Presentations of stroke and acute myocardial infarction in the first 28 days following the introduction of State of Emergency restrictions for COVID-19

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Abstract

Objectives: To determine if Victorian State of Emergency (SOE) measures to combat COVID-19 were associated with delayed presentations or management of acute stroke and acute myocardial infarction (AMI).

Methods: This was a retrospective, pre- and post-implementation study using data from an adult, tertiary cardiology and neurosciences centre with 24-h capacity for endovascular procedures. All primary presentations with acute stroke or AMI during the first 28 days of stage 2 and stage 3 SOE restrictions (26 March to 23 April 2020) were compared to an equivalent period without restrictions (26 March to 23 April 2019). The primary outcome variable was time from onset of symptoms to ED presentation.

Results: There were 52 (1.6% of all ED presentations) patients who met inclusion criteria during the SOE period and 57 (1.0%) patients in the comparator period. Patients were equally matched for demographics, disease severity and prior history of stroke or AMI. Median time from symptom onset to presentation was 227 (93–1183) min during the SOE period and 342 (119–1220) min during the comparator period (P = 0.24).

Among eligible patients with ischaemic stroke or ST-elevation AMI, median time to primary reperfusion intervention was 65 (37–78) min during SOE and 44 (39–60) min in the comparator period (P = 0.54). There were no differences in mortality at hospital discharge (9.6% vs 10.5%) and hospital length of stay (5.4 vs 4.3 days).

Conclusions: In the first 28 days, SOE measures to combat COVID-19 were not associated with delays in presentation or life-saving interventions for patients with acute stroke and AMI.

Key words: coronavirus, delay, lockdown, myocardial infarction, stroke.

Introduction

Coronavirus disease (COVID-19) is caused by the SARS-CoV-2 virus, a potentially fatal disease that is of significant global public health concern. The outbreak was declared a pandemic on 11 March 2020. In order to combat community transmission of the virus, countries around the world have implemented a variety of physical distancing interventions. Measures such as school closure, workplace avoidance, case isolation and community contact reduction have been shown to be highly effective in flattening the epidemic curve, reducing the maximum daily case numbers and lengthening outbreak duration.3

On 16 March 2020, the Victorian Government declared a State of...
Emergency (SOE) and implemented stage 1 physical distancing restrictions. These were escalated to stage 2 restrictions (effective from 26 March 2020) and stage 3 restrictions (effective from 31 March 2020). Under Victorian SOE stage 3 measures, individuals were only permitted to leave their place of residence for four reasons: to shop for essential supplies, to exercise, to work or study (if this cannot be done remotely) and to seek medical care.

A potential adverse effect of physical distancing interventions, such as the Victorian SOE measures, is delayed assessment and management of non-COVID-19 conditions. Consistent with this, Victorian hospitals have reported decreases of up to 40% in ED attendance. Contributing factors may include apprehension of patients to visit health services where patients with symptoms of COVID-19 are being assessed, delayed detection of symptoms and signs by family and friends and misinterpretation of public health messaging to ‘stay at home’. A shift to primary care being practised by telehealth (potentially resulting in sub-optimal assessment of patients), and reduced priority of regular health screening and risk factor assessment, may also be implicated.

It has been repeatedly demonstrated that early recognition of symptoms with reduced time to intervention results in better outcomes following stroke and acute myocardial infarction (AMI). The aim of the present study was to determine whether there was an association of Victoria’s SOE measures with delayed presentations of acute stroke and AMI. Secondary aims were to assess the association between the implementation of SOE restrictions and times to essential investigation (computed tomography of the brain [CTB]) for acute stroke), reperfusion interventions and hospital outcomes.

Methods

Design

A retrospective pre- and post-implementation study was undertaken. The study protocol was reviewed and approved by The Alfred Hospital Research and Ethics Committee (Project ID 245/20). The requirement to seek informed consent from patients was waived.

Setting

The study was conducted at an adult major referral hospital in metropolitan Melbourne, Victoria, Australia, with an annual ED attendance of approximately 65 000 patients. The Emergency and Trauma Centre (E&TC) is serviced by emergency physicians between 07.00–02.00 hours on weekdays and 07.00–24.00 hours on weekends.

