**Impact of COVID19 Pandemic on the Incidence and Management of Out of Hospital Cardiac Arrest in Patients Presenting with Acute Myocardial Infarction in England**

**Short running title:**  Incidence of out of hospital cardiac arrest during COVID19 pandemic

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**Abstract**

**Background:** Studies have reported significant reduction in acute myocardial infarction (AMI) related hospitalizations during the COVID19 pandemic. However, whether these trends are associated with increased incidence of Out of Hospital Cardiac Arrest (OHCA) in this population is unknown.

**Methods & Results:** AMI hospitalizations with OHCA during the COVID19 period (1st February-14th May 2020) from the Myocardial Ischaemia National Audit Project and British Cardiovascular Intervention Society datasets were analysed. Temporal trends were assessed using Poisson models with equivalent pre-COVID19 period (1st February-14th May 2019) as reference.

AMI hospitalizations during COVID19 period were reduced by more than 50% (n=20,310 vs n=9,325). OHCA was more prevalent during the COVID-19 period compared with the pre-COVID period (5.6% vs. 3.6%), with a 56% increase in the incidence of OHCA (incidence rate ratio: 1.56, 95%CI 1.39-1.74). OHCA patients during COVID19 period were likely to be older, female, of Asian ethnicity and more likely to present with STEMI. The overall rates of invasive coronary angiography (58.4% vs. 71.6%, p<0.001) were significantly lower amongst the OHCA during COVID19 period with increased time to reperfusion (mean 2.1 hours vs. 1.1 hours, p=0.05) in STEMI. The adjusted in-hospital mortality probability increased from 27.7% in February 2020 to 35.8% in May 2020 in the COVID19 group (p <0.001).

**Conclusions:** In this national cohort of hospitalized AMI patients, we observed a significant rise in incidence of OHCA during COVID period paralleled with reduced access to guidelines recommended care and increased in-hospital mortality.

**Keywords:** Out of hospital cardiac arrest, Incidence, COVID19, acute myocardial infarction, mortality

**Abbreviations**

|  |  |
| --- | --- |
| AMI | Acute myocardial infarction  |
| OHCA | Out of hospital cardiac arrest |
| COVID19 | Corona virus disease 2019 |
| NICOR | National Institute of Cardiovascular Outcome Research  |
| NHS | National Health System  |
| MINAP  | Myocardial Ischaemia National Audit Project  |
| BCIS  | British Cardiovascular Intervention Society  |
| PCI  | Percutaneous coronary intervention  |

**Clinical Perspectives**

**What is new?**

* This population based cohort study provides important information about the incidence, clinical and procedural characteristics of patients presenting with AMI and pre-hospital cardiac arrest during COVID-19 pandemic in England.
* There was a marked increase in the incidence of out of hospital cardiac arrest during the COVID-19 pandemic compared to pre-COVID-19 period.
* Out of hospital cardiac arrest patients during COVID-19 were less likely to receive guideline indicated care and had increased mortality compared to pre-CVOID-19 era.

**What are the clinical implications?**

* Immediate counter measures are required to increase patient awareness and improve cardiac care of this high-risk group during the ongoing COVID-19 pandemic.

**Introduction**

During the global pandemic of COVID19 caused by the novel acute respiratory syndrome coronavirus 2 (SARS-Cov2), a significant reduction in acute myocardial infarction (AMI) related hospitalisations have been observed (1-4). It has been postulated that patients with AMI are not seeking medical attention because of their concerns around the risk of nosocomial acquired COVID19 infection, as well as limitations to social movement due to Government lockdowns(3, 5, 6). Delays to timely reperfusion are associated with an increased risk of life threatening arrhythmias, out of hospital cardiac arrest (OHCA, heart failure and death among patients presenting with AMI(7-9).

A recent multicentre observational report from Italy found that AMI related hospitalisations were reduced by almost 50% during the COVID19 period and accompanied by a three-fold rise in mortality and complications(2). Such significant changes to AMI related hospitalizations may result in an increase in OHCA and death (10, 11). Data from the Lombardia Cardiac Arrest Registry reported a 58% increase in OHCA during the first 40 days of the COVID19 outbreak(12). It was thought that this may be related to the spread of the COVID19 infection as there was no information regarding the incidence of AMI in this cohort. Similar observations were made by Lai et al from NYC EMS system, where a threefold rise in incidence of OHCA was noted in those undergoing EMS resuscitation during the COVID19 period(13). It remains unclear, however, whether reduced hospitalisations with AMI are associated with changes in incident OHCA. Equally, it is not known if the changes in service structure and delivery of healthcare emergency response during the COVID19 pandemic have influenced the management of patients presenting with OHCA in the context of AMI. Using multisource nationwide data derived from UK national acute coronary syndrome and percutaneous coronary intervention datasets, we studied the characteristics, care and outcomes of admissions to hospital with AMI complicated by OHCA during the first wave of the COVID19 outbreak in the England.

