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ACUTE CORONARY SYNDROMES AND COVID-19

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Abstract: At the end of 2019, cases of a new acute viral respiratory disease, later recognized as COVID-19, were described. The pandemic has greatly affected healthcare services around the world and is in addition to existing challenges for emergency services such as ST-elevation myocardial infarction. Both conditions can coexist, initial presentations can overlap, and there is no such thing as a true and reliable point-of-care test. Pre-hospital diagnosis and timely treatment of acute coronary syndrome are necessary to achieve optimal outcomes. The use of risk stratification tools (such as GRACE scores) can assist in prioritizing cases to minimize their hospital stay. Critically ill patients with ST-elevation myocardial infarction, no catheter lab facilities in place or too unstable for transfer must be considered for thrombolysis and activation of services for facilitated PCI, if needed. Patients with cardiovascular disease are particularly vulnerable during this period, regardless of their infectious status. Adapting cardiac services to ensure continuity of care for these patients, even in the context of a new wave of COVID-19, is essential to minimize preventable cardiovascular death.
Keywords: COVID-19; acute coronary syndrome.

INTRODUCTION

The coronavirus (COVID-19) pandemic has had an unprecedented impact on healthcare systems, including acute cardiology services (RASHID et al. 2020). COVID-19 directly leads to cardiac complications in patients with underlying heart disease or cardiac risk factors. COVID-19 indirectly impacts patients through the necessary shift in healthcare resource allocation and the need for social distancing. A reduction in health-seeking behavior, reduced attendances for cardiac emergencies, and a reduction in traditional

chronic care will have implications that go beyond the infectious scope of the virus. Therefore, cardiovascular care during the pandemic must remain a priority to mitigate significant morbidity and mortality from both the direct and indirect effects of COVID-19 (PONTONE et al. 2020). As future waves of the coronavirus are anticipated, it is prescient to review its impact on cardiovascular care delivery, in particular the treatment of acute coronary syndromes (ACS).

CARDIOVASCULAR CONCERNS IN COVID-19

Early reports suggested a strong relationship between traditional cardiovascular risk factors and poor COVID-19 outcomes (SINGH et al. 2020; VECCHIO et al. 2020). Myocardial injury related to COVID-19 is evident post mortem (SINGH et al. 2020). Those with critical illness demonstrate elevated troponin and B-type natriuretic peptide (BNP) levels, and increasing levels correlate with worse clinical outcomes (SCHIAVONE et al. 2020).

Mechanisms of myocardial injury remain poorly understood, but candidates may involve ACE2 expression in the myocardium and coronary vessels, triggering local inflammation, hypercoagulopathy, and thrombosis. Coronary thrombosis will cause ACS and localized ischemia in the form of type I myocardial infarction (MI) (MOUNTANTONAKIS et al. 2020). Ischemia can also result from respiratory failure and hypoxia; in the context of underlying coronary heart disease, the increase in troponin may reflect a type II AMI due to a supply/demand mismatch (MATSUSHITA et al. 2021). Pulmonary emboli may also occur, leading to high pulmonary pressures with right ventricular distention (GUIMARÃES et al. 2020). An immune-mediated inflammatory response appears to lead to secondary myocarditis and contributes to acute heart failure and multiple organ failure (GRIFFIN et al. 2020). Myocarditis in COVID-19 generates marked ECG changes with marked and even regional ST elevation ('STEMIS'). Furthermore, the sympathetic impulse can lead to a Takutsubo-type cardiomyopathy or lead to cardiac arrhythmia.

