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## Collision of COVID-19 pandemic with cardiovascular risk in chronic kidney disease patients; a heavy “triple peine”

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Patients with chronic kidney diseases exhibit a very high cardiovascular risk. The COVID-19 outbreak has worsened this risk by the addition of a new cardiac pathology and the exacerbation of pre-existing cardiovascular diseases in patients with chronic impairment of kidney function.

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Please do not remove my echocardiography control from your activity schedule” announced a diabetic and chronic kidney disease (CKD) patient with recently diagnosed coronary artery disease in an email sent to hospital management. This anxious thought highlights how some routine clinical services such as laboratory resources, control echocardiography and cardiac rehabilitation could be simply postponed during time of crisis such as the current COVID-19 outbreak.

In this paper, we will describe how CKD patients suffer from a kind of three medical charges “triple peine in French” related to; first, the heavy burden of cardiovascular risk well-known in such condition, second, CKD is one of some underlying health conditions and risk factors, cited in a recent CDC report, that might expose patients to higher risk for severe disease or death from COVID-19 and third, the lack of appropriate medical facilities while the only emergency for the health policy makers is facing the COVID-19 pandemic.

### Patients with CKD struggle with very high cardiovascular risk

CKD is defined as impaired kidney function assessed by the reduction of estimated glomerular filtration rate (eGFR  $\leq 60$  mL/min/1.73 m<sup>2</sup>) or kidney damage (especially raised urinary albumin-to-creatinine ratio  $\geq 30$  mg/g) present for three months with implications for health (1). In 2017,

the global prevalence of CKD was 9.1% (700 million cases) and increased by 29.3 % during the period 1990-2017 (2). Such alarming epidemiological pattern has a huge impact on mortality from CKD (global increase by 41.5% during the same period) and up to half of advanced CKD patients are reported to die of cardiovascular diseases (CVDs) (3). As the burden of CVDs is well known to be very high among CKD patients, the cardiovascular risk prediction in such condition became a key step and several reports showed that the transition from CKD to end-stage renal disease (ESRD) is a critical period where the risk of death from CVDs is even greater than the risk of progression to ESRD (3,4). Impaired renal function, even when adjusted for traditional cardiovascular risk factors continue to increase the cardiovascular (CV) risk by two to three times (5). European Society of Cardiology (ESC) guidelines for cardiovascular risk prediction, published in 2016, has included eGFR less than 30 mL/min/1.73 m<sup>2</sup> and albuminuria as very high risk (10% risk or more for 10-years CV mortality) and eGFR 30 to 59 mL/min/1.73 m<sup>2</sup> as high risk (5% to 10% risk for 10-years CV mortality) (5). Among CVDs, some specific ones deserve a closer relationship with CKD. A meta-analysis from the CKD prognosis consortium (CKD-PC) explored four items (CV mortality, heart failure, coronary heart disease and stroke) as CV outcomes of interest. Both eGFR and albuminuria were associated independently with all four

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CV outcomes with more evidence for the outcomes of CV mortality and heart failure (5).

### COVID 19 is also a new cardiac pathology

On March 11, 2020, the World Health Organization (WHO) declared COVID-19, a pandemic that represents a threat to global health (6). COVID-19 is dominated by respiratory symptoms, nevertheless severe CV damages have been widely described (7). Although the fact that several reports regarding clinical features of COVID-19 did not describe clearly comorbid CVDs, such conditions have been reported to be the most common noncommunicable epidemic that COVID-19 runs into (8). A recent Center for Disease Control (CDC) report has shown that, among U.S COVID-19 cases, some underlying health conditions represent a potential risk factor. CVDs, hypertension and CKD are found to be associated with poor outcomes (9).

CVDs and acute pulmonary infection deserve closer scrutiny. As the previous viral infections such as influenza epidemic, COVID 19 can trigger acute coronary syndrome, arrhythmia, and exacerbation of heart failure. In turn, deterioration of CVDs could lead to complicated COVID-19 management (10).

COVID 19 is responsible of both new cardiac disease and (or) exacerbation of underlying CVDs (10). The first effect remains unknown and is probably related to several mechanisms including direct myocardial cells damage by the virus, systemic inflammatory responses leading to cytokine storm, and hypoxia (10,11). Myocardial injury as demonstrated by elevation of myocardial biomarkers such as troponin T (TnT) is strongly associated with deterioration of clinical courses and death (10,11). Guo et al (11) reported that TnT levels which is a sign of myocardial injury is strongly associated with C-reactive protein (CRP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) that are respectively biomarkers of inflammation and ventricular dysfunction (11). Their data also show that CKD and/or some of their causal conditions such as hypertension and diabetes are well recognized as a serious risk factor. Furthermore, acute kidney injury (AKI) complicating the COVID-19 courses through pyrexia, diarrhea or poor fluid intake could lead to worsening of both renal and cardiac function through additional elevation of serum creatinine and TnT (11).

### Delayed access or provision of care resulting from COVID-19 and fear of COVID-19

During the COVID-19 pandemic, nephrology units could be put under disproportionate pressures related to staff shortage and hospital capacity reduction (12). Some in and out-patient non-urgent activity could be simply canceled (12). Several guidelines provided the plans for both strengthening the health system response

to COVID-19 and quality care provision for patients with chronic conditions. However, the pandemic is expected to be prolonged with a real risk of equipment shortage and supply chain deficiencies (12,13). Moreover, previous reports have shown that patients' behavior was significantly influenced by the fears of severe acute respiratory syndrome (SARS) and that this fear seriously compromised their accessibility to quality care (14,15). Hence, patients with CKD are at a real risk of worsening renal function and life-threatening evolution if the delay in access care is not monitored.

### Conclusion

COVID-19 has been declared a global pandemic and public health crisis. Patients with CKD are at a very higher CV risk and are reported to have the highest number of comorbidities. CKD is well recognized as a risk factor of poor outcomes during the COVID-19 courses, in turn, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) represents a new cardiac pathology and additional CV risk for patients with CKD. This unprecedented situation is challenging for health systems and health-care providers are required to maintain continuity of essential services including renal units care. The main actions would be the protection of in- and out-patients with chronic conditions, the prevention of delays in accessing hospital care, the provision of high-quality care, and the switch to online/digital platforms for primary care and non-urgent activities.

### Authors' contribution

MA and OM prepared the manuscript. MB and NZ critically revised the manuscript.

### Conflicts of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### Ethical considerations

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