCA. Median length of stay was 5 days (interquartile range, 2–11) and the maximum length of stay was 388 days. In patients identified with a discharge diagnosis of ACS who presented with OHCA (n=9421), overall in-hospital mortality was 29.2% (2753/9421). In patients identified with a discharge diagnosis of ACS who presented with OHCA (n=9421), we compared clinical outcomes in patients who underwent a coronary procedure with those who did not. This was further divided into no coronary angiogram (1699/9421), CA alone (1964/9421), and CA+PCI (5758/9421). Overall, in patients who underwent CA+PCI, in-hospital death was significantly lower than in patients who underwent CA alone (21.8% CA+PCI, 1258/5758 versus 37.3% CA alone, 734/1964; $P<0.001$) and significantly lower than in patients who underwent no coronary procedure (21.8% CA+PCI, 1258/5758 versus 44.8% 761/1699 no coronary procedure; $P<0.001$). Over the 5-year period, trend analysis demonstrated a significant increase in in-hospital mortality from 27.8% (443/1595) in 2009 to 31.0% (414/1334) in 2013 in the overall cohort of OHCA ACS patients (n=9421). In patients who underwent CA+PCI (n=5758), trend analysis showed a slight but significant increase in in-hospital mortality over the 5-year period from 20.2% (177/876) in 2009 to 22.6% (200/884) in 2013

Table 2. Temporal Trends in Baseline Characteristics of the MINAP OHCA Patients Who Underwent CA±PCI

Baseline Characteristic (CA±PCI)	Year of Admission										*P* Value
	2009		2010		2011		2012		2013*		
Age >75	266/1227	18.4%	301/1468	20.5%	381/1738	21.9%	472/2138	22.0%	239/1151	20.8%	0.724
Sex (male)	933/1227	76.0%	1124/1468	76.6%	1323/1738	76.1%	1692/2138	79.1%	910/1151	79.1%	<0.05†
ST-elevation	832/1227	67.8%	1041/1468	71.0%	1191/1738	68.5%	1539/2138	72.0%	797/1151	69.2%	0.355
Previous AMI	242/1227	19.7%	262/1468	17.9%	328/1738	18.9%	377/2138	17.6%	184/1151	16.0%	<0.05†
Previous angina	228/1227	18.6%	259/1468	17.7%	295/1738	17.0%	304/2138	14.2%	169/1151	14.7%	<0.05†
Hypertension	503/1227	41.0%	621/1468	42.3%	710/1738	40.9%	877/2138	41.0%	458/1151	39.8%	0.576
Hypercholesterolemia	360/1227	29.3%	433/1468	29.5%	483/1738	27.8%	580/2138	27.1%	289/1151	25.1%	<0.05†
Peripheral vascular disease	32/1227	2.6%	44/1468	3.0%	74/1738	4.3%	79/2138	3.7%	42/1151	3.6%	0.125
Cerebrovascular disease	74/1227	6.0%	88/1468	6.0%	106/1738	6.1%	159/2138	7.4%	63/1151	5.5%	0.806
Chronic renal failure	40/1227	3.3%	46/1468	3.1%	58/1738	3.3%	80/2138	3.7%	45/1151	3.9%	0.593
Heart failure	61/1227	5.0%	60/1468	4.1%	89/1738	5.1%	110/2138	5.1%	49/1151	4.3%	0.602
Smoker	803/1227	65.4%	946/1468	64.5%	1117/1738	64.3%	1353/2138	63.3%	709/1151	61.6%	<0.05†
Diabetes mellitus	136/1227	11.1%	201/1468	13.7%	247/1738	14.2%	323/2138	15.1%	137/1151	11.9%	0.124
Previous PCI	108/1227	9.1%	120/1468	8.2%	134/1738	7.7%	175/2138	8.2%	84/1151	7.3%	0.222
Previous CABG	74/1227	8.8%	69/1468	4.7%	81/1738	4.7%	98/2138	4.6%	54/1151	4.7%	0.170
Family history	341/1227	27.8%	398/1468	27.1%	483/1738	27.8%	485/2138	22.7%	284/1151	24.7%	<0.001†
VT/VF	1119/1227	91.2%	1350/1468	92.0%	1552/1738	89.3%	1940/2138	90.7%	1030/1151	89.5%	<0.05†

Baseline characteristics, including the cardiovascular risk factors, of the patients with troponin positive acute coronary syndrome (ACS) presenting as out-of-hospital cardiac arrest (OHCA) that were selected to undergo any coronary procedure (coronary angiogram [CA]±percutaneous coronary intervention [PCI], 7722/9421) over the 5-year period. The total number is comprised of CA alone (n=1964) and CA+PCI (n=5758). Data are described as counts (n/N) and percentages (%); where n is the number of patients with a characteristic, and N is the total number of patients in that year who underwent CA±PCI (2009, N=1227; 2010, N=1468; 2011, N=1738; 2012, N=2138; 2013, N=1151). AMI indicates acute myocardial infarction; CABG, coronary artery bypass graft surgery; MINAP, Myocardial Ischaemia National Audit Project; and VT/VF, pulseless ventricular tachycardia/ventricular fibrillation.

