



NewsLetter

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EDITORIAL

AM I SAFE AFTER OVERCOMING COVID-19 ? (LIFE AFTER SURVIVING COVID-19)

As all of us are aware that an outbreak of coronavirus disease 2019 (COVID-19), caused by a novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) occurred late last year in Wuhan city of China. Subsequently it has gone on to be a pandemic that has spread very rapidly globally. At the present time, the therapeutic strategies to deal with the infection are mainly supportive. Hence our best weapon appears to be prevention aimed at reducing transmission in the community.

The clinical spectrum of persons infected with this virus varies, from having absolutely no symptoms (asymptomatic) or mild illness (paucisymptomatic) to very severe illness characterized by respiratory failure needing ICU support and mechanical ventilation to multiorgan failure.

Asymptomatic patients form the majority of all Covid-19 victims. Available data suggests that 80% of infections are mild or asymptomatic, 15% are severe infection, requiring oxygen and 5% are critical infections, requiring ventilation. As per the standard Covid-19 protocol it is believed that an average patient recovers in two weeks and can be discharged. The WHO says critical cases can take up to six weeks for recovery. All recovered patients are advised home isolation for some time and report any new health condition immediately.

Various studies have looked at who are the persons more likely to be affected by severe illness. Children appear to be less affected (1-5%) and have milder forms of illness. Male, aged over 65, smokers and those with co-morbidities such as hypertension, diabetes, cardiovascular disease, chronic lung diseases and high BMI have been seen to have the severe variety of the disease. Therefore they have been recommended stricter compliance with social distancing and avoiding non-essential travel.

The question that people frequently ask is what happens once I recover from COVID-19. Am I safe?

Do people who have beaten Covid-19 have to worry about their long-term health?

Do Covid-19 survivors really recover fully?

The disease is new and we still do not have clear answer to this question. Some of the earliest patients who recovered in China got re-infected a few months ago. There is not enough verifiable data to know what percentage of Covid-19 patients comeback to hospitals with serious health conditions after recovery and what the long-term effects are. What we do know about long-term effects of Covid-19 on patients who developed acute respiratory distress syndrome (ARDS) could have a

greater risk of long-term health issues.

Based on a recent article from Italy published in Lancet Respir Med (May 2020), it is recognized that pulmonary fibrosis is a sequelae of ARDS. Available data also indicate that among patients with COVID-19 who develop ARDS, 20% of cases are severe. When any pneumonia is severe, recovery may take long and when recovery does occur it may leave scarring that could have implications especially in elderly, those with chronic lung conditions and especially smokers. Investigators from Leeds, Manchester observed that problems in respiratory and exercise capacity are usually present in the first six months after hospitalization.

Impaired lung function from SARS-CoV-2 infection can negatively affect other organs like the heart, kidneys, and brain, with significant health impacts that may last after getting over the infection.

Although COVID-19 is predominantly a respiratory illness, a large number of patients with COVID-19 present with preexisting cardiovascular disease or develop new-onset cardiac dysfunction during the course of the illness. Although the exact mechanism is unclear, the ACE2 receptor, the binding point for SARS-CoV-2, is abundantly found in myocytes. Therefore, myocyte damage from a direct viral attack could very well be the predominant mechanism.

Research shows one in five ARDS survivors experiences long-term cognitive impairment, even five years after being discharged. Continuing impairments can include short-term memory problems and difficulty with learning and executive function. These can lead to challenges like difficulty working, impaired money management, or struggling to perform daily tasks.

ARDS survivors, especially those who require intensive care, frequently have increased rates of depression and anxiety, and many experience post-traumatic stress. Although it's still too early to have much data on Covid-19, during the SARS outbreak, former patients struggled with psychological distress and stress for at least a year after the outbreak.

The UK National Health Service assumes that of Covid-19 patients who have required hospitalization, 45% will need ongoing medical care, 4% will require inpatient rehabilitation, and 1% will permanently require acute care. The UK National Health Service assumes that of Covid-19 patients who have required hospitalization, 45% will need ongoing medical care, 4% will require inpatient rehabilitation, and 1% will permanently require acute care.

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ENDOSCOPIC SURGERY FOR SINONASAL AND SKULL BASE MALIGNANCY – WITH SAFE ONCOLOGICAL OUTCOME AND MINIMAL MORBIDITY

Sino nasal malignancies are a group of rare heterogenous cancers that originate near critical neurovascular structures. The incidence is estimated to be 0.83 per 100,000 persons. Proximity to the orbit, brain, cranial nerves, and carotid arteries make surgical resection inherently challenging and potentially morbid. Surgery has played and continues to play an important role in the management of sinonasal malignancies and techniques have changed over time. Craniofacial techniques, originally described in the 1960s, became the gold standard in the surgical management of malignancies involving the anterior skull base over the ensuing decades. These techniques remain the treatment of choice for many patients with advanced disease. In the 1990s, endoscopic techniques began to be applied to various skull base pathologies. In the late 1990s and early 2000s, endoscopic approaches were applied to resection of sinonasal malignancies. Current expanded endonasal endoscopic approaches provide excellent access to selected lesions involving the anterior, middle, and posterior cranial fossa and the craniocervical junction.