**Methods**

Study Data

Because of the sensitive nature of the data collected for this study, requests to access the dataset from qualified researchers trained in human subject confidentiality protocols may be sent to National Institute of Cardiovascular Outcomes Research (NICOR). Data for this study were drawn from two nationwide cardiovascular registries of the NICOR, namely the Myocardial Ischaemia National Audit Project (MINAP) and the British Cardiovascular Intervention Society (BCIS) percutaneous coronary intervention (PCI) dataset(14, 15). Full details regarding the framework of these datasets and their utility in conducting research has been described previously(16-18). Briefly, MINAP is one of the largest single health system heart attack registries and collects information about baseline demographics, reperfusion treatment, pharmacological and invasive management of patients admitted with AMI to one of the 195 acute NHS hospitals in England(19-21). The BCIS PCI database contains high-resolution information regarding the procedural aspects, peri-procedural pharmacology and in-hospital PCI related complications of patients admitted with AMI(16, 22, 23).

Ethics

The National Institute for Cardiovascular Outcomes (NICOR) databases including MINAP and BCIS are collected and used for research purposes without requiring informed patient consent fell under section 251 of National Health Service Act 2006(24, 25) and therefore institutional board review was not required for this study. Access to data required for this project has been fast tracked using a novel collaboration as part of a national drive for COVID19 related research.

Study population

We included all adult patients aged 18-100 years admitted with a diagnosis of AMI between 1st February 2019 and 14th May 2020 (the latest live data upload available) from the MINAP and BCIS PCI database, respectively. We only included patients with an index admission diagnosis of AMI or a PCI procedure during these dates. Further exclusions were made based on missing record information regarding sex, cardiac arrest in hospital and final diagnosis not being AMI (**Supplementary Figure 1 and Supplementary Figure 2**). Given that first cases of COVID19 in the United Kingdom were reported on the 29th January 2020, we defined patients from 1st February 2020 to 14th May 2020 as the COVID19 group. To further understand the temporal differences in the baseline characteristics, procedural profile and outcomes, we generated an equivalent cohort of pre-COVID19 patients from 1st February 2019 to 14th May 2019 from both datasets. Time to reperfusion treatment was calculated from time of symptoms onset to time of the reperfusion treatment in the form of PPCI or thrombolysis for ST elevation acute myocardial infarction.

Statistical analysis

Continuous variables were presented as means and standard deviations (SD) whereas categorical variables were reported as absolute numbers and percentages. Chi^2 and student t-tests were used to examine differences across groups for categorical and continuous variables, respectively. All statistical comparisons were made between the pre-COVID19 and COVID19 groups only, whereas patients without OHCA were reported for total cohort comparison. All tests were two sided and p<0.05 considered statistically significant. Poisson regression models were used to estimate the unadjusted incidence rate ratio (IRR) of OHCA across each month of 2020, using the equivalent month in 2019 as the reference. We used multiple imputations with chained equations to account for missing data related bias, creating 10 datasets(26, 27). Variables with complete information such as age, sex, OHCA, month and year were registered as regular whereas all other variables with missing information were imputed using logistic regression for binary, multinomial for nominal and linear regression for continuous variables (supplementary table 1). We used multivariable logistic regression with an interaction term between OHCA and the month variable to study the association between OHCA and in-hospital mortality in the pre-COVID19 and COVID19 periods. The margins command was using following the regression models, to obtain adjusted probability for in-hospital mortality.

In order to investigate, whether the lag in the data uploads may be associated with inflated incidence of OHCA due to different hospital reporting pre- and post-COVID19 period, we performed a sensitivity analysis. We only included the 88 ‘rapid reporting’ hospitals which have consistently provided data on a weekly basis during the COVID and pre-COVID period across 2019 and 2020. All analyses were performed using Stata v16.0.