*Numeric data only available from January to July 2013.

†Unadjusted *P*<0.05.

(P_{trend} <0.001). However, this increase in mortality was significantly less than the increase in mortality in the CA alone cohort (33.6% [118/351] in 2009 versus 44.3% [117/267] in 2013; *P*<0.001) and in patients who underwent no coronary procedure (40.2% [148/368] in 2009 versus 53% [97/183] in 2013; *P*<0.001).

Multivariable logistic regression analysis of the patients identified in-hospital with a discharge diagnosis of ACS who presented with OHCA was performed to determine predictors of in-hospital mortality (n=9421). These were older age (>75 years; OR, 1.59; 95% CI, 1.34–1.89; *P*<0.001) and the presence of preexisting comorbidities including diabetes mellitus (OR, 2.04; 95% CI, 1.75–2.36; *P*<0.001), heart failure (OR, 1.84; 95% CI, 1.36–2.47; *P*<0.001), cerebrovascular disease (OR, 1.63; 95% CI, 1.29–2.07; *P*<0.001), chronic renal failure (OR, 1.66; 95% CI, 1.04–1.78; *P*<0.05), and peripheral vascular disease (OR, 1.70; 95% CI, 1.26–2.30; *P*<0.001; Table 5). Conversely, the risk of in-hospital death was decreased if the patient presented with VT/VF (OR, 0.21; 95% CI, 0.17–0.26; *P*<0.001), male sex (OR, 0.78; 95% CI, 0.68–0.89; *P*<0.001) and had risk factors for coronary disease including hypercholesterolemia (OR, 0.69; 95% CI, 0.59–0.81; *P*<0.001), smoking history (OR, 0.72; 95% CI, 0.61–0.84; *P*<0.001), and family history (OR, 0.37; 95% CI, 0.32–0.44; *P*<0.001). CA+PCI was also associated with decreased risk of in-hospital mortality in the STE cohort (OR, 0.58; 95% CI, 0.36–0.96; *P*<0.05) but not the non-STE cohort (Table 5).

In patients identified with a discharge diagnosis of ACS who presented with OHCA, we compared neurological outcomes between patients who underwent a coronary procedure with those who did not (n=9421). This was further divided into no procedure (1699), CA alone (1964), and CA+PCI (5758). In patients who underwent CA+PCI, good neurological outcome was significantly higher than in patients who underwent CA alone (61.6% CA+PCI, 3546/5758 versus 41.4% CA alone, 814/1964; *P*<0.001) and significantly higher than in patients who underwent no coronary procedure (61.6% CA+PCI, 3546/5758 versus 35.6% no procedure, 604/1,699; *P*<0.001). Trend analysis over the 5-year period showed a significant decrease in the proportion of patients with good neurological outcome in the overall OHCA ACS cohort from 54.2% (864/1595) in 2009 to 51.3% (685/1334) in 2013 (*P*=0.05). In patients who underwent CA+PCI, trend analysis showed no significant change in good neurological outcome over the 5-year period from 2009 to 2013 (63.4% in 2009 [555/876] versus 61.0% [539/884] in 2013; P_{trend}=0.07). However, in both the CA alone (45.6% [160/351] in 2009 versus 34.3% [92/268] in 2013; *P*<0.001) and no coronary angiogram (40.2% [148/368] in 2009 versus 29.5% [54/183] in 2013; *P*<0.001) cohorts, a significant decrease in good neurological

Table 3. Comparison of Baseline Characteristic Between Patients That Underwent No Coronary Procedure vs CA Alone and CA+PCI in the MINAP OHCA Cohort

Baseline Characteristic	Procedure Specific Data						*P* Value
	No CA (1)		CA Alone (2)		CA+PCI (3)		
Age >75	607/1699	35.7%	600/1964	30.5%	1059/5758	18.4%	<0.001*
Sex (male)	724/1699	42.6%	531/1964	27.0%	4868/5758	84.5%	<0.001*
ST-elevation	350/1699	20.6%	535/1964	27.2%	5274/5758	91.6%	<0.001*
Previous AMI	470/1699	27.7%	607/1964	30.9%	787/5758	13.7%	<0.001*
Previous angina	435/1699	25.6%	500/1964	25.5%	754/5758	13.1%	<0.001*
Hypertension	738/1699	43.4%	955/1964	48.6%	2214/5758	38.5%	<0.001*
Hypercholesterolemia	433/1699	25.5%	564/1964	28.7%	1580/5758	27.4%	<0.001*
Peripheral vascular disease	76/1699	4.5%	94/1964	4.8%	177/5758	3.1%	<0.05*
Cerebrovascular disease	195/1699	11.5%	177/1964	9.0%	314/5758	5.5%	<0.001*
Chronic renal failure	135/1699	7.9%	139/1964	7.0%	130/5758	2.3%	<0.001*
Heart failure	148/1699	8.7%	208/1964	10.6%	160/5758	2.8%	<0.001*
Smoker	982/1699	57.8%	1022/1964	52.0%	3906/5758	67.8%	<0.001*
Diabetes mellitus	264/1699	15.5%	396/1964	20.2%	649/5758	11.3%	<0.001*
Previous PCI	116/1699	6.8%	184/1964	9.4%	437/5758	7.6%	<0.001*
Previous CABG	168/1699	9.9%	223/1964	11.4%	153/5758	2.7%	<0.001*
Family history	278/1699	16.4%	355/1964	18.1%	1636/5758	28.4%	<0.001*
VT/VF	1322/1699	77.8%	1638/1964	83.4%	5353/5758	93.0%	<0.001*

