MEDICATION MANAGEMENT IN AGED CARE WHILE MITIGATING COVID-19

CARDIOVASCULAR DISEASES

People with COVID-19 (coronavirus) and pre-existing vascular disease are at increased risk of severe viral disease and death[1]. In addition, there is emerging information on acute and long-term cardiovascular complications of COVID-19 infection.[2]

Studies have consistently shown that cardiovascular disease is a common underlying condition among COVID-19 patients. It is clear that cardiovascular disease is a potent prognostic factor regardless of COVID-19, and many risk factors for cardiovascular disease also impact on outcomes in COVID-19 (for example older age, hypertension, diabetes).

Many of these cardiovascular disorders have an underlying pro-inflammatory pathophysiology and the activation of the inflammatory processes that occur with COVID-19 infection is likely to impact on outcomes as a result (see **Figure 1**). Hypertension has been shown to exacerbate airway hyperinflammation in patients with COVID-19, resulting in reduced viral clearance.[3]

The excessive immune response that occurs in the presence of COVID-19 infection also results in endothelial dysfunction, platelet activation and hypercoagulability.[4]

In addition to vascular inflammatory issues, it is known that cardiovascular disease increases the risk of pneumococcal disease and pneumonia, and this is also likely to impact on outcomes of COVID-19.

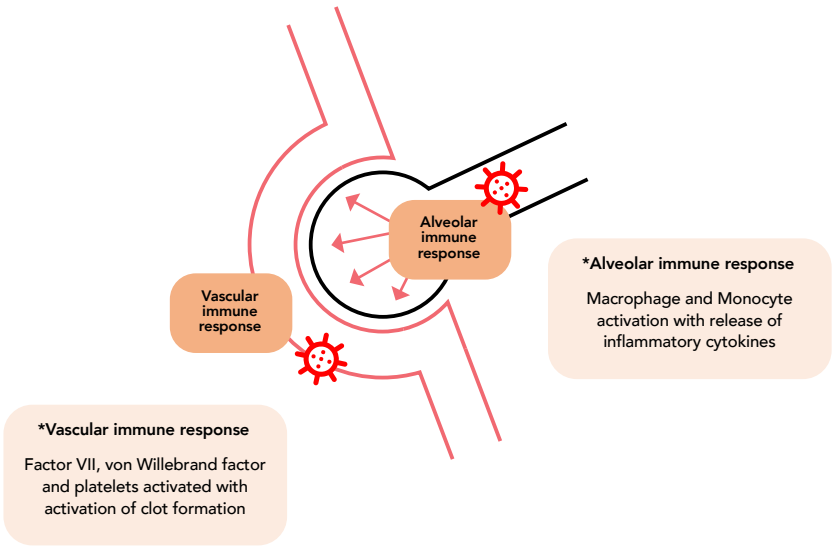

Figure 1: Alveolar and vascular immune responses to COVID-19

KEY POINTS

The underlying pro-inflammatory nature of many cardiovascular conditions predisposes patients to the excessive immune response that occurs in the presence of COVID-19 infection.

The presence of cardiovascular disease (ischaemic heart disease, hypertension or heart failure) is independently associated with a more than twofold increase in mortality from COVID-19.

Despite initial concerns, the use of renin angiotensin system inhibitors has not been shown to influence all-cause mortality in patients with COVID-19.

COVID-19 AND CARDIOVASCULAR DISEASE

A meta-analysis of 16 studies examined the impact of vascular disease and a poor composite outcome (consisting of mortality and severe COVID-19). They found that cardiovascular disease was associated with an increased risk of the outcome with a relative risk of 2.23 (95% CI 1.71-2.91) and that cerebrovascular disease was similarly associated with an odds ratio of 2.04 (95% CI 1.43-2.91). The associations were not influenced by gender, age, hypertension, diabetes, and respiratory co-morbidities, indicating a mechanism independent of these other factors.

A number of studies have reported the impact of COVID-19 on the cardiovascular system. Its impact may vary from cardiac damage (with acute coronary syndrome, arrhythmias, cardiac arrest, myocarditis) to thrombosis (venous thromboembolism, stroke).[5] In addition (or as a consequence), there seem to be long-term cardiovascular complications associated with COVID-19, with an increased incidence of heart failure and abnormal cardiovascular imaging.[2,7,8]

A meta-analysis of 45 studies of patients *hospitalised* with COVID-19 concluded the following with regard to outcomes:[9]

- COVID-19 was associated with a high risk of in-hospital death, which occurred in about 12% of patients
- unsurprisingly, studies with a high percentage of more severe disease and a high percentage of intensive care unit admission reported the highest risk of death during hospitalisation
- age and diabetes were independent predictors of mortality
- after adjustment for age, hypertension did not show any significant association with the risk of in-hospital death.

Optimising the management of cardiovascular disease and its risk factors will likely improve outcomes in the presence of COVID-19 outbreak. Adherence to existing immunisation recommendations for influenza and pneumococcal vaccines is particularly relevant.

ACE inhibitors

Despite initial concerns, the use of renin angiotensin system inhibitors has not been shown to influence all-cause mortality in patients with COVID-19.[10,11] Indeed, there is some evidence that treatment with renin angiotensin system blockers can reduce the severity of COVID-19 and increase viral clearance.Several randomised control trials are ongoing to compare the use of angiotensin-converting enzyme inhibitors versus an angiotensin receptor blocker in patients with hypertension and COVID-19.