The goals of surgical resection of anterior skull base malignancies are similar to those of oncologic surgery at other body sites. In general terms, the goal of surgery is to obtain a negative margin resection of the tumour. This must be achieved with as little morbidity as possible with preservation of critical anatomic structures where appropriate. Endonasal endoscopic approach provide improved visualization of the tumour margins with the endoscope as facilitating complete resection of the tumour origin resulting in negative margins. EEA avoids facial incisions and potential cosmetic issues that arise from lateral rhinotomy and coronal incisions. Open approaches have additional morbidity associated with performing a craniotomy. The endoscopic approach proceeds with debulking with the goal of identifying and resecting the tumour pedicle en bloc. Obtaining negative margins optimizes survival independent of the surgery being performed piecemeal or en bloc.

Endoscopic resection of Sino-nasal tumours that are centrally located in the nose and sinuses should be considered before the external approach. Contraindications to a pure endoscopic approach include extension into facial, orbital soft tissues, involvement of lacrimal pathway, nasal bone, extension through orbital contents, the superior and lateral aspects of the frontal sinus and the floor of the nasal cavity. Patients with involvement of the medial wall of the maxilla and the medial portion of the posterior wall are often excellent candidates for endoscopic resection. However, involvement of the superior, anterior, inferior and lateral walls may require conversion to an open approach. Involvement of the brain or other extension which would require resection of the anterior cranial fossa dura lateral to approximately the mid-orbital roof is also contraindicated. Lesions involving optic chiasm are not resectable by any mean.

We routinely perform endoscopic skull base surgery at our institution. Here, we describe 2 Esthesioneuroblastoma cases done endoscopically.

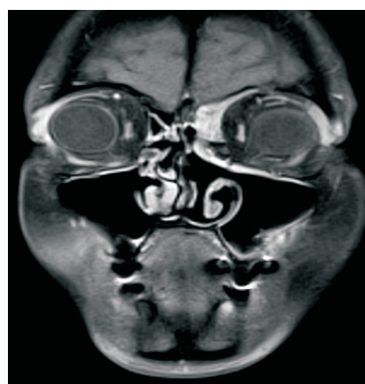


Fig. 1:
Showing soft tissue in left Ethmoid Sinus

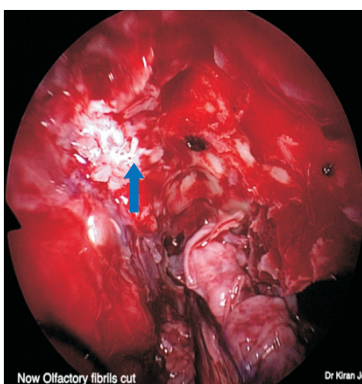


Fig. 2: Arrow showing cut end of olfactory fibrils

Case 1: 40 years old female underwent endoscopic sinus surgery outside for left side nasal polyp. Postoperative histopathology report revealed esthesioneuroblastoma. MRI of paranasal sinus showed tumour limited to left nasal cavity only (Hyams III/IV, Kaddish B). Distant work up showed no metastasis. Patient was planned for endoscopic endonasal resection and frozen section of olfactory fibrils (Fig. 1 & 2). Intraoperative frozen showed normal olfactory fibril. Defect repaired with fascia lata. Patient is on one year follow up and doing fine.

Case 2: 40 years old male underwent endoscopic sinus surgery for bilateral nasal polyp outside. Postoperative pathology report showed Esthesioneuroblastoma (Hyams II, Kaddish C). MRI of paranasal sinus revealed tumour in bilateral nasal cavity with extensive intradural intracranial extension. Patient was given 3 cycles of neoadjuvant chemotherapy (cisplatin + etoposide) followed by endoscopic craniofacial resection (Fig. 3, 4, 5 & 6). Frozen report showed negative dural margins. Defect was repaired with fascia lata flap. Patient was discharged on sixth postoperative day. Currently patient is undergoing adjuvant radiotherapy.