ACUTE CORONARY SYNDROMES

In the pre-COVID-19 era, the diagnosis of ACS was based on classic symptoms of chest discomfort (often associated autonomic features), electrocardiographic features, and increased cardiac biomarkers (usually troponin). Treatment requires antiplatelet agents (aspirin with a potent $P2Y1_{12}$ antagonist such as clopidogrel, prasugrel, or ticagrelor), injectable anticoagulants (such as fondaparinux), and modification of cardiac demand (with beta-blockers) (CHIEFFO et al. 2020). Statins are administered early as they can promote plaque stabilization. Although initial reports raised concerns about ACE inhibitor and angiotensin receptor use in COVID-19 patients, age-corrected models did not support this, and ARBs may even have a protective role (ASHRAF et al. 2020).

Those with higher-risk features, such as significant troponin markers, continuous ECG changes, or high GRACE scores, receive invasive angiography, as revascularization reduces poor outcomes, including reinfarction (BRAITEH et al. 2020). In ST-segment elevation myocardial infarction (STEMI), prompt revascularization with primary percutaneous coronary intervention (PCI) is essential. Untreated, ST-following Elevation Myocardial Infarction (STEMI) has high mortality and risks of mechanical complications such as mitral regurgitation or ventricular septal defects (CAPACCIONE et al. 2021). Door-to-balloon time must be less than 60 minutes when feasible. Non-

ST-segment elevation myocardial infarction (STEMI) must undergo angiography within 72 hours, preferably sooner.

All of these factors hold true in the COVID-19 era, with the additional assessment of infectious status and adequate staff protection. COVID-19 treatment algorithms have incorporated the use of anticoagulants due to thrombotic risk (CHIEFFO et al. 2020). Ischemic events can be reduced by adding rivaroxaban 2.5 mg twice daily and ongoing studies are evaluating this in the era of COVID-19.

Although chest pain is common in COVID-19, symptoms of true MI remain distinct and detectable on history assessment. The key issue is to distinguish these MI type I events from troponin elevation due to arrhythmia, heart failure, myocarditis, pericarditis, or systemic disease (MI type II) (COURAND et al. 2020). Clinical assessment, serial ECG, and troponin measurement are critical to the diagnosis. In the context of COVID-19, conservative management may be appropriate for non-true SCA.

Point of care echocardiography can support decision making: the presence of regional wall motion changes would suggest typical ACS. As echocardiography is an intimate examination with a prolonged period of contact between the patient and the healthcare professional, there is an increased risk of viral transmission and the use of full personal protective equipment (PPE) is recommended. Focused scans with limited views to answer the question are appropriate. Patients must wear masks during the scan and during their assessment and treatment.

REPERFUSION FOR STEMI

In STEMI, rapid mechanical reperfusion via primary percutaneous coronary intervention (PPCI) is the preferred treatment option (COURAND et al. 2020). The National Health Service and the British Cardiovascular Intervention Society reiterated that PPCI remains the treatment of choice for STEMI in the COVID-19 era (GRIFFIN et al. 2020). In the UK, most cardiac networks have STEMI diagnosed by ambulance services, and patients are taken directly to designated cardiac catheter labs. Occasionally, patients may need acute transfer from district general hospitals to central hospitals if the first hospital cannot provide revascularization in a timely manner. Usually, intensive care ambulances are needed for this.

As there is an asymptomatic period when infected patients are shedding the virus, those who present with emergency STEMI can lead to viral transmission for both first responders and those performing PPCI. COVID-19 diagnostic tools are still not fast enough to allow screening prior to emergency PPCI for STEMI, and while CT-thorax screening is useful in more elective scenarios, it is unfeasible in a STEMI scenario. As PPCI can involve cardiac arrest, a recognized 'aerosol generating procedure', it is agreed that full PPE is recommended for all those undergoing PPCI (DE HAVENON et al. 2020; GUIMARÃES et al. 2020). Services must consider protecting staff members most at risk of COVID-19: those with lung disease or those over the age of 65 have been transferred to non-patient-oriented activities appropriately.