A comparison of the baseline characteristics of all patients selected to undergo a coronary procedure with those who were not, from the 5-year cohort of acute coronary syndrome (ACS) patients presenting with out-of-hospital cardiac arrest (OHCA; 9421). This is subdivided into groups (1) no coronary angiogram (CA; 1191/9421); (2) CA only (1785/9421); and (3) CA+PCI (6445/9421). For clarification, see Figure 1. Data are displayed as counts n/N and percentages (%), where n is the number of patients documented as having the presence of a baseline characteristic, N is the total number of patients in each cohort and % is the proportion. AMI indicates acute myocardial infarction; CABG, coronary artery bypass graft surgery; MINAP, Myocardial Ischaemia National Audit Project; and VT/VF, pulseless ventricular tachycardia/ventricular fibrillation.

*Unadjusted *P*<0.05.

outcome was seen over the 5-year period. Figure 2 demonstrates temporal trends in good neurological outcome in the overall cohort of OHCA ACS patients, those who underwent CA+PCI and the rate of coronary intervention.

In the OHCA cohort of ACS patients, the association of coronary procedure with life status (mortality both in-hospital and after discharge) was examined (Figure 3). Cox proportional hazards model was used to generate time-varying HRs for short-term and long-term follow-up. This demonstrated significant reduction in mortality in the entire OHCA ACS cohort between those selected to undergo any coronary procedure (CA±PCI) versus no (coronary) procedure both before 30 days (HR, 0.35; 95% CI, 0.20–0.60; *P*<0.05) and after 30 days (HR, 0.36; 95% CI, 0.25–0.50; *P*<0.001). This was further supported by Cox proportional hazards model analysis with time-varying exposure to CA, which demonstrated a significant reduction in mortality both in the STE (HR, 0.30; 95% CI, 0.28–0.32; *P*<0.05) and non-STE cohort (HR, 0.44; 95% CI, 0.42–0.46; *P*<0.001).

Discussion

In this large, 5-year, retrospective observational study, examining patients identified in-hospital with a final diagnosis of ACS, with a specific focus on those presenting with OHCA, the main findings were as follows (1) the proportion of ACS patients identified as presenting with OHCA increased over the 5-year period. (2) An increase in the rate of CA+PCI was demonstrated. (3) Patient selection for CA±PCI favored male patients, under 75, with STE on the postresuscitation ECG with a presenting rhythm of VT/VF. (4) A significant increase in CA±PCI in the STE patients was seen over time. (5) Overall in-hospital mortality was significantly lower and neurological outcome better in patients selected to undergo CA+PCI from the ACS cohort presenting with OHCA (both STE and non-STE patients). (6) Over the 5-year period, the rate of good neurological outcome in the CA+PCI cohort remained unchanged.

The MINAP registry was established with the intention of capturing all patients admitted to hospital, diagnosed with and treated as ACS. MINAP is a hospital-based ACS registry completed by cardiology personnel, thus will not capture all patients resuscitated from cardiac arrest and admitted to hospital. As part of a focus on improving care, the Department of Health for England introduced survival from cardiac arrest as part of the Ambulance Service National Quality Indicators from 2011 onwards. This provides data from 2011 to 2013, on the number of patients surviving to the hospital with return of spontaneous circulation (5910 in 2011, 7662 in 2012, and

Table 4. Multivariable Logistic Regression Analysis to Determine the Odds of Undergoing CA±PCI and CA+PCI

Variable	Adjusted Odds Ratio	95% Confidence Interval	*P* Value
CA±PCI			
STE	2.51	1.89–5.31	<0.05
Male sex	1.53	1.22–1.90	<0.05
Cerebrovascular disease	0.70	0.544–0.893	<0.05
Previous CABG	0.70	0.523–0.924	<0.05
CA+PCI			
VT/VF	2.16	1.29–3.63	<0.05
STE	8.34	7.00–9.94	<0.05
Previous PCI	1.88	1.24–2.85	<0.05
Hypercholesterolemia	1.31	1.04–1.66	<0.05
Smoking history	1.45	1.20–1.76	<0.05
Previous coronary artery bypass graft	0.46	0.35–0.61	<0.05
Heart failure	0.69	0.49–0.98	<0.05
Previous AMI	0.55	0.44–0.69	<0.05

Multivariable logistic regression analysis is demonstrating significant associations between categorical covariates and (1) CA±PCI and (2) CA+PCI (n=9421). AMI indicates acute myocardial infarction; CA, coronary angiogram; CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention; STE, ST-elevation; and VT/VF, pulseless ventricular tachycardia/ventricular fibrillation.

