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Global Spotlights

COVID-19 and the heart: insights from the National Societies of Cardiology Journals

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The outbreak of COVID-19 has generated an enormous publication activity from both international-oriented journals and National Societies of Cardiology Journals (NSCJ). The later provided many national- or regional-specific features of the pandemic spread.

In a bibliometric analysis of publications of COVID-19 and their scientific impact during the first 3 months of the pandemic, Dieguez-Campa *et al.* from Mexico identified 2530 publications on COVID-19 recorded from PubMed/MEDLINE. They were written by authors from 67 countries (China 39%, USA 16.7%), and they subsequently generated 59 104 citations. While taking into account all 67 countries of origin, the authors showed a correlation between the number of publications per country, and the numbers of confirmed cases of COVID-19 and deaths related to the disease.[1] Böhm *et al.* attributed the increase in submission rate to *Clinical Research in Cardiology* during the shutdown to travel restrictions, cancellation of medical congresses, reduction of clinical and scientific meetings, and advisory boards. Of note, a shorter review time and a shorter time to acceptance or rejection were observed concomitantly.[2]

The containment policy and related shutdown directly impacted cardiovascular practice. In a multicenter study from France, Huet *et al.* showed that before containment, the nine participating intensive cardiac care units (ICCUs) admitted 4.8 ± 1.6 patients per day for acute myocardial infarction (AMI) or heart failure (HF) vs. 2.6 ± 1.5 only during containment.[3]

In a Spanish nationwide registry (75 ICCUs) of patients with ST-segment elevation myocardial infarction (STEMI), Rodriguez-Leor *et al.* showed that suspected and confirmed patients with STEMI decreased by 27% during the COVID-19. There was no difference in time from first medical contact to reperfusion nor in reperfusion strategies, with 94% primary percutaneous coronary interventions (PCI). However, in-hospital mortality was higher during COVID-19 (7.5% vs. 5.1%). Among patients treated during the COVID, the incidence of confirmed SARS-CoV2 infection was only 6.3%.[4] These changes significantly impacted interventional cardiology procedures with a reduction in diagnosis procedures (−56%), PCI (−48%), structural interventions (−81%), and primary PCI for STEMI.[5]

In a meta-analysis of cardiovascular complications of COVID-19 published by Momtazmanesh *et al.* in the *Egyptian Heart Journal*, acute cardiac injury occurred in 25% of the 10 898 patients included from 35 studies. Admission to intensive care units of patients with cardiac involvement was 13.5-fold and mortality was 20-fold higher as compared with patients without cardiac manifestations.[6]

Arrhythmias accounted for 11.7% of 692 patients admitted to 35 hospitals with COVID-19 according to the Portuguese Association of Arrhythmias. Older patients were the most exposed (median age 73.5 years) as well as patients with hypertension (64%). Observed arrhythmias included paroxysmal supraventricular tachycardia (26.6%), atrial fibrillation (AF, 62.5%), sinus bradycardia (7.8%), and ventricular tachycardia (3.1%). An arrhythmia or a prolongation of QT interval was observed in 10.8% of 53 patients to whom any experimental drug regimen against SARS-CoV2 was administered.[7]

Diagnosis of myocardial involvement with SARS-CoV2 remains often challenging until MRI is performed. Along with d-dimer and troponin assessment, the level and significance of anti-cardiac antibodies has been examined in a Russian study by Blagova *et al.* Among 86 patients admitted to hospital for moderate-to-severe COVID-19, cardiac damage (45.3% of patients) included new-onset AF (9.3%), HF (9.3%), low QRS voltage (11.4%), repolarization abnormalities (41.5%), and pericardial effusion (30%). Anti-cardiac antibodies were found with three-fold higher titres in 25 patients (73.5%), and their level correlated with pericardial effusion and mortality.[8]

Pulmonary artery circulation in patients with COVID-19 has been extensively reviewed by Jansa and Ascherman, from Praha, who showed that prevalence of COVID-19 is not increased in patients with pulmonary arterial hypertension (PAH). A potential explanation of this could pertain to vasodilatation, anti-remodelling, and anti-aggregation effects of specific therapies administered to patients with PAH.[9]

