Editorial: The impact of COVID-19 on cardiovascular health

Professor Ian D Jones

Professor of Cardiovascular Nursing

Liverpool Centre for Cardiovascular Science,

School of Nursing and Allied Health,

Liverpool John Moores University,

Tithebarn Building,

Tithebarn St Liverpool L2 2ER

ORCID: 0000-0002-3081-0069

Introduction

When the editors asked me to produce an editorial that focussed on the current cardiac related issues in intensive care nursing, I pondered for some time about the content of the paper and how I might move the debate beyond Coronavirus Disease 2019 (Covid-19). Unfortunately, whilst many, if not most of the critical care workforce is physically, psychologically, and emotionally tired of the effects of the pandemic, viral mutation, an unwillingness, or inability for some to receive the vaccines mean that we are likely to see Covid-19 patients in critical care units for some time. Moreover, the number of people attending hospital with acute coronary syndrome[1-5] heart failure,[6] arrhythmia[7] and those requiring emergency cardiac surgery[8] dramatically reduced during the pandemic. Consequently, it is likely that some of these patients will suffer the long-term effects of missed treatment and require critical care nursing at some point in the future. It therefore still seems appropriate to consider the cardiac ramifications of Covid-19 and its implications for the critical care nurse.

Covid-19

Covid-19 is caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (Sars-CoV-2) first identified in Wuhan, China in 2019. Sars-CoV-2 is unlike the coronavirus' that cause the common cold but similar to the Zoonotic SARS Coronavirus' that transfers from animals to humans including the Severe Acute Respiratory Syndrome (SARS) Coronavirus reported in 2002[9] and the Middle Eastern Respiratory Coronavirus Syndrome (MERS) reported in 2012[10]. Like SARS and MERS, Sars-COv-2 is

believed to have originated in bats and was transmitted to humans via an intermediate host thought in this case to be a pangolin[11].

Sars-Cov-2 enters the cell by binding to Angiotensin Converting Enzyme 2 (ACE2) receptors[12,13] in the heart, vascular endothelium, intestinal epithelium, kidneys and in the lungs[14]. Whilst much of the early research understandably focussed on the respiratory impact of the infection, the systemic effects are now more clearly understood.

Cardiovascular disease as a risk factor

Cardiovascular Disease (CVD) is both a predictor of increased mortality and can occur as a consequence of contracting Covid-19. Figliozzi and colleagues[15] reported in their meta-analysis, a threefold increased composite risk of death and worsened Covid-19 outcome for those with a previous CVD history. These poor outcomes are likely to be related to a combination of pathology and underlying CVD risk factors including diabetes[16], hypertension[17-19] and obesity[20] which have been found to negatively impact clinical outcome. Whilst much has been written about the risk of thrombo-embolic events associated with Covid-19, less focus appears to have been placed on additional cardiovascular complications, which are discussed in this editorial.

Acute myocardial injury

Acute myocardial injury, evidenced by raised Troponin levels, is believed to occur in 9-40%[21] of hospitalised patients and has been shown to be a negative prognostic indicator[22-24], including increased admission to intensive care and death[25,26]. The mechanism in which SARS-Cov-2 induces myocardial injury is unclear but may include the alteration of the ACE2 signalling pathways[27,28], the effect of a cytokine storm associated with systemic inflammation[22.23] and/or additional myocardial workload resulting from respiratory failure and hypoxia. Irrespective of the underlying pathology, myocardial injury leads to increased risk of cardiovascular complications, including, myocarditis, arrythmia, heart failure and acute coronary syndrome[29].

Myocarditis

Early case reports suggested that myocarditis was a common complication of Covid-19[30,31]. These results were unsurprising given that in one Canadian study 35% of patients who died during the 2002 SARS outbreak were found to have evidence of the virus within their hearts[32]. However, the Task Force for the management of Covid-19 of the European Society of Cardiology[29] have suggested that a

definitive diagnosis of myocarditis can only be made following examination of endomyocardial biopsies and, as such, the evidence that myocarditis is a common complication of Covid-19 is yet to be convincingly demonstrated.