Patients presenting to the E&TC with symptoms consistent with stroke are managed by a multidisciplinary team via a stroke call-out system. This includes a stroke consultant or registrar, a critical care registered nurse, an emergency medicine registrar or consultant and a pharmacist (in-hours). The system aims to facilitate rapid access to multi-modal computed tomography (CT) imaging, including plain CTB, arch to vertex CT angiography and CT perfusion imaging using automated and standardised software reporting (Rapid©). Reperfusion strategies (thrombolysis and endovascular clot retrieval) are delivered according to a hospital protocol.

All patients with ST-elevation myocardial infarction (STEMI) are managed through a STEMI call-out system. Patients are assessed by a critical care registered nurse, a cardiology registrar and emergency medicine registrar or consultant, with the objective of expediting reperfusion via percutaneous coronary intervention (PCI). PCI was the preferred therapy for STEMI patients and patients with STEMI were not expected to receive thrombolysis at this centre.

Outcome measures

The primary outcome variable was time from onset of symptoms (self-reported by patients or collateral history) to time of registration in the ED. Where history regarding time of onset was unknown (e.g. patient awoke with symptoms), the onset time was recorded as ‘midnight’ (if overnight) or the last known time the patient was reported to be asymptomatic. For the primary outcome, we also reported sub-group analyses of patients with known onset times and subgroups with ischaemic stroke and STEMI.

Secondary outcome measures were the proportion of patients who presented beyond 12 h after symptom, time to CTB for patients presenting with acute stroke, time to first reperfusion intervention (thrombolysis or endovascular treatment), death in hospital and hospital length of stay (LOS). For secondary outcome measures, the initial time was taken as registration time of the patient in the ED. Time to CTB was calculated from the time of images being available. Time to first reperfusion intervention was calculated from the commencement of the relevant infusion or procedure groin puncture time.
Data extractions
Participants were identified from comprehensive databases maintained by the stroke and cardiology services. Data were augmented by review of electronic medical record using explicit chart review methods by two investigators (BM and JPM). Additional explanatory variables assessed included mode of arrival to hospital, presenting complaint, whether the patient was managed as being COVID-suspect and severity of disease. To quantify severity of stroke, the first National Institutes of Health Stroke Scale was used as recorded by the admitting stroke registrar or consultant. To quantify the severity of an AMI, the peak troponin level in the index presentation was used. Troponin concentrations are measured at The Alfred hospital using Architect STAT high sensitivity troponin I with a limit of detection of 1.9 ng/L, and a CV of 12.6% has been reported at 3.5 ng/L. Data on COVID-19 testing were extracted from the COVED registry. After-hours was defined as the period between 18.00 and 07.00 hours, 7 days a week.

Analysis
Continuous and normal or near-normally distributed variables were summarised using mean (standard deviation) with differences assessed using Student’s t-test. Skewed continuous and ordinal variables were summarised using median (inter-quartile range) and differences assessed the Wilcoxon rank-sum test. Nominal variables were summarised using counts (proportions) and differences assessed using the χ²-test or, if a value in a cell was <5, Fisher’s exact test was used. A P-value of <0.05 was defined to be statistically significant. Assuming that among patients presenting without delay of >12 h from onset of symptoms, time to presentation was 200 (30) min, to test for a minimum clinically significant 10% difference, with 90% power, we required 48 patients in each arm with a minimum sample size of 96. All analyses were undertaken using Stata v 15.1 (College Station, TX, USA).

Results
There were 95 patients admitted under the Stroke and General Cardiology units during the SOE period and 156 in the comparator period. After exclusion of patients not diagnosed with an acute stroke or AMI, there were 52 patients (1.6% of all E&TC presentations) who met inclusion criteria during the SOE and 57 (1.0%) patients in the comparator period (Fig. 1). There was a 9.6% (95% CI 3.2–21.0) decrease in the number of patients who met inclusion criteria in the first 28 days of the SOE period compared to the comparator period.