**Results**

*Clinical characteristics*

Five hundred and twenty-four patients (5.6%) of patients were admitted with OHCA from a total of 9,325 AMI admissions the during the COVID19 period from 1st Feb 2020 to 14th May 2020, compared with 731 (3.6%) patients out of 20,310 during the equivalent pre-COVID19 period from 1st February 2019 to 14th May 2019. Patients presenting with OHCA during the COVID19 period were older (mean age 67.1 vs. 63.1 years, p<0.001), women (28.8% vs 20.5%, p<0.001) and of Asian ethnicity (10.0% vs 4.6%, p<0.001). There was an increased prevalence of insulin treated diabetes mellitus (6.4% vs 3.0%, p<0.001) and hypertension (47.9% vs 41.2%, p<0.001) in the COVID19 OHCA group compared with the pre-COVID19 OHCA group. In-hospital pharmacological treatments were comparable between the pre-COVID19 and COVID19 groups with similar use of glycoprotein IIbIIIa inhibitors, ACE inhibitors, P2Y12 inhibitors and dual anti-platelet therapy (**Table 1**). An increasing proportion of patients with OHCA during the COVID19 period had ST-elevation MI compared with OHCA patients in the pre-COVID19 period (**Supplementary Figure 3**).

*Trends in incidence of OHCA*

During the COVID19 period, the monthly proportions of OHCA increased from 5.4% in February 2020 to 6.9% in May 2020 (**Figure 1**) whilst there was a significant decrease in the total number of patients presenting with AMI. There was a 56% increase in the overall incidence of OHCA during the COVID19 period (5.6% vs 3.6% IRR 1.56 (95%CI 1.39-1.74)) compared to pre-COVID19 period (**Figure 2**). The incidence rate ratio of OHCA also increased from 1.55 (95%CI 1.29-1.87) in February 2020 to 1.96 (95%CI 1.31-2.86) May 2020 compared to equivalent monthly periods in 2019 (**Figure 2**). In the sensitivity analysis of “rapid reporting”, hospitals which consistently reported data in all months during pre-COVID and COVID period, we found a similar rise in the incidence of OHCA in patients presenting with AMI during the COVID period (IRR 1.36 95%CI 1.08-1.72 in Feb 2020, increasing to IRR 1.80 95%CI 1.20-2.99 in May 2020) compared to the pre-COVID period (**Supplementary Figure 4 and Supplementary Figure 5**).

*Processes of care*

Patients admitted with OHCA during the COVID19 period were slightly less likely to be seen by a cardiologist (91.0% vs. 96.8%, p<0.001), less likely to be investigated with an invasive coronary angiography (58.4% vs. 71.6%, p<0.001) and for STEMI had increased time to reperfusion treatment (mean 2.1 hours vs. 1.1 hours, p=0.05) (**Table 1**). Temporal analysis of use of invasive coronary angiography revealed a consistent lower use of an invasive strategy across all months in the COVID19 period with almost a 50% reduction in May 2020 compared to May 2019 (**Figure 3**). The use of PCI was also lower across COVID19 months in 2020 compared to pre-COVID19 months in 2019 (**Supplementary** **Figure 6**). In-hospital mortality was higher in the OHCA group during the COVID19 period compared with the pre-COVID19 (37.7% vs 27.8%, p<0.001). In the multivariable analysis, the adjusted probability of mortality also increased from 27.7% to 35.8% in the COVID19 cohort compared to 16.9% to 29.8% in the the pre-COVID19 cohort (P <0.001) (**Supplementary Figure 7**).

*Clinical and angiographic characteristics from BCIS registry*

In the BCIS registry, of 15,114 PCI procedures, 674 (4.5%) were undertaken for OHCA in the pre-COVID19 period compared with 270 (3.4%) of 7,856 during the COVID19 period. The baseline demographics and clinical characteristics were similar between the pre-COVID19 and COVID19 periods (**Table 2**). Patients with OHCA who received PCI during the COVID19 period more frequently had complex coronary disease such as left main stem (3.8% vs. 1.2%, p<0.001) and multi-vessel PCI (21.2% vs. 12.6%, p<0.001). There was similar use of peri-procedural pharmacology, haemodynamic support in the form of pharmacological inotropes, intra-aortic balloon pump, and impella device across the pre-COVID19 and COVID19 groups (**Supplementary Table 2**). The procedural success was similar in both groups with no difference in the in-hospital mortality, major adverse cerebrovascular events (MACCE), bleeding and other peri-procedural complications (**Supplementary Table 2**).

**Discussion**

In this national prospective cohort of patients hospitalised with AMI during the COVID19 outbreak, there was an increase in the incidence of OHCA accompanied with a substantial decline in AMI related hospitalisations during the same time period. In fact, following announcement of lockdown and implementation of social distancing measures in England, the incidence of OHCA among those presenting with AMI almost doubled in the late phase of COVID19 pandemic compared with an equivalent period in the previous year. More frequently, patients presenting with OHCA during the COVID19 period were older, women and of Asian ethnicity. Although the pharmacological management strategies were not changed, during the COVID19 pandemic patients hospitalised with AMI after OHCA had longer delays to emergency reperfusion, less frequently received invasive coronary angiography, were less likely to receive specialist care, and had a higher risk of in-hospital death.