Arrhythmia

Tachy and brady arrhythmias are common in patients with Covid-19. One study from China[33] reported 16.7% of hospitalised patients experienced arrhythmias, which increased to 44% in those requiring intensive care management. However, the authors failed to report the type of arrhythmia. More recent studies[34,35] have reported arrhythmia prevalence of between 7- 25% with atrial fibrillation accounting for 5-15% of all reported arrhythmia. Both papers report a correlation between arrhythmia and disease severity with Peltzer and colleagues[34] also reporting a correlation between arrhythmia and 30-day mortality. Whilst arrythmia prevalence is not uncommon in hospitalised Covid-19 patients, this frequency increases in those requiring intensive care. In one observational study of 113 intensive care patients in Germany[36,] the authors report that 44.2% of patients experienced sustained atrial arrhythmia, the most common of which (35%) was atrial fibrillation. Sustained ventricular tachycardia, ventricular fibrillation or Torsade's de Pointes were observed in 4 patients (3.5%), whilst ten patients (8.9%) experienced second or third-degree AV block. A second cohort study[37] including 155 patients from seven intensive care units in Denmark found that 57 patients (37%) experienced an arrhythmia with 55 (33%) of these patients experiencing atrial fibrillation/flutter. Arrhythmia appeared to increase 30-day mortality (39% v 61%). However, this finding was not statistically significant, possibly due to the small sample size. Management of arrhythmia, especially those incorrectly perceived as benign, may not be prioritised in a critically ill patient but the short-term physiological impact on cardiac output and the longer-term risk, for example stroke in AF should not be underestimated. Cardiac arrhythmias are a red flag and should be treated immediately in line with the relevant European Society of Cardiology Guidelines.

Heart failure

Heart failure related admissions reduced significantly during the height of the Covid-19 pandemic in 2020[38] with patients presenting with more advanced signs of decompensation[39] and an increased level of Brain Naturetic Peptide (BNP) both of which are associated with higher mortality[40]. Some have speculated that patients may have delayed seeking help for fear of contracting Covid-19; however, in our recent work[41], we found that patients with cardiovascular disease delayed seeking help during the pandemic as they were often unable to interpret their symptoms. When faced with public health messaging which suggested that people should only attend hospital if the situation was life threatening, they chose to stay at home.

The prevalence of chronic heart failure (CHF) as a comorbid condition in the Covid-19 population has been reported as 3-21%[42,43] with CHF associated with an increased risk of mortality[44,45] and need for mechanical ventilation[46]. In addition to those that present with CHF, between 2-23% of patients will develop acute heart failure because of the infection. The large variation in prevalence between studies is probably related to the diverse methods of data collection rather than variations in populations. For example, Zhou et al[47] report prevalence of heart failure as an outcome but do not record the number of patients with chronic heart failure on admission. It is therefore feasible that some of the 23% of patients reported as suffering from heart failure in this study were suffering from chronic heart failure and that increased metabolic demand exposed subclinical heart failure. It is clear from the combined data that up to one-fifth of Covid-19 patients will experience heart failure during their illness and the presence of heart failure increases a patient's need for critical care management. Whilst the most severe cases will require mechanical ventilation and system support to maintain organ perfusion, it is essential that fundamental heart failure treatment is included in their management plan. Whilst during the early days of the pandemic there was a belief that ACE inhibitors might lead to up regulation of the ACE2 receptors, therefore increasing risk, there is no evidence that this occurs, and ACE inhibitors along with other evidence-based therapies should form part of routine heart failure management as per European Society of Cardiology [48].