Although most reports have confirmed that COVID-19 causes mild symptoms only among children, more severe illnesses may sometimes occur, especially in children with congenital heart disease or associated comorbidities. A scientific statement on the optimal management of children with COVID-19 has been published by Koçak *et al.* from Turkey. Echocardiography is recommended in children with HF, unexplained tachycardia incompatible with fever, cardiomegaly, ST-T segment changes, and arrhythmia. Acute myocardial injury should be detected using biomarkers if symptoms are present. In this later case, myocarditis, pericardial effusion, and coronary artery dilatation

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resulting from a multisystem inflammatory syndrome similar to Kawasaki disease should get tested.[10]

A safe use of potentially effective drugs is also required in adults. Several publications have emerged describing the likely effects of the use of well-known drugs, including chloroquine, hydroxychloroquine, and their combination with azithromycin. QT prolongation induced by these drugs may result in *torsades de pointes* and, in turn, sudden cardiac death. An approach to monitor and to screen patients at risk to avoid such life-threatening events has been proposed by Garvanski and Petrov,[11] from Bulgaria.

Other more unlikely treatments took place against SARS-CoV2. Among them, plants used in traditional Chinese medicine are quite popular. Their use was supported in part by previous trials on other viral diseases. In a study by Akalin *et al.* from Turkey, data available from PubMed/MEDLINE on antiviral, anti-inflammatory, and immunomodulatory effects of the 10 most used plants against COVID-19 were extensively reviewed. Despite effectiveness seen in laboratory and animal studies, clinical studies remains at least insufficient, or for the time being not available.[12]

In the sickest patients, a hyperimmune response characterized by a cytokine storm leads to critical illness and end-organ dysfunction with a high mortality rate. Given their anti-inflammatory and immune-modulating effects, various cell types have emerged as therapeutic candidates, among which the cardiosphere-derived cells, stromal/progenitor cells derived from heart tissue (antigenic profile CD105+, CD45−, CD90low). These cells, already tested in patients with miscellaneous heart diseases, including AMI, HF, and PAH, have been successfully administered to six critically ill patients with COVID-19 (decreased PaO2/FiO2 ratio, diffuse bilateral pulmonary infiltrates on CT scan). By contrast with patients with similar severity (18% mortality) who all received the IL-6 inhibitor tocilizumab, those who received cardiosphere-derived cells improved, as evidenced by extubation, survival, and early discharge from hospital in four of six.[13]

Cardiopulmonary resuscitation with the use of personal protective equipment for aerosol-generating procedures (PPE AGP) in a patient with a sudden cardiac death during the COVID-19 pandemic is uneasy. This has been analysed in a Polish study by Malysz *et al.* This single-blinded, multicenter, randomized, cross-over simulation study involved 67 paramedics wearing PPE AGP. They performed 2-min continuous chest compressions, either manual or with a LUCAS mechanical chest compression device, in adults with suspected COVID-19. Both depth and rate of chest compressions were more frequently correct with the mechanical device. Accordingly, the authors suggest changing the healthcare giver performing manual chest compressions every minute when he or she is wearing a PPE AGP.[14]

Kaufmann and Huber from Austria published in German the most often asked questions from patients with respect to COVID-19 and cardiovascular diseases to provide helpful answers that were given by ESC experts. Such an approach was perceived very useful among readers.[15]

Although most NSCJ published updated reviews on cardiovascular manifestations of COVID-19 as international-oriented journals did, they also provided original contributions focusing on unusual fields, which were encountered during the pandemic.

Appendix

Jean-Jacques Monsuez (Editor-in-Chief of *Archives des Maladies du Cœur et des Vaisseaux Pratique*), France; Plamen Gatzov (Editor-in-Chief of *Bulgarian Cardiology Journal*), Bulgaria; Gergely Agoston (Associate Editor of *Cardiologia Hungarica*), Hungary; Michael Aschermann (Editor-in-Chief of *Cor et Vasa*), Czech Republic; Hala Mahfouz Badran (Editor-in-Chief of *Egyptian Heart Journal*), Egypt; Michael Böhm (Editor-in-Chief of *Clinical Research in Cardiology*, Germany); Alfonso Buendia-Hernandez (Editor-in-Chief of *Archivos de Cardiologia de Mexico*), Mexico; Nuno Cardim (Editor-in-Chief of *Revista Portuguesa de Cardiologia*), Portugal; Jose-Maria De La Torre (Editor-in-Chief of *REC Interventional Cardiology*), Spain; Cetin Erol (Editor-in-Chief of *Anatolian Journal of Cardiology*), Turkey; Gerd Heusch (Editor-in-Chief of *Basic Research in Cardiology*, Germany); Kurt Huber (Editor-in-Chief of *Austrian Journal of Cardiology*), Austria; Yves Juillière (Editor-in-Chief of *Archives of Cardiovascular Diseases*), France; Evgeny Shlyakhto (Editor-in-Chief of *Russian Journal of Cardiology*), Russia; Anetta Undas (Editor-in-Chief of *Kardiologia Polska*), Poland; Dilek Ural (Editor-in-Chief of *Archives of The Turkish Society of Cardiology*), Turkey; Fernando Alfonso (past Chairman of the Editors' Network of the *European Society of Cardiology*), Spain; Ignacio Ferreira-Gonzalez (Editor-in-Chief of *Revista Española de Cardiología* and Chairman of the Editors' Network of the *European Society of Cardiology*), Spain.