Many studies have noticed a fall in AMI related admissions during COVID19 pandemic(2-4, 28). Data from 15 hospitals in the northern Italy revealed over 30% reduction in the incidence of AMI related hospitalizations during the COVID19 pandemic(29). Similar observations were made by Mafham et al from England reporting 40% reduction in AMI related hospitalization during the COVID19 pandemic(28). The slight difference between the incidence of AMI related hospitalizations in this study may be related to differences in datasets and coding differences in the SUSAPC (Secondary Uses Service Admitted Patient Care) dataset that was used(28). These findings have raised concerns that the decrease in AMI admissions may have resulted in an increased risk of OHCA and / or mortality. Our study substantiates these concerns by showing reduced AMI admissions paralleled an increased incidence of OHCA among those presenting with AMI during the COVID19 pandemic in England. These results are consistent with those of Baldi et al who reported a 58% increase in the incidence of OHCA among COVID19 positive patients in Italy(12). However, there were no data regarding the concurrent history of coronary heart disease or AMI diagnosis in these patients and the authors concluded that these findings may be related to actual viral infection.

Our data provide important information regarding the characteristics and in-hospital management of OHCA patients during the COVID19 pandemic. The demographic differences in the pre-pandemic and during COVID19 period are of particular interest. It is possible that older patients with increased co-morbidities may have refrained from seeking early help due to fears of being exposed to infection, breaking their shielding and social confinement. Our observation about the ethnic origin of OHCA patients may be linked to increase risk of COVID19 related mortality in ethnic minorities such as south Asians that has been widely reported (30, 31). It is probable that media coverage, cultural and social beliefs as well as a lack of awareness may have prompted many to delay contact with the emergency medical services, thus presenting with OHCA.

There were also differences in in-hospital management and outcomes of OHCA patients during the COVID19 period. Patients with OHCA during the COVID19 period experienced an increase in time to reperfusion therapy, slightly less specialist care and use of an invasive coronary strategy, whereas the demographics of those selected for PCI seems to have been unchanged. Following Government directives and a declaration of a healthcare emergency in the UK, hospitals undertook major reconfigurations of their services in preparation for COVID19 related admissions. It is possible that the restructuring of emergency services, re-deployment of specialist doctors to COVID19 wards to focus on the care of COVID19 positive patients and conflicting and evolving guidance regarding how and when to resuscitation in the context of OHCA, specifically with concerns about the aerosol generation may have contributed to these differences in management(32, 33). Indeed, we noted a significant reduction in invasive coronary strategy for OHCA in this study which is associated with improved survival and more favourable neurological outcomes particularly in those presenting with ST elevation on the ECG(34). Reassuringly, we observed no substantial differences in procedural characteristics and outcomes for patients with OHCA who received PCI during the COVID19 period.

To the best of our knowledge, this is first national report of impact of COVID19 pandemic on the care and outcomes of patients with OHCA presenting to hospitals in the setting of AMI. We acknowledge the limitation of our study. MINAP collects data only for hospitalised cases of acute coronary syndrome and we were therefore unable investigate the incidence, care and outcomes of those with OHCA occurring in patients in whom OHCA was not related to an ACS or did not survive to hospital admission. Therefore, our data are likely to have underestimated the overall incidence of OHCA. Nevertheless, a recent report from a community cardiac arrest registry suggested a similar rise in OHCA incidence reaffirming our findings (12). Finally, the observational nature of our study precludes inferences about causation.

**Conclusion**

Our study provides important insight into admissions, care and outcomes for patients with AMI complicated by OHCA during the COVID19 pandemic. These data suggest that a decline in AMI related hospitalisation in England was accompanied by an increased in the number of cases of OHCA particularly after the implementation of social confinement measures during the COVID outbreak in England. It appears that elderly, women and ethnic minorities may have refrained from seeking early help after developing cardiac symptoms of AMI. The reorganisation of hospital services and staff in preparation for the COVID19 pandemic may inadvertently have affected the care of this high-risk group. Urgent interventions to improve public awareness and treatment pathway to allow timely access to specialist care will be required to minimise the collateral cardiac damage of COVID19 for patients with AMI.

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**Conflict**

All authors confirm no potential conflict relevant to this manuscript.

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