Table 5. Multivariable Logistic Regression Analysis to Determine the Odds of In-Hospital Mortality

Variable	Adjusted Odds Ratio	95% Confidence Interval	*P* Value
Predictors of in-hospital mortality			
VT/VF	0.15	0.13–0.18	<0.001
Family history	0.39	0.31–0.49	<0.001
CA+PCI	0.62	0.40–0.95	<0.05
Hypercholesterolemia	0.69	0.59–0.81	<0.05
Smoking history	0.73	0.63–0.85	<0.001
Male sex	0.79	0.70–0.89	<0.001
Chronic renal failure	1.40	1.04–1.89	<0.05
Cerebrovascular disease	1.54	1.25–1.90	<0.001
Age >75	1.59	1.40–1.81	<0.001
Heart failure	1.59	1.25–2.02	<0.001
Peripheral vascular disease	1.75	1.31–2.33	<0.001
Diabetes mellitus	1.98	1.65–2.37	<0.001

Multivariable logistic regression analysis is demonstrating significant associations between categorical covariates and in-hospital mortality (n=9421). CA indicates coronary angiogram; PCI, percutaneous coronary intervention; and VT/VF, pulseless ventricular tachycardia/ventricular fibrillation.

8033 in 2013).[11] Comparison of these data with MINAP data would suggest that MINAP captures approximately one-third of resuscitated cardiac arrest patients and admitted to hospital. Interestingly, the number of resuscitated cardiac arrests admitted to hospital increased yearly according to Ambulance Service data. Our study also demonstrated an increase in the number of OHCA patients diagnosed and treated as ACS over the 5-year period. This could, in part, reflect a shift in postcardiac arrest management, with a greater percentage of patients admitted and survived to hospital with OHCA who are investigated for and treated as ACS. However, this could also be attributable to improved case ascertainment in both prehospital and hospital-based audit systems.

Of patients identified in-hospital with a discharge diagnosis of ACS who presented with OHCA, the proportion of OHCA patients presenting with VT/VF per year within the in-hospital ACS cohort, remained unchanged. Comparison of these data with Ambulance Service National Quality Indicators demonstrate a similar picture, with the proportion of resuscitated cardiac arrests delivered to the hospital with a presenting rhythm of VT/VF also remaining unchanged. This is despite the overall decrease in the observed incidence of VT/VF arrest out-of-hospital. This could be explained by prehospital factors, which include the decision by the ambulance crews to perform resuscitation and a more favorable outcome in this cohort, thus patients surviving to hospital with return of spontaneous circulation. It could also partially be explained by selection bias whereby a cardiac arrest with presenting rhythm of VT/VF is thought more likely to be ischemic in origin, and thus more likely to be treated and diagnosed with ACS, and thus entered into the MINAP database.

Over the 5-year period, distribution of baseline characteristics of the OHCA patients captured within the MINAP registry and therefore diagnosed with ACS broadened to include patients without traditional risk factors for coronary disease. This and the observed increase in the proportion of OHCA patients receiving coronary intervention could reflect a more proactive approach both in England and internationally to postarrest care during this period, with increased recognition and emphasis placed on the benefits of specialist cardiac care to manage ensuing cardiovascular dysfunction and treatment of the potential underlying cause through reperfusion.[12] This is in addition to the national increase in the use of PCI as the preferred reperfusion strategy.

This study identified well-established predictors of survival and good neurological outcome in OHCA including VT/VF as the presenting rhythm. This has been shown in numerous observational studies.[6,13,14] Our study also showed that CA+PCI was associated with reduced in-hospital mortality after OHCA in patients with STE. CA+PCI was also associated with good neurological outcome and improved long-term survival. However, this study also showed that predictors of good outcome were synonymous with the selection criteria for patients undergoing CA±PCI, suggesting a degree of selection bias for CA toward patients believed to have characteristics associated with a more favorable outcome.

Over the 5-year period, in-hospital mortality increased in the OHCA cohort of ACS patients. However, the overall in-hospital mortality of those presenting with OHCA in

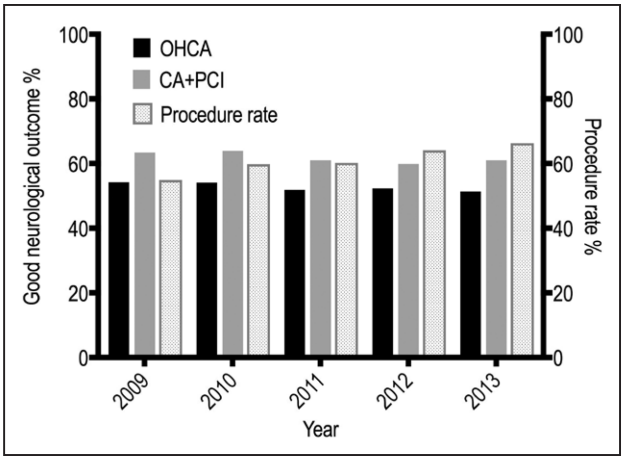

Figure 2. Temporal trends in the good neurological outcome. Temporal trends in neurological outcome are displayed graphically for the overall out-of-hospital cardiac arrest (OHCA) cohort (black), and the cohort of OHCA that underwent coronary angiogram (CA)+percutaneous coronary intervention (PCI; gray), the temporal trends in the procedural rate of CA+PCI is also shown (pattern).