In a recent meta-analysis examining the effect of ACE inhibitor (ACEI) treatment on the incidence of pneumonia in non-COVID-19 patients (25 studies, 330,780 patients), ACEIs were associated with a 26% *reduction* in pneumonia risk (odds ratio [OR]=0.74, P=< .001).[12] Results from 11 of these studies (8.4 million patients) showed that the risk of getting infected with the SARS-CoV-2 virus was reduced by 13% (OR=0.87, P=.014) in patients treated with an ACEI, whereas analysis from 10 studies (8.4 million patients) treated with ARBs showed no effect (OR=0.92, P=.354). Results from 34 studies in 67,644 COVID-19 patients showed that RAAS blockade reduces all-cause mortality by 24% (OR=0.76, P=.04).[12]

Given these data and the well-established beneficial effects of renin angiotensin system inhibitors (ACEIs and ARBs), Australian guidelines strongly recommend that these medications be continued.[1]

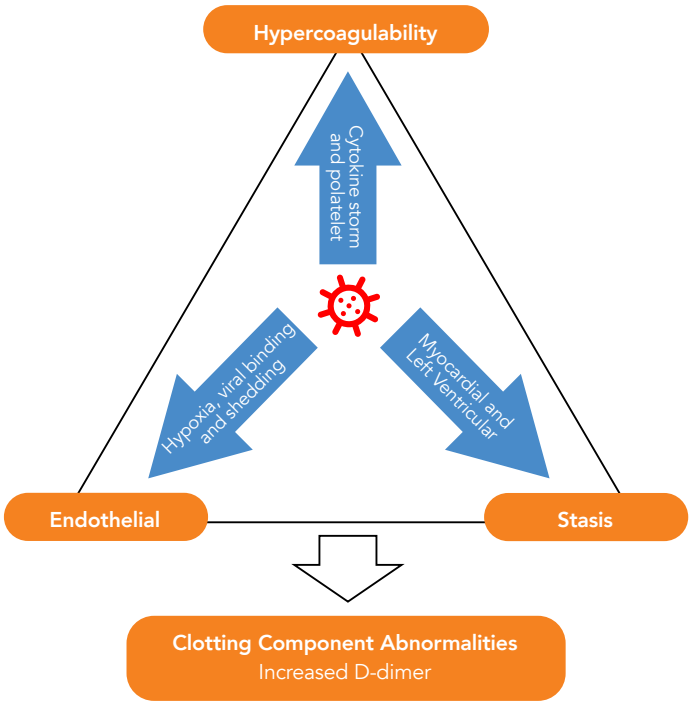

Figure 2: COVID-19 and abnormalities of coagulation components

Thromboembolic complications of COVID-19

Pulmonary embolism is a frequent complication of COVID-19, with the risk of pulmonary embolus among COVID-19 patients admitted to ICU being twofold compared to patients hospitalised to ICU for other causes.[2] The increased risk of thrombotic events has been attributed to activation of inflammatory cytokine storm as outlined above and described in **Figure 2**.[13] Biomarkers identifying thrombophilia such as elevated D-dimer and thrombocytopenia have been implicated as important prognostic markers.[4]

Current Australian guidelines for management of patients with moderate to severe COVID-19 include a recommendation for prophylactic anticoagulation with low molecular weight heparin unless contraindications exist.[14] There is no clear guidance on the current use of antiplatelet agents or anticoagulants for patients already using them for other indications (e.g. atrial fibrillation). In this setting, given the hypercoagulable state induced by COVID-19 would combine with any underlying vascular coagulopathy, the general recommendation would be to continue treatment as per normal clinical judgement.

MANAGING CARDIOVASCULAR DISEASE WHILE MITIGATING COVID-19

Minimise shortness of breath due to heart failure

Any pathophysiology that impacts on efficiency of oxygen transfer will have an adverse impact on patients with COVID-19. Optimising management of pulmonary oedema associated with heart failure is likely to improve outcomes compared to patients who remain short of breath.

Maintain adequate blood pressure control

Excessively high blood pressure can predispose to a range of cardiovascular morbidities and given the impact of severe hypertension on endothelial function, maintaining an adequate blood pressure remains an appropriate treatment goal.

In aged care, maintaining adequate blood pressure should take into account the risk of postural hypotension contributed to by antihypertensive and other agents. In addition, excessively low blood pressure can predispose to poor outcomes in older patients suffering from infections (including COVID-19).

Continue ACEIs and ARBs

Angiotensin modifying agents have been investigated for their possible impact on COVID-19 entry to cells and studies do not support cessation of these agents. Indeed, given these agents are commonly- used in the management of symptomatic heart failure and hypertension, their ongoing critical role in controlling these conditions is likely to improve outcomes for patients with COVID-19.

Continue antiplatelet agents or anticoagulants

There is evidence that COVID-19 causes a hypercoagulable state and current treatment guides suggest anticoagulation in moderate to severe infection.[14] Ensuring pre-existing conditions that require antiplatelet or anticoagulant therapy are adequately treated will likely reduce the likelihood of a thrombotic or embolic event. There is no evidence for pre-emptive treatment with antiplatelet agent or anticoagulants.

Minimising the number of invasive blood tests (and physical contacts in the event of a COVID-19 outbreak) by changing from warfarin to a direct-acting oral anticoagulant in appropriate patients would be reasonable.

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