Acute Coronary Syndrome

Reductions in hospital attendance for acute coronary syndrome during social containment mandates, during 2020[1-5] may result in an increasing number of patients presenting with undiagnosed heart failure. Moreover, increased myocardial workload with subsequent oxygen supply and demand imbalance, in combination with atherosclerotic plaque destabilisation may increase a person's risk of suffering an acute coronary syndrome (ACS)[49] and whilst ensuring the use of personal protective equipment to protect staff from possible infection, patient management should not vary from current guidelines, which are designed to restore coronary blood flow as soon as possible.

Congenital heart disease

Adults with congenital heart disease (CHD) are assumed to be at greater risk from Covid-19 due to residual haemodynamic lesions such as valve disorders, reduced left ventricular function and arrhythmia[50]. However, recent evidence obtained from 58 CHD centres including 1044 Covid-19 positive patients suggests that CHD mortality rates are no greater than the wider population[51].

Nevertheless, it might be unwise to treat those with congenital heart disease as a homogenous group with evidence that those with worse physiological state, such as cyanosis and pulmonary hypertension, renal insufficiency, and previous heart failure, are at greater risk[51]. The latest European guidelines[47] suggest early admission to hospital and an intensive care management plan to be discussed with a CHD specialist in all those except the lowest risk.

Conclusion

Patients with cardiovascular disease are at greater risk of dying of Covid-19 and are more likely to require intensive care nursing. Critically ill patients with Covid-19 often suffer cardiovascular complications that require immediate and ongoing management. As the incidence of Covid-19 increases once more, it is essential that nurses recognise the influence of co-morbid heart disease on clinical outcome so that we can prevent or manage their potential complications and reduce subsequent morbidity and mortality.

1 Mafham MM, Spata E, Goldacre R, et al. COVID-19 pandemic and admission rates for and management of acute coronary syndromes in England. Lancet. 2020;396 (10248):381–389.

2 Metzler B, Siostrzonek P, Binder RK, Bauer A, Reinstadler SJ. Decline of acute coronary syndrome admissions in Austria since the outbreak of COVID-19: the pandemic response causes cardiac collateral damage. Eur Heart J. 2020;41(19):1852–1853.

3 Rodríguez-Leor O, Cid-_Alvarez B, Ojeda S, et al. Impacto de la pandemia de COVID-19 sobre la actividad asistencial en cardiología intervencionista en Espa~na. REC Interv Cardiol. 2020;2(2):82–89.

4 Solomon MD, McNulty EJ, Rana JS, et al. The COVID-19 pandemic and the incidence of acute myocardial infarction. New Engl J Med. 2020.

5 Tam CCF, Cheung KS, Lam S, et al. Impact of coronavirus disease 2019 (COVID-19) outbreak on ST-segment_elevation myocardial infarction care in Hong Kong, China. Circ Cardiovas Qual Outcomes. 2020;13:(4) e006631.

6 Cox ZL, Lai P, Lindenfeld J. Decreases in acute heart failure hospitalizations during COVID-19. Eur J Heart Fail. 2020.

7 Bollmann A, Hohenstein S, Meier-Hellmann A, Kuhlen R, Hindricks G. On behalf of Helios hospitals G. emergency hospital admissions and interventional treatments for heart failure and cardiac arrhythmias in Germany during the COVID-19 outbreak: insights from the German-wide Helios hospital network. Eur Heart J Qual Care Clin Outcomes. 2020;6(3):221–222.

8 Casey L, Khan N, Healy DG. The impact of the COVID-19 pandemic on cardiac surgery and transplant services in Ireland's national centre. Irish J Med Sci. 2020.(1971 -).

9 Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. Lancet Infect Dis. 2020 May;20(5):533-534. doi: 10.1016/S1473-3099(20)30120-1. Epub 2020 Feb 19. Erratum in: Lancet Infect Dis. 2020 Sep;20(9):e215. PMID: 32087114; PMCID: PMC7159018.