PPCI must be performed with reperfusion within 120 minutes of the onset of symptoms and within 60 minutes of arrival at a center capable of PPCI (GUIMARÃES et al. 2020). Radial access is preferred to facilitate early patient ambulation. Observational data suggest that those with COVID-19 have a higher thrombus burden: rates of multivessel thrombosis and stent thrombosis are higher (JENAB et al. 2020). Higher rates of aspiration thrombectomy and greater need for GPIIb/IIIa and higher doses of intraprocedural heparin

are reported (LANG et al. 2020). Prolonged hospitalization and higher mortality are seen in those with COVID-19 and STEMI (MATSUSHITA et al. 2021; LI et al. 2021)

A dedicated catheter lab is recommended and all possible equipment must be available to limit the need for a team to fetch the equipment and potentially spread the virus. A designated area for donning and doffing PPE is essential; employees must observe each other to support this process. All team members must have sufficient PPE with mask, lab coat, goggles and/or FF2 or FFP3 visor. As PPE remains scarce, some may choose to limit PPE use to carriers only. However, in the event of a cardiac arrest, team members will need to leave the cardiac catheter lab to put on PPE prior to exposure to cardiopulmonary resuscitation (CPR) maneuvers.

Negative pressure facilities have been recommended to minimize the spread of the virus, but few have this capability. The alternative is to clean deeply after each box. In the event that multiple STEMI patients arrive at the same time, a risk assessment must be performed and, if delays are unavoidable, thrombolysis must be considered.

In those who have developed cardiogenic shock in the context of COVID-19 infection, futility must be considered. However, as decision-making in acute situations can be challenging, all available supportive therapies must be used when appropriate.

THROMBOLYSIS FOR STEMI

Although ICPP remains the treatment of choice for STEMI, the number of COVID-19 cases in Wuhan and Lombardy has raised sufficient concerns that thrombolysis must be considered in certain circumstances (RASHID et al. 2020; MOUNTANTONAKIS et al. 2020; PONTONE et al. 2020; PONTONE et al. al. 2020).

Under normal circumstances, transfer to ICPP centers is effective and safe. However, during the peak of COVID-19, hospital transfers were affected and, for unwell COVID-19 patients who are actively shedding viruses, are potentially dangerous. In addition, critically ill patients who require noninvasive ventilation are difficult to transfer safely with aerosolized secretions that pose a threat to staff. Intubated patients have closed circuits that reduce the risk of transmission, but these patients remain a challenge to transfer in a timely manner. Patients in intensive care units (ICU) in district generals without acute primary angioplasty services will be at a disadvantage as acute transfer to local ICPP centers will be delayed.

In these situations, thrombolysis must be considered early and administered immediately in the absence of contraindications; the highest value is within 1 hour of the onset of pain. Fibrin-specific agents such as alteplase and tenectaplase can be easily administered; the latter is preferable as a single bolus reduces the need for close nursing contact.

The use of thrombolysis remains controversial with concerns about bleeding risks in the context of possible COVID-19 myocarditis. Furthermore, a quarter of patients will not reperfuse and still require facilitated PCI (ROWLAND et al. 2020). However, despite these concerns, thrombolysis is used for STEMI worldwide and has been used successfully in COVID-19 patients in China (SCHIAVONE et al. 2020). Although PPCI has a clear advantage in reducing the risk of bleeding and increasing the likelihood of reperfusion, the balance of efficacy between thrombolysis and PPCI is closer to balance when PPCI is delayed. The strategic reperfusion study shortly after myocardial infarction (STREAM) demonstrated that even a single hour delay meant that there was no

significant difference in major events after randomized to thrombolysis or PPCI (SINGH et al. 2020).

Patients must be urgently discussed with a senior cardiologist and an interventional cardiologist. Fast communication is essential and may need to be fully remote to facilitate speed. Documentation must reflect why thrombolysis is used and the system constraints that mandate it. Initial decisions must be documented for subsequent treatment for those patients in whom the ST segments do not resolve sufficiently. A cardiac catheter lab must be activated and steps taken for safe transfer. Patients who achieve reperfusion must be considered for invasive angiography at stabilization.