References

1. Dieguez-Campa CE, Perez-Neri I, Reyes-Teran G, Flores-Apodaca IA, Castillo-Ledon-Pretelini J, Mercado-Bautista O, Alvarez-Santana R, Zenteno MA, Bowles B, Lee A. The 2020 research pandemic: a bibliometric analysis of publications on COVID-19 and their scientific impact during the first months. *Arch Cardiol Mex* 2020. doi:10.24875/ACM.20000375.
2. Böhm M, Ewen S, Schweitzer A, Katus HUGO. Scientific publication activity during COVID-19 shutdown. *Clin Res Cardiol* 2020;**109**:1443–1445.
3. Huet F, Prieur C, Schurtz G, Gerbaud E, Manzo-Silberman S, Vanzetto G, Elbaz M, Tea V, Mercier G, Lattuca B, Duflos C, Roubille F. One train may hide another: acute cardiovascular diseases could be neglected because of the COVID-19 pandemic. *Arch Cardiovas Dis* 2020;**113**:303–307.
4. Rodriguez-Leor O, Cid-Alvarez B, Perez de Prado A, Rossello X, Ojeda S, Serrador A, Lopez-Palop R, Martin-Moreiras J, Rumoroso JR, Cequier A, Ibanez B, Cruz-Gonzalez I, Romaguera R, Moreno R. Impact of COVID-19 on ST-segment elevation myocardial infarction care. The Spanish experience. *Rev Esp Cardiol* 2020;**73**:994–1002.
5. Rodriguez-Leor O, Cid-Alvarez B, Ojeda S, Martin-Moreiras J, Rumoroso JR, Lopez-Palop R, Serrador A, Cequier A, Romaguera R, Cruz I, Perez de Prado A, Moreno R. Impact of the COVID-19 pandemic on interventional cardiology in Spain. *REC Interv Cardiol* 2020;**2**:82–89.
6. Momtazmanesh S, Shobeiri P, Hanaei S, Mahmoud-Elsayed H, Dalvi B, Malakan Rad E. Cardiovascular disease in COVID: a systematic review and meta-analysis of 10 898 patients and proposal of a triage risk stratification. *Egypt Heart J* 2020;**72**. doi:10.1186/s43044-020-00075-z.
7. Mesquita D, Carmo P, Cabanelas N. Cardiac arrhythmias in patients presenting with COVID 19 treated in Portuguese hospitals. A National Registry from APAPE. *Rev Port Cardiol* 2021, in press.
8. Blagova OV, Varionchik NV, Zaydenov VA, Savina PO, Sarkisova ND. Anticardiac antibodies in patients with severe and moderate COVID-19. *Russ J Cardiol* 2020;**25**:4054.
9. Jansa P, Ascherman M. COVID-19 in disorders of pulmonary circulation. *Cor Vasa* 2020;**62**:19–21.
10. Koçak G, Ergul Y, Nişli K, Hatemi AC, Tutar E, Tokel NK, Celebi A. Evaluation and follow-up of pediatric COVID-19 in terms of cardiac involvement: a scientific statement from the Association of Turkish pediatric cardiology and Pediatric cardiac surgery. *Anatol J Cardiol* 2020; **24**:13–18.
11. Garvanski I, Petrov I, Simova I. Recommendations for the follow-up of patients with cardiovascular disease when administering potentially effective medications