10 Chan, J. W., Ng, C. K., Chan, Y. H., Mok, T. Y., Lee, S., Chu, S. Y., Law, W. L., Lee, M. P., & Li, P. C. (2003). Short term outcome and risk factors for adverse clinical outcomes in adults with severe acute respiratory syndrome (SARS). *Thorax*, *58*(8), 686–689. https://doi.org/10.1136/thorax.58.8.686

11 Zhang T, Wu Q, Zhang Z. Probable Pangolin Origin of SARS-CoV-2 Associated with the COVID-19 Outbreak. Curr Biol. 2020 Apr 6;30(7):1346-1351.e2. doi: 10.1016/j.cub.2020.03.022.

12 Walls AC, Park YJ, Tortorici MA, Wall A, McGuire AT, Veesler D. Structure, function, and antigenicity of the SARS-CoV-2 spike glycoprotein. Cell 2020;181: 281–292.e286.

13 Yan R, Zhang Y, Li Y, Xia L, Guo Y, Zhou Q. Structural basis for the recognition of SARS-CoV-2 by full-length human ACE2. Science 2020;367:1444–1448.

14 Tikellis C, Thomas MC. Angiotensin-Converting Enzyme 2 (ACE2) Is a Key Modulator of the Renin Angiotensin System in Health and Disease. Int J Pept. 2012;2012:256294. doi: 10.1155/2012/256294

15 Figliozzi S, Masci PG, Ahmadi N et al. Predictors of adverse prognosis in COVID-19: a systematic review and meta-analysis. Eur J Clin Invest 2020;50: e13362.

16 Barron E, Bakhai C, Kar P et al. Associations of type 1 and type 2 diabetes with COVID-19-related mortality in England: a whole-population study. Lancet Diabetes Endocrinol 2020;8:813–822.

17 Del Sole F, Farcomeni A, Loffredo L et al. Features of severe COVID-19: a systematic review and meta-analysis. Eur J Clin Invest 2020;50:e13378.

18. Figliozzi S, Masci PG, Ahmadi N et al. Predictors of adverse prognosis in COVID-19: a systematic review and meta-analysis. Eur J Clin Invest 2020;50: e13362.

19 . Ssentongo P, Ssentongo AE, Heilbrunn ES, Ba DM, Chinchilli VM. Association of cardiovascular disease and 10 other pre-existing comorbidities with COVID-19 mortality: a systematic review and meta-analysis. PLoS One 2020; 15:e0238215.

20 Popkin BM, Du S, Green WD et al. Individuals with obesity and COVID-19: a global perspective on the epidemiology and biological relationships. Obes Rev 2020;21:e13128.

21 Sandoval Y, Januzzi JL Jr, Jaffe AS. Cardiac Troponin for Assessment of Myocardial Injury in COVID-19: JACC Review Topic of the Week. J Am Coll Cardiol. 2020 Sep 8;76(10):1244-1258. doi: 10.1016/j.jacc.2020.06.068.

22 Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study.
Lancet 2020.

23 Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497e506.

24 Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. J Am Med
Assoc 2020.

25 Lala A, Johnson KW, Januzzi JL; et al. Mount Sinai Covid Informatics Center. Prevalence and impact of myocardial injury in patients hospitalized with COVID-19 infection. J Am Coll Cardiol 2020;76:533–546.

26 Shi S, Qin M, Shen B et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. JAMA Cardiol 2020;5:
802–810.

27 Xiong TY, Redwood S, Prendergast B, Chen M. Coronaviruses and the cardiovascular system: acute and long-term implications. Eur Heart J 2020.

28 Li B, Yang J, Zhao F, et al. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. Clin Res Cardiol 2020.

29 The Task Force for the management of COVID-19 of the European Society of Cardiology, European Society of Cardiology guidance for the diagnosis and management of cardiovascular disease during the COVID-19 pandemic: part 1—epidemiology, pathophysiology, and diagnosis, *European Heart Journal*, 2021;, ehab696, https://doi.org/10.1093/eurheartj/ehab696

30 Fried JA, Ramasubbu K, Bhatt R The variety of cardiovascular presentations of COVID-19. Circulation 2020;141:1930–1936.