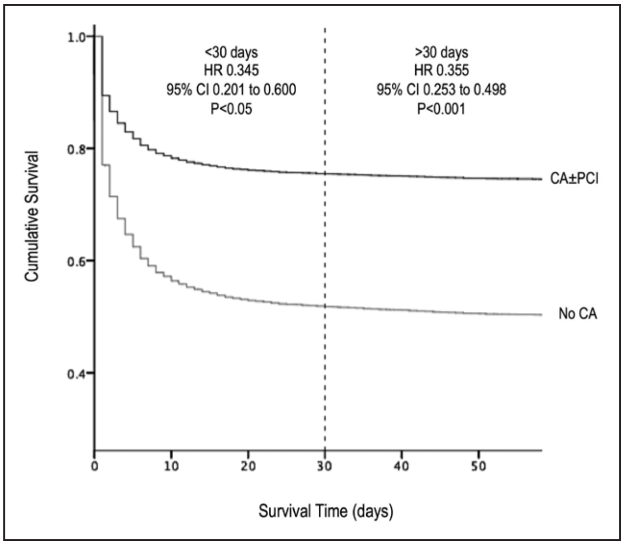

Figure 3. Kaplan–Meier survival curves. Survival curves according to coronary angiogram (CA)±percutaneous coronary intervention (PCI; black) and no CA (gray). Cox proportional hazards model was used to calculate time-varying hazard ratios (HRs). Survival represents life status, which includes survival both in-hospital and following discharge. CI indicates confidence interval.

the MINAP registry was shown to be much lower than the Ambulance Service National Quality Indicators would suggest, which is indicative of the selective nature of the data, with MINAP only capturing a proportion of all resuscitated cardiac arrests admitted to hospital. In OHCA patients who underwent CA+PCI, there was a slight but significant increase in in-hospital mortality, despite an increase in CA±PCI. This likely reflects a broadening of selection criteria for CA±PCI extending to higher risk patients.

The observational nature of these data makes it impossible to derive conclusions about causality. The data for CA±PCI in the non-STE OHCA cohort are conflicting. Although non-STE patients in this study appeared to fare better with CA±PCI, they remain an extremely heterogeneous cohort, with multiple possible causes for arrest including noncardiac causes, chronic coronary artery disease, and scar-induced arrhythmia. The non-STE patients in the MINAP registry were a select group, with a confirmed diagnosis of ACS, entered into the database retrospectively, thus these findings cannot be transferable to all non-STE patients. However, these data would suggest that regardless of postresuscitation ECG findings, patients with ACS as the cause of OHCA could benefit from CA±PCI. In the absence of STE following cardiac arrest, the ECG is less reliable in guiding diagnosis and a focus is placed on hemodynamic status and possible preceding symptoms before arrest. Recently published European Society of Cardiology guidelines recommend rule out of noncoronary causes before CA.[8] In the absence of convincing randomized data we are yet to determine the best postarrest strategy for these patients. Further investigation in the form of a randomized trial of routine invasive angiography and revascularization, where appropriate following OHCA is necessary. The key factor here is to identify which patients benefit from an early invasive strategy. The coordination of this however, is complex, and close interaction is necessary prehospital between centers and emergency services and internally between the emergency department, cardiologists, and the critical care unit. Several planned randomized control trials including PEARL (Early Coronary Angiography Versus Delayed Coronary Angiography; https://www.clinicaltrials.gov, unique identifier: NCT02387398) and ARREST (A Randomized Trial of Expedited Transfer to a Cardiac Arrest Center for Non-ST Elevation Out- of-Hospital Cardiac Arrest; http://www.isrctn.com, unique identifier: ISRCTN 96585404) will address the optimal postarrest pathway for these patients and if CA should be routinely performed in all patients with resuscitated arrest of presumed cardiac cause.[15]

Limitations

There are several limitations in this study that are inherent to retrospective database analysis that preclude conclusions with regard to causality. There was a large proportion of missing data, analyses of individuals with only full data sets can introduce bias thus multiple imputation analysis was performed. Multiple imputation works on the assumption that data are missing at random. Despite consistency in results in comparison with complete case analysis, and inclusion of a large number of variables in the MI model, we cannot confirm if the systematic differences between the missing values and the observed values can be explained by differences in observed data thus may be subject to bias. Therefore, the results of this study must be considered hypothesis generating, thus supporting the need for a randomized controlled trial in this cohort.