for the treatment of COVID-19 with a purpose to reduce the risk of QT prolongation and sudden cardiac death. *Bulg Cardiol J* 2020; **26**:21–26.
12. Akalın E, Ekici M, Alan Z, Özbir Elevli E, Yaman Bucak A, Aobuliaikemu N, Üresin AY. Traditional Chinese medicine practices used in COVID-19 treatment in clinic and their effects on the cardiovascular system. *Turk Kardiyol Dern Ars* 2020; **48**:410–424.
13. Singh S, Chakravarty T, Chen P, Akhmerov A, Falk J, Friedman O, Zaman T, Ebinger JE, Gheorghiu M, Marbán L, Marbán E, Makkar RR. Allogeneic cardiosphere-derived cells (CAP-1002) in critically ill COVID-19 patients: compassionate-use care series. *Basic Res Cardiol* 2020; **115**:36.
14. Malysz M, Smereka J, Jaguszewski M. An optimal chest compression technique using personal protective equipment during resuscitation in the COVID-19 pandemic: a randomized crossover simulation study. *Kardiol Pol* 2020;**78**:1254–1261.
15. Kaufmann CC, Huber K. COVID-19: what heart patients need to know? *J Kardiol* 2020;**27**:146–150.

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A much-loved Nobel Laureate, known simply as Aunt Trudy

Gertrude B. 'Trudy' Elion won the Nobel Prize in 1988. But what was she really like? Her nephew, cardiologist Dr Jon Elion, reveals what an inspirational figure she was to him and numerous others

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The headline in the Kentucky newspaper proclaimed: 'Nobel Laureate is Just "Aunt Trudy" to Local Cardiologist'. The story was celebrating the award of the 1988 Nobel Prize in Physiology or Medicine to Gertrude B. Elion, which she received jointly with George H. Hitchings and Sir James W. Black 'for their discoveries of important principles for drug treatment'.

While she may have been just 'Aunt Trudy' for headline purposes, she was so much more: an inspirational figure who loved family life, fostered a joyous pursuit of science, and had a common touch with students, colleagues, and even Royalty.

The 'local cardiologist' was Dr Jon Elion, her nephew, who recalls her as 'unassuming, pleasant, outgoing, and with an easy laugh'.

'She was very egalitarian in her views of gender, race, or lifestyle preferences. She treated everybody equally, whether it was the King of Sweden or the security guard at the research lab', he added.

But above all, she was an important inspiration to him.

Born in New York City on 23 January 1918, the daughter of a dentist, Trudy Elion enjoyed time with the wider family, often visiting her brother (Jon's father), always bringing gifts and spending Christmases with them.

'Aunt Trudy was a big part of our extended family and someone with whom I was very close from my early childhood', said Jon.

Worldwide friendships

An avid photographer and traveller with interests in opera and ballet, she went to many conferences—the Gordon Research Conference was a favourite—and had worldwide friendships that crossed the boundaries of countries and industries.

'She would swap stories and share preliminary results with others at national and international meetings', he continued. 'But in looking back, she never talked much about the science. Instead, she regaled us with stories about the people that she met, "old friends" who would figure prominently in later years, helping each other out, sending promising compounds to each other to explore and test'.

He suspects this may have underpinned one of her favourite sayings: 'It's amazing how much you can get done if you don't care who gets the credit'.

Understandably excited when she called with the news of her Nobel Prize, great plans were made for the family to head to Stockholm for the ceremony. Trudy insisted that her family join her for the week-long Nobel festivities in Sweden, though her brother was unable to attend because of severe back pain.

Blue chiffon

Having delivered her Nobel lecture, The Purine Path to Chemotherapy, she attended the ceremonial ball, resplendent in a blue chiffon dress.

Jon said: 'I remember my daughter being wide-eyed with amazement when the Queen of Sweden, covered in jewels and a sparkling dress, came over to her, took her by the hand, and brought her over to where we were to pose for a picture with the King and Queen'.

In securing the 1988 Nobel Prize in Physiology or Medicine, Hitchings and Elion had diverged from the historical trial-and-error approach of drug development towards what became termed as rational drug design. New molecules with specific molecular structures were used to create compounds that would interfere with the natural production of deoxyribonucleic acid (DNA) in cells and interrupt cell growth.

Crowning glory

Over the years the research philosophy formed the basis for new drugs against diseases, including: thioguanine and 6-mercaptopurine

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