31 Inciardi RM, Lupi L, Zaccone G et al. Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). JAMA Cardiol 2020;5:819–824.

32 Oudit GY, Kassiri Z, Jiang C, et al. SARS-coronavirus modulation of myocardial ACE2 expression and inflammation in patients with SARS. Eur J Clin Invest 2009;39:618e25.

33 Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. J Am Med Assoc 2020

34 Peltzer B, Manocha KK, Ying X et al. Arrhythmic complications of patients hospitalized with COVID-19: incidence, risk factors, and outcomes. Circ Arrhythm Electrophysiol 2020;13:e009121.

35 Rav-Acha M, Orlev A, Itzhaki I, Zimmerman SF, Fteiha B, Bohm D, Kurd R, Samuel TY, Asher E, Helviz Y, Glikson M, Michowitz Y. Cardiac arrhythmias amongst hospitalised Coronavirus 2019 (COVID-19) patients: Prevalence, characterisation, and clinical algorithm to classify arrhythmic risk. Int J Clin Pract. 2021 Apr;75(4):e13788. doi: 10.1111/ijcp.13788. Epub 2021 Feb 8. PMID: 33128270.

36 Parwani, A. S., Haug, M., Keller, T., Guthof, T., Blaschke, F., Tscholl, V., Biewener, S., Kamieniarz, P., Zieckler, D., Kruse, J., Angermair, S., Treskatsch, S., Müller-Redetzky, H., Pieske, B., Stangl, K., Landmesser, U., Boldt, L. H., Huemer, M., & Attanasio, P. (2021). Cardiac arrhythmias in patients with COVID-19: Lessons from 2300 telemetric monitoring days on the intensive care unit. *Journal of electrocardiology*, *66*, 102–107. https://doi.org/10.1016/j.jelectrocard.2021.04.001

37 Wetterslev, M., Jacobsen, P. K., Hassager, C., Jøns, C., Risum, N., Pehrson, S., Bastiansen, A., Andreasen, A. S., Tjelle Kristiansen, K., Bestle, M. H., Mohr, T., Møller-Sørensen, H., & Perner, A. (2021). Cardiac arrhythmias in critically ill patients with coronavirus disease 2019: A retrospective population-based cohort study. *Acta anaesthesiologica Scandinavica*, *65*(6), 770–777. https://doi.org/10.1111/aas.13806

38 Bromage DI, Cannatà A, Rind IA, Gregorio C, Piper S, Shah AM, et al. The impact of COVID-19 on heart failure hospitalization and management: report froma Heart Failure Unit in London during the peak of the pandemic. Eur J Heart Fail. (2020) 22:978–84. doi: 10.1002/ejhf.1925

39 Bhatla A, Mayer MM, Adusumalli S et al. COVID-19 and cardiac arrhythmias. Heart Rhythm 2020;17:1439–1444.

40. Shoar S, Hosseini F, Naderan M, Mehta JL. Meta-analysis of cardiovascular events and related biomarkers comparing survivors versus non-survivors in patients with COVID-19. Am J Cardiol 2020;135:50–61.

41 S Burton, J Hayes, N Scott-Morell, J Sanders, H Walthall, J Wright, I Jones, Should I stay or should I go? An exploration of the decision-making behaviour of acute cardiac patients during the Covid-19 pandemic, *European Journal of Cardiovascular Nursing*, Volume 20, Issue Supplement_1, July 2021, zvab060.144, https://doi.org/10.1093/eurjcn/zvab060.144

42 Shi S, Qin M, Shen B, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. JAMA Cardiol 2020;1–8.

43 Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;6736:1–9.