Among patients with acute stroke, 52 were diagnosed as ischaemic stroke (27 during SOE and 25 in comparator period) and 10 were diagnosed as haemorrhagic stroke (three during SOE and seven in comparator period). Among patients with an AMI, there were 16 patients who presented with a STEMI (eight during SOE and eight in the comparator period) and 31 patients with a NSTEMI (14 during SOE and 17 in the comparator period).
TABLE 2. Outcome measures

|                          | SOE period (n = 52) | Comparator period (n = 57) | P-value |
|--------------------------|---------------------|---------------------------|---------|
| Time from onset of symptoms to presentation (min, median and IQR) | 227 (93–1183) | 342 (119–1220) | 0.24 |
| Onset of symptoms to presentation of over 24 h, n (%) | 11 (21.6) | 14 (24.6) | 0.67 |
| Time to CTB† (min, median and IQR) | 52 (21–97) | 65 (45–90) | 0.11 |
| Time to primary reperfusion intervention (min, median and IQR) | | | |
| All eligible stroke and STEMI (n = 20) | 65 (37–78) | 44 (39–60) | 0.54 |
| Eligible ischaemic stroke‡ (n = 5) | 67 (37–97) | 60 (46–212) | 0.56 |
| Eligible STEMI (n = 15) | 40.6 (29.3–45.1) | 64.7 (37.5–76.0) | 0.30 |
| NSTEMI (n = 25) | 340 (89–1301) | 830 (144–3831) | 0.58 |
| Death in hospital | 5 (9.6%) | 6 (10.5%) | 0.99 |
| LOS in hospital§ | 3 (2–6) | 4 (2–6.5) | 0.39 |

†Among patients with acute stroke. ‡Eligible for thrombolysis or endovascular procedure. §Excludes two patients who were inpatients at the time of reporting. CTB, computed tomography of the brain; IQR, interquartile range; LOS, length of stay; NSTEMI, non-ST-elevation myocardial infarction; SOE, State of Emergency; STEMI, ST-elevation myocardial infarction.

were no patients diagnosed with a concurrent stroke and AMI. Demographic and patient characteristics in the two time-periods are listed in Table 1, demonstrating similarities in age, presentation modes and times, disease severity and prior history of stroke or AMI.

Median time from symptom onset to presentation was 227 (93–1183) min during the SOE period and 342 (119–1220) min during the comparator period (P = 0.24). There were 17 (32.7%) patients who presented >12 h after onset of symptoms in the SOE period, compared to 19 (33.3%) during the comparator period (P = 0.94). Among patients with ischaemic stroke, median time from onset to presentation was 404 (139–1561) min during SOE and 405 (215–820) min during the comparator period (P = 0.73). Among patients with STEMI, median time to presentation was 93 (66–118) min during SOE and 69 (51–152) min during the comparator period (P = 0.75). In the subgroup of patients where onset times were accurately reported (n = 78), median time from onset to presentation was 178 (82–736) min during SOE and 149 (71–341) min in the comparator period (P = 0.60).

Median time to CTB for patients presenting with acute stroke was 52 (21–97) min during the SOE period and 65 (45–90) min in the comparator group (P = 0.11). Among eligible patients with ischaemic stroke or STEMI, median time to primary reperfusion intervention was 65 (37–78) min during the exposure period compared to 44 (39–60) min in the comparator period (P = 0.54). There were 11 patients who died in hospital – five during the SOE and six in the comparator period (P = 0.99). Hospital LOS during SOE was 4 (2–6.5) days and 3 (2–6) days in the comparator period (P = 0.39). Outcomes of the overall population and subgroups are summarised in Table 2.

Discussion

The effects of the SOE through significant restrictions on individual movement have been associated with controlling the spread of COVID-19. In the first 28 days of restrictions, we observed a reduction in the number of presentations of acute stroke and AMI, but there appeared to be no significant adverse effects of delayed presentations associated with the SOE. Times to assessment and life-saving interventions were unchanged.