The MINAP database only captures patients with a discharge diagnosis of ACS, which is at most one-third of resuscitated cardiac arrests admitted to the hospital, thus conclusions are not transferable to the entire OHCA population. Furthermore, we cannot compare outcomes between patients with OHCA of the presumed cardiac cause who received acute cardiac care and those who did not. Because of the lack of randomized data, selection for coronary intervention is subjective, and we, therefore, cannot account for why individual patients were or were not chosen for this management strategy. This study did not include differentiation of outcome by the center; this would have been informative and could be predictive of outcome and also of missing values.

Conclusions

In this MINAP registry, there was an increase in the proportion of OHCA cases treated as ACS over the 5-year period. The rate of CA+PCI increased and was associated with improved survival compared with cohorts not selected for this management strategy; however, as selection criteria broadened to include patients with additional comorbidities, outcomes declined. The future challenges are to identify those patients who will benefit from such a strategy. These data support the need for a randomized controlled trial in this patient cohort.

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Disclosures

None.

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Temporal Trends in Identification, Management, and Clinical Outcomes After Out-of-Hospital Cardiac Arrest: Insights From the Myocardial Ischaemia National Audit Project Database

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Supplemental Material

Supplemental Methods

Missing data values and multiple imputation (MI) methodology

Table 1 demonstrates the distribution of missing data and the models used for imputation. Data on coronary angiography were missing in 47% of patients (4,465/9,421). Thus analysis of only complete cases could lead to potential bias if these were not a random subset of patients. The multiple imputation (MI) method was used to address the missing data. SPSS v24.0 (IBM Corp.©) was used to auto-scan the data. Identification of arbitrary missing patterns led to use of fully conditional specification (FCS) MI method. This was performed in the SPSS v24.0 (IBM Corp.©) standard statistical package. The FCS MI method in SPSS v24.0 is an iterative Markov Chain Monte Carlo method. This method enabled appropriate regression model (linear for continuous and logistic for categorical) selection for each variable. [1] Furthermore, previous simulations have provided evidence that FCS MI yields unbiased estimates with appropriate coverage and this has been strongly recommended as the preferred method for dealing with missing data in large observational studies. [2] The FCS imputations are generated sequentially by specifying an imputation model for each variable given the other variables. MI was performed for the incomplete characteristics at the patient level using the aforementioned software. Five imputations were obtained to give an efficiency of 99% when compared to an infinite number of imputations with 10 iterations. [3] Statistical interactions were not included in the imputation models. We used all available variables in our imputation model to ensure minimal bias. All known covariates thought to be associated with the missingness mechanism and outcomes were used to help predict the values for the missing data. The observed covariates used in the MI sequence were: age >75 years, sex (male), ST-elevation, neurological status, VT/VF as presenting rhythm, life status (tracked), diabetes mellitus, previous acute myocardial infarction, previous coronary artery bypass grafting procedure, previous percutaneous coronary intervention (PCI), hypertension, heart failure, cerebrovascular disease, smoking history, family history, previous angina, chronic renal failure, peripheral vascular disease, hypercholesterolemia, coronary angiography +/-PCI, length of stay and survival time in days. Life status was also included to preserve its relationship with the incomplete patient characteristics and coronary angiography. The output dataset contained the original (non-missing) data and the data for the 5 imputations. Multiple imputation datasets were analyzed as described in the statistical methods section as usual using supported analysis procedures to obtain final (combined) parameter estimates to take into account the inherent uncertainty in the various sets of imputed values.

Comparison of observed and imputed values and complete case analysis

As large fractions of the data were imputed, we compared baseline characteristics between patients in whom coronary procedural data were documented (observed) with those in whom data was not documented (missing) (Table 2). We then proceeded to compare baseline characterises between the observed data and imputed values (final data set used for analysis) (Table 3).

Complete Case Analysis

This was performed in patients with complete data on the presence or absence of coronary angiography+/-PCI, this yielded similar results to the MI method. Baseline characteristics are compared between the CCA and multiply imputed cohort. To determine characteristics for missing data for CA+/-PCI, comparison was made between the baseline characteristics of those missing and those with complete data.

Of the 9,421 OHCA patients who were captured by the MINAP registry, 4,956 of these had complete data on coronary procedures and in-hospital mortality. Complete case analysis of the primary endpoint demonstrated that CA+PCI reduced in-hospital mortality when compared to no procedure (OR 0.172, 95% CI 0.138 to 0.214; $P<0.001$). When MI was used, a smaller (albeit statistically significant) treatment effect was observed with CA+PCI when examining both the primary endpoint (OR 0.58; 95% CI 0.36 to 0.96; $P<0.05$).

Supplemental Tables

Table 1. Summary of missing data values

These are depicted as numbers and percentage of total data, variable type and multiple imputation method. *** denotes variables used as predictors**. Abbreviations: CA+/-PCI coronary angiography +/- percutaneous coronary intervention, AMI acute myocardial infarction, CABG coronary artery bypass grafts, VT/VF ventricular tachycardia /ventricular fibrillation as presenting rhythm.