UNIQUE ISSUES RELATED TO ACS IN THE COVID-19 ERA

STEMI

Unwell patients with COVID-19 manifested severe ST elevation, but unobstructed coronary arteries were found on invasive angiography (TAN et al. 2020). The mechanism remains unclear, but is attributed to myocarditis or a Takutsubo-like response to intense inflammation. As the number of COVID-19 cases increased in Wuhan and Lombardy, there was concern that ICPP services would become overwhelmed by similar patients and expose them to the risks of unnecessary invasive procedures (BRAITEH et al. 2020; CAPACCIONE et al. 2021). However, this has been less evident in the UK. Echocardiography can help support the diagnosis of global myocarditis, but coronary angiography is still advocated to prevent the loss of a true coronary occlusion (GUIMARÃES et al. 2020).

DELAYED SERVICE

With the evolution of the pandemic, a global reduction in admissions by ACS was observed (ASHRAF et al. 2020). This is perhaps in response to strong government messages to 'stay at home'. Interestingly, patients avoided hospitals despite significant cardiac symptoms. Patients may fear contracting the virus or wish to avoid overwhelming medical services. Referents in primary or intermediate care settings may misinterpret chest pain as part of COVID-19. Those in smaller district hospitals may not be able to transfer patients to catheter lab centers due to saturation of emergency services (TOUŠEK et al. 2021). Globally, a 20% to 40% reduction in STEMI presentations has been reported; greater reductions in NSTEMI are observed (ROFFI et al. 2020; TAM et al. 2020). Participants experienced significantly longer door-to-balloon times, with longer assessment times in emergency rooms, longer times for staff to prepare PPE, and potentially longer procedure times due to clot burden, disease complexity, or need for respiratory support (ROFFI et al. 2020; CHOR et al. 2020).

Late presentations for STEMI have increased and may have a large thrombotic burden with failure to reperfusion despite PCI (ROFFI et al. 2020). Mechanical complications such as the septal defects and ventricular rupture have been reported. It is expected that the incidence of heart failure may increase due to this late presentation with ACS. National PCI and MI registries in the UK are being used to study the pattern of ACS admissions since the beginning of the pandemic (VECCHIO et al. 2020).

NEW PATHS AND NEW WAYS OF WORKING

Significant changes in work patterns meant that new avenues of care were instituted. Some of them may have value beyond the pandemic. Paths must be modified according to locally available resources.

MINIMIZED PERMANENCE TIME

Prompt treatment and minimization of tests that are unlikely to change short-term clinical decisions must help minimize patient length of stay. This is important to reduce the likelihood that patients will acquire coronavirus infection de novo from other patients. In efficient healthcare systems with early reperfusion, it must be feasible for uncomplicated AMI to be discharged within 24 hours of admission. Immediate review in emergency departments with same-day angiography must be considered when possible. As elective care has been reduced, catheter labs are able to turn around quickly and radial access allows for early discharge. Bedside point-of-care echocardiography can provide LV assessment. A short period of rhythm monitoring is appropriate in low-risk patients with uncomplicated PCI. Tests such as positron emission tomography (PET), myocardial perfusion imaging (MIBI) and magnetic resonance imaging (MRI) are less available in the current pandemic. Unless they are essential for decision making, it is suggested that these tests be postponed to reduce length of stay.

Low-risk patients with low Global Registry of Acute Coronary Events (GRACE) scores and small increases in troponin can be stratified and, if appropriate, early emergency angiography can be considered on an outpatient, outpatient basis. Some Trusts have kept angiographic facilities in 'clean zones', allowing patients to be discharged from emergency departments and semi-electively the next day for the invasive procedure, minimizing hospital stays. Maximum antiplatelet therapy and appropriate counseling are required.