The reduction in presentations of AMI and stroke is broadly consistent with observations around the world, but the magnitude of difference less pronounced. For instance, in the period prior to the pandemic, the city of Piacenza, Italy, had recorded 612 new cases of ischemic stroke annually (21% of which were secondary to large vessel occlusion), with a monthly average of 51 cases. In the first month of the pandemic, only six cases of stroke were received (with one case of large vessel occlusion). The authors hypothesised that increased inflammatory cytokines associated with COVID-19 may result in decreased platelet function leading to fewer episodes of stroke.10 Similarly, a 38% reduction in cardiac catheterisation laboratory STEMI activations was observed in the USA, and a 40% reduction in Spain.11,12 Authors suggested that explanations may include avoidance of medical care.
due to physical distancing rules or concerns of contracting COVID-19 in hospital and reduction in STEMI misdiagnosis.

Times to early life-saving interventions were unchanged in the present study. This contrasts with experience overseas, where times were likely to have been affected by the greater burden of COVID-19 than experienced in Australia to date. Centres from Italy have reported longer onset-to-door and door-to-treatment times for major strokes in the setting of the COVID-19 pandemic. Similarly, in Hong Kong, longer median times for symptom onset to first medical contact, door to device and catheterisation laboratory arrival to device times were observed in STEMI patients when compared with historical data from the prior year. Based on this evidence, investigators have recommended health authorities promote early presentations for AMI compatible symptoms and no delays for reperfusion treatment.

Although no significant differences were observed in the present study, one plausible explanation for potential delays in door-to-treatment times may relate to COVID-19 infection prevention and control requirements, including the requirement for staff to don personal protective equipment. Very few catheterisation laboratories are equipped with negative ventilation systems and, consequently, the risk of transmission remains relatively high with each encounter. Tailored management protocols (including infection prevention and control and personal protective equipment procedures) have been developed, but implementation may have the effect of delaying time-to-treatment.

The present study is limited in being retrospective and can therefore only imply association. It is subject to the established limitations of medical record review methodology. Only a short period of 28 days of post-implementation data were analysed and may not be representative over a longer period of time. However, all patients in both periods were available for analysis and present valuable data on early effects of the SOE. Pre-hospital deaths were unacknowledged for in the present study design, and review of coronial records may add further information to potential adverse effect of physical distancing. In addition, the present study was not designed to explore the reasons for delayed presentations.

Small numbers in sub-group analyses may be associated with type II errors and require ongoing surveillance. For example, the difference in median time to reperfusion of 21 min is clinically significant, but because of the small number of patients, we cannot be confident that the true population difference is reflected in this sample. Being a single centre study and limited to two conditions only, generalisability to other health services and other conditions remains unknown. Variations in demographics and population of selected patients, together with small samples, may explain differences observed in other health services.

The framework presented in this manuscript may be used for further research into other conditions and monitor effect of the SOE over the next coming months. More granular assessment of times would mandate separation of different acute reperfusion interventions, with comparison of times for specific procedures. Additionally, qualitative research may have a role in determining which factors and social interventions contributed to delays to the ED attendance. The novel Registry for Emergency Care Project aims to assess times to critical assessment for all ED patients, across multiple sites, and can further inform strategies to reduce times to intervention.

Notwithstanding the limitations of the present study, there is a clear role for public health authorities to emphasise the importance of timely medical contact for patients experiencing acute illness and injury. The indirect effects of communicable disease outbreaks and public health responses are well documented, and it is critical that governments seek to limit any collateral impact. The COVID-19 pandemic and the associated physical distancing measures are predicted to have far-reaching health effects. Unintended second order effects related to delayed presentations can be minimised by clear and consistent communication from public health authorities.

**Conclusions**

SOE measures to achieve physical distancing and restrict community contact were not associated with significant changes in time to the ED presentation after acute stroke and AMI. Time to initial investigation and life-saving interventions were also unchanged in the first 28 days. Public health messaging encouraging patients with acute illness or injury to seek medical assessment should be continued.

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**Competing interests**

BM, GMOR and PAC are section editors for *Emergency Medicine Australasia*.

**Data availability statement**

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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