Variable Summary					
	Missing		**Valid N (variable observed/measured)**	**Variable type**	**Imputation method**
	N	**Percent**			
CA+/-PCI	4465	47.4%	4956	Categorical	Logistic regression
Family history	2979	31.6%	6442	Categorical	Logistic regression
Smoking history	2074	22.0%	7347	Categorical	Logistic regression
Hypercholesterolemia	1434	15.2%	7987	Categorical	Logistic regression
Peripheral vascular disease	1377	14.6%	8044	Categorical	Logistic regression
Chronic renal failure	1335	14.2%	8086	Categorical	Logistic regression
Angina	1294	13.7%	8127	Categorical	Logistic regression
Cerebrovascular disease	1286	13.7%	8135	Categorical	Logistic regression
Heart failure	1286	13.7%	8135	Categorical	Logistic regression
Hypertension	1232	13.1%	8189	Categorical	Logistic regression
Previous PCI	1200	12.7%	8221	Categorical	Logistic regression
Previous CABG	1166	12.4%	8255	Categorical	Logistic regression
Previous AMI	1161	12.3%	8260	Categorical	Logistic regression
Diabetes Mellitus	1008	10.7%	8413	Categorical	Logistic regression
Survival time (days)*	855	9.1%	8566	Continuous	Linear regression
Life Status*	849	9.0%	8572	Categorical	Linear regression
VT/VF	802	8.5%	8619	Categorical	Logistic regression
Neurological status	578	6.1%	8843	Categorical	Logistic regression
ST-Elevation	423	4.5%	8998	Categorical	Logistic regression
In-hospital death	222	2.4%	9199	Categorical	Logistic regression
Length of Stay*	177	1.9%	9244	Continuous	Linear regression
Sex (Male)	21	0.2%	9400	Categorical	Logistic regression
Age >75 years	6	0.1%	9415	Categorical	Logistic regression

Table 2. The left hand column refers to patients in the MINAP database in whom the presence or absence of coronary procedure was documented and the characteristics of this cohort. The right hand column refers to patients in the MINAP database in whom data on the presence or absence of coronary procedure were missing and the characteristics of this cohort. This analysis was performed in order to identify covariates associated with missingness (of coronary procedural documentation).

	Observed (n=4956)	Missing (n=4465)	P value
Age >75	988 (20)	1277 (29)	<0.0001
Sex (Male)	3834 (77)	3298 (74)	<0.0001
STE	3939 (79)	1968 (44)	<0.0001
Previous AMI	693 (14)	934 (21)	<0.0001
Previous Angina	596 (12)	838 (22)	<0.0001
Hypertension	1730 (35)	1663 (37)	0.0183
Hypercholesterolemia	1182 (24)	995 (22)	0.0719
PVD	143 (3)	134 (3)	0.7399
CVD	241 (5)	326 (7)	<0.0001
CRF	109 (2)	215 (5)	<0.0001
Heart Failure	148 (3)	275 (6)	<0.0001
Smoker	2730 (55)	2091 (47)	<0.0001
Diabetes	536 (11)	605 (14)	<0.0001
Previous PCI	358 (7)	271 (6)	0.025
Previous CABG	173 (3)	293 (7)	<0.0001
Family History	984 (20)	672 (15)	<0.0001
VT/VF	4220 (85)	3387 (76)	<0.0001

Table 3. The left hand column refers to the baseline characteristics of patients in the MINAP database with original data (observed) and the right hand column refers to the baseline characteristics of the multiply imputed (pooled) dataset. The data are presented as n/N (%), where n is the total number with the observed baseline characteristic in the original or imputed cohort and N is the total number of observations (documented presence or absence) and the percentage is a percentage of the total population with the documented presence or absence of a characteristic. In the observed cohort N varies with each characteristic. In the multiply imputed cohort with complete data, N=9,421. P values have not been added to the table because the observed and imputed values are not independent.

	Observed	Imputed (n=9421)
Age >75	2265/9415 (24)	2266/9,421 (24)
Sex (Male)	7132/9400 (80)	7148/9,421 (80)
STE	5907/8998 (66)	6124/9,421 (65)
Previous AMI	1627/8260 (20)	1864/9,421 (20)
Previous Angina	1434/8127 (18)	1689/9,421 (18)
Hypertension	3393/8189 (41)	3908/9,421 (41)
Hypercholesterolemia	2177/7987 (27)	2577/9,421 (27)
PVD	277/8044 (3)	348/9,421 (4)
CVD	567/8135 (7)	686/9,421 (7)
CRF	324/8086 (4)	411/9,421 (4)
Heart Failure	423/8135 (5)	516/9,421 (6)
Smoker	4718/7347 (64)	5910/9,421 (63)
Diabetes	114/8413 (14)	1294/9,421 (14)
Previous PCI	629/8221 (8)	738/9,421 (8)
Previous CABG	466/8255 (6)	544/9,421 (6)
Family History	1656/6442 (26)	2268/9,421 (24)
VT/VF	7607/8619 (88)	8313/9,421 (88)

Table 4. MINAP data fields used.

Of the 123 MINAP core data entry fields, 49 were extracted for the purposes of this study. These can be broadly categorized into descriptive baseline demographics (left, and clinical outcomes including current life status (right).