HOSPITALIZATION OF CONTAMINATED PATIENTS

In some cases, hospitalization is unavoidable. Hospitals have developed clearly demarcated 'zones' to reflect the likelihood of viral cross-contamination. Patients with confirmed COVID-19 must be grouped with other carriers of the virus. However, delays in viral diagnosis can apparently mean good, but infected and shedding patients can enter ostensibly "clean" zones.

FINAL CONSIDERATIONS

Patients with ACS may have coronary artery disease that is better revascularized by coronary artery bypass graft surgery. At the beginning of the pandemic, all elective surgeries were canceled to reduce the impact on intensive care facilities. This has evolved to allow for urgent surgery once discussed in a multidisciplinary team (MDT) meeting, but in a limited number of centers. MDT must be performed at baseline and preferably daily to minimize uncertainty and length of stay. In patients with COVID-19, there is concern that surgery poses undue risks and harm. In these cases, PCI must be preferred whenever possible. As the surgical disease can be complex, additional care and attention will be required when performing PCI, taking into account adjuvant technologies.

FUTURE PERSPECTIVES POST-COVID-19

The emergence of a new virus implies decisions that seek to mitigate its pathogenic effects, prevent intense transmissibility and population illness.

The COVID-19 pandemic has generated a rapid setup of services in hospitals, aided by the reduction of bureaucracy. Acute services have been reconfigured to reduce the spread of the coronavirus by segregating acute assessment areas, wards and catheter labs into "clean" and "dirty" zones. Patients are stratified by the probability of infection. Upstream smear and temperature assessment

are essential. Unfortunately, keeping sites strictly clean will be difficult in acute care, particularly for STEMI, and PPE must continue to be used when patients are at risk of infection. Increasingly faster swab protocols can facilitate more selective use.

Elective work, which has been delayed by the pandemic, has been restored using enhanced pre-procedure assessment with comprehensive scanning and patient self-isolation prior to elective procedures. The duration of isolation appears to be variable between hospitals. Biweekly staff cleaning can help identify illness among staff and reduce the chance of service closures or patient infection. Outpatient elective surgery was stratified by urgency and in some places moved to different hospital locations to ensure there is no impact on intensive care services. In the long term, normal clinical services must return to minimize a growing inequality of access to the service.

Outpatient flows have benefited from the adoption of the technology. Clinics go remote to reduce patient viral exposure. Telephone and video clinics are now fully established and, in many cases, can replace traditional clinics. In-person consultations may be reserved for specific patients, but must include appropriate PPE and social distancing to reduce the risk of exposure to cardiology patients who are specifically vulnerable to complications. Post-infarction "virtual" cardiac rehabilitation and heart failure clinics have proven to be feasible.

In the future, it is necessary to work to anticipate the possibility of new 'waves' of the virus. Cardiologists may need new models of work, going beyond work plans and may require shift patterns.

FINAL CONSIDERATIONS

The management of CHWs remains a key priority and services must be adaptively configured to respond to the ever-changing demands of the pandemic. Treatment for ACS is well established, and while an effort must be made to adhere to standard pathways, judicious use of pharmacological and diagnostic adjuvants may allow bypassing these pathways to identify and treat those that are not true ACS and those that are simply ACS. unstable to benefit from standard treatment strategies.

Prompt and early revascularization, with appropriate personal protective equipment, remains the standard treatment approach for patients with acute coronary syndrome in the COVID-19 era. The use of risk stratification tools (such as GRACE scores) can assist in prioritizing cases to minimize their hospital stay. Critically ill patients with ST-elevation myocardial infarction, no catheter lab facilities in place or too unstable for transfer must be considered for thrombolysis and activation of services for facilitated PCI, if needed. Patients with cardiovascular disease are particularly vulnerable during this period, regardless of their infectious status. Adapting cardiac services to ensure continuity of care for these patients, even in the context of a new wave of COVID-19, is essential to minimize preventable cardiovascular death.

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