44 Chen T, Wu D, Chen H et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ. 2020; 368. https://doi.org/10.1136/bmj.m1091

45 Dan S, Pant M, Upadhyay SK. The case fatality rate in COVID-19 patients with cardiovascular disease: global health challenge and paradigm in the current pandemic. Curr Pharmacol Rep. 2020; Sep 15:1–10. https://doi.org/10.1007/s40495-020-00239-0

46 Alvarez-Garcia J, Lee S, Gupta A, Cagliostro M, Joshi AA, Rivas-Lasarte M, et al. Prognostic impact of prior heart failure in patients hospitalized with COVID-19. J Am Coll Cardiol. (2020) 76:2334–48. doi: 10.1016/j.jacc.2020.09.549

47 Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L, Wei Y, Li H, Wu X, Xu J, Tu S, Zhang Y, Chen H, Cao B. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020 Mar 28;395(10229):1054-1062. doi: 10.1016/S0140-6736(20)30566-3. Epub 2020 Mar 11. Erratum in: Lancet. 2020 Mar 28;395(10229):1038. Erratum in: Lancet. 2020 Mar 28;395(10229):1038. PMID: 32171076; PMCID: PMC7270627.

48 McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, Burri H, Butler J, Čelutkienė J, Chioncel O, Cleland JGF, Coats AJS, Crespo-Leiro MG, Farmakis D, Gilard M, Heymans S, Hoes AW, Jaarsma T, Jankowska EA, Lainscak M, Lam CSP, Lyon AR, McMurray JJV, Mebazaa A, Mindham R, Muneretto C, Francesco Piepoli M, Price S, Rosano GMC, Ruschitzka F, Kathrine Skibelund A; ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021 Sep 21;42(36):3599-3726. doi: 10.1093/eurheartj/ehab368. Erratum in: Eur Heart J. 2021 Oct 14;: PMID: 34447992.

49 Giustino G, Pinney SP, Lala A et al. Coronavirus and cardiovascular disease, myocardial injury, and arrhythmia: JACC focus seminar. J Am Coll Cardiol 2020; 76:2011–2023.

50 Diller GP, Gatzoulis MA, Broberg CS, Aboulhosn J, Brida M, Schwerzmann M, Chessa M, Kovacs AH, Roos-Hesselink J. Coronavirus disease 2019 in adults with congenital heart disease: a position paper from the ESC working group of adult congenital heart disease, and the International Society for Adult Congenital Heart Disease. Eur Heart J. 2021 May 14;42(19):1858-1865. doi: 10.1093/eurheartj/ehaa960. PMID: 33313664; PMCID: PMC7799120.

51 Broberg CS, Kovacs AH, Sadeghi S, Rosenbaum MS, Lewis MJ, Carazo MR, Rodriguez FH 3rd, Halpern DG, Feinberg J, Galilea FA, Baraona F, Cedars AM, Ko JM, Porayette P, Maldonado J, Sarubbi B, Fusco F, Frogoudaki AA, Nir A, Chaudhry A, John AS, Karbassi A, Hoskoppal AK, Frischhertz BP, Hendrickson

B, Bouma BJ, Rodriguez-Monserrate CP, Broda CR, Tobler D, Gregg D, Martinez-Quintana E, Yeung E, Krieger EV, Ruperti-Repilado FJ, Giannakoulas G, Lui GK, Ephrem G, Singh HS, Almeneisi HM, Bartlett HL, Lindsay I, Grewal J, Nicolarsen J, Araujo JJ, Cramer JW, Bouchardy J, Al Najashi K, Ryan K, Alshawabkeh L, Andrade L, Ladouceur M, Schwerzmann M, Greutmann M, Meras P, Ferrero P, Dehghani P, Tung PP, Garcia-Orta R, Tompkins RO, Gendi SM, Cohen S, Klewer S, Hascoet S, Mohammadzadeh S, Upadhyay S, Fisher SD, Cook S, Cotts TB, Aboulhosn JA. COVID-19 in Adults With Congenital Heart Disease. J Am Coll Cardiol. 2021 Apr 6;77(13):1644-1655. doi: 10.1016/j.jacc.2021.02.023. PMID: 33795039; PMCID: PMC8006800.