Baseline Demographics	**Outcomes**
Arrival at Hospital (month)	Survival Time
Arrival at Hospital (year)	Length of Stay
Discharge Date (relative)	Admission Diagnosis
Symptom Onset (relative)	Outcome of arrest
Call for Help (relative)	Admission Ward
Arrival 1st Responder (relative)	Procedure Performed
Arrival Ambulance (relative)	Intended Reperfusion Procedure
Arrival at Hospital (relative)	Assess at non intervention hospital
1st Cardiac Arrest (relative)	Assess at Intervention Centre
Arrival at non interventional hospital (relative)	Peak Troponin
Arrival at non interventional hospital (relative)	Why no Angio
Local Angio date (relative)	Why no Intervention
Gender	Discharge Diagnosis
ECG Determining Treatment	Bleeding Complications
Previous AMI	Death in Hospital
Previous Angina	Discharge Destination
Hypertension	Reinfarction
Hypercholesterolemia	Life Status
Peripheral Vascular Disease	
Cerebrovascular Disease	
Chronic Renal Failure	
Heart Failure	
Smoking Status	
Diabetes	
Previous PCI	
Previous CABG	
LVEF	
Family History of CHD	
Where cardiac arrest	
Presenting Rhythm	
Age At Admission	

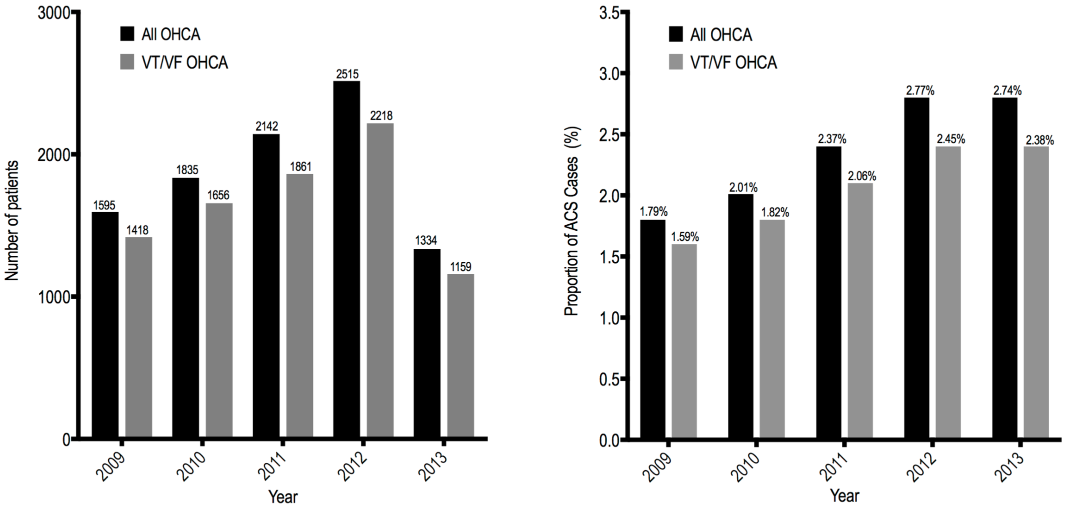
Table 5. Temporal trends in the in-hospital procedural rates

This table demonstrates the temporal trends in the in-hospital procedural rates of coronary angiography alone and coronary angiography + percutaneous coronary intervention (PCI) of the 9,421 patients with troponin positive acute coronary syndrome (ACS) presenting as out-of-hospital cardiac arrest (OHCA) over the 5-year period. Data are displayed per year, as counts n/N and percentages (%), where n is the number of patients documented as having undergone or not undergone a coronary procedure, N is the total number of patients in that year with a discharge diagnosis of ACS presenting with OHCA and % is the proportion, * indicates $P<0.05$. †Numerical data only available from January to July 2013.

Procedure Specific Data	Year of Admission										
	2009		2010		2011		2012		2013†		P value
No Angiogram	368/1595	23.1%	367/1835	20.0%	404/2142	18.9%	377/2515	15.0%	183/1334	13.7%	<0.001*
Coronary Angiogram	351/1595	22.0%	370/1835	20.2%	449/2142	21.0%	526/2515	20.9%	267/1334	20.0%	<0.001*
Coronary Angiogram + PCI	876/1595	54.9%	1098/1835	59.8%	1289/2142	60.2%	1612/2515	64.1%	884/1334	66.3%	<0.001*

Supplemental Figures

Figure 1.



Supplemental Figure Legend

Figure 1. The temporal trends in OHCA characteristics

This figure demonstrates both the number (left) and proportion (right) of acute coronary syndrome (ACS) presenting as out-of-hospital cardiac arrest (OHCA) (black) and the numbers (left) and proportion (right) of ACS presenting with pulseless ventricular tachycardia/ventricular fibrillation (VT/VF) OHCA (gray). OHCA as a proportion of total ACS cases (%) was calculated as the number of patients with OHCA divided by the number of patients with ACS per year x100; P_{trend}<0.001). VT/VF OHCA (%) was calculated as the number of patients with VT/VF OHCA divided by the number of patients with ACS per year x100; P_{trend}<0.001).

Supplemental References

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