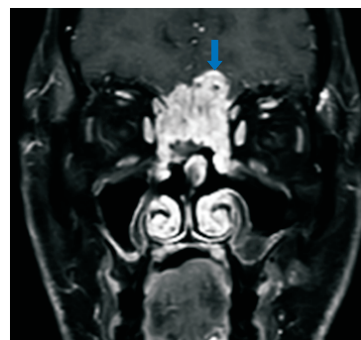


Fig. 3:
Pre chemotherapy MRI



Fig. 4:
Post chemotherapy MRI

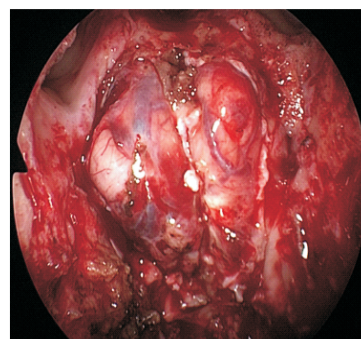


Fig. 5: Basifrontal lobe after endoscopic dural resection

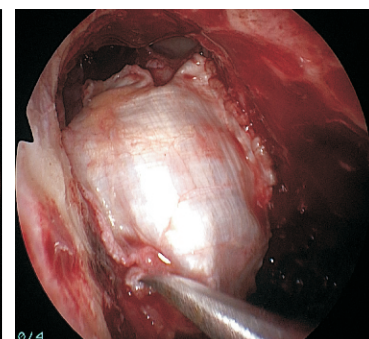


Fig. 6
Showing endoscopic dural repair

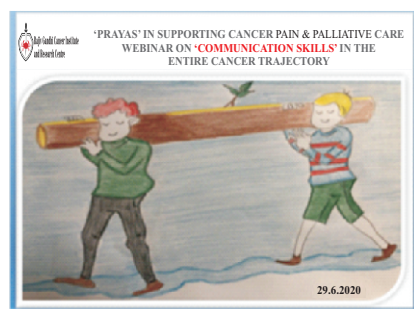
Conclusion: The endoscopic approach is at least as good as the open approach in obtaining negative margins. The endoscopic approach does carry less morbidity and a shorter hospital stay. The gold standard for surgery of Sino nasal and skull base malignancies is therefore to select the approach that is most capable of obtaining negative margins while minimizing patient morbidity.

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PRAYAS - SUPPORTING CANCER PAIN & PALLIATIVE CARE

'PRAYAS' series in supporting cancer pain & palliative care, webinar on 'Communication Skills' in the entire cancer trajectory.



The Covid pandemic has led to marked changes in our lives and created a challenging state of affairs for medical activities and education system. Moving forward and learning to live with Covid and cancer, the Pain and Palliative Care Department of RGCIRC has developed a new normal way of spreading the awareness about cancer pain and palliative care. 'PRAYAS'

series is the one which will not only spread awareness but also engross the doctors and sisters who would like to work and serve the mankind.

on Monday, 29th June 2020 which focused on communication skills in the entire cancer trajectory. I am thankful to the faculty members and delegates for their active participation.



We got the overwhelming response by the attendees which shows that such meetings are required to enhance our learning skills more. Henceforth, virtual series will continue quarterly addressing different and difficult issues faced by a cancer patient and their families.

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CONCEPT OF SYNTHETIC LETHALITY: PARP INHIBITORS – NEW ERA IN PERSONALIZED MEDICINE

The term “synthetic lethality” was originally coined by geneticists in the 1940s. It arises when a combination of deficiencies in the expression of two or more genes leads to cell death, whereas a deficiency in only one of these genes does not. Although the concept originated some 8 decades ago, it was applied to cancer somewhat later to explain the selective killing of cancer cells with particular molecular defects. Only simultaneous mutations in gene pair confer lethality while any other combination of mutations is viable (as conceptualized in fig 1).

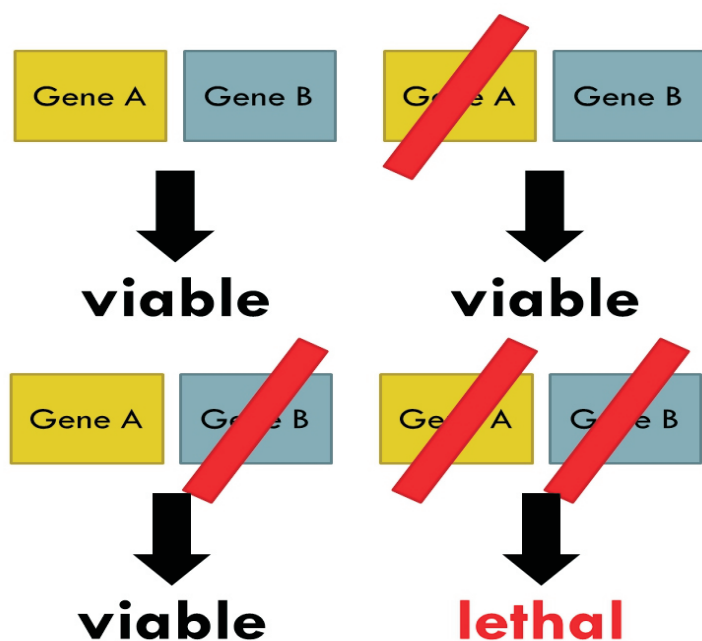


Fig. 1

Normally in response to DNA damage, the PARP pathway and BRCA tumor suppressor proteins are activated which repair the damaged DNA. Cells with BRCA mutations become dependent on the PARP pathway to fix damages to DNA, since the protein product of BRCA genes is altered and defective. Cells exposed to PARP inhibitors repair DNA via the protein products encoded by BRCA genes if they become damaged. In cells with BRCA mutations that are treated with PARP inhibitors, both DNA repair mechanisms are blocked and the cell dies (as conceptualized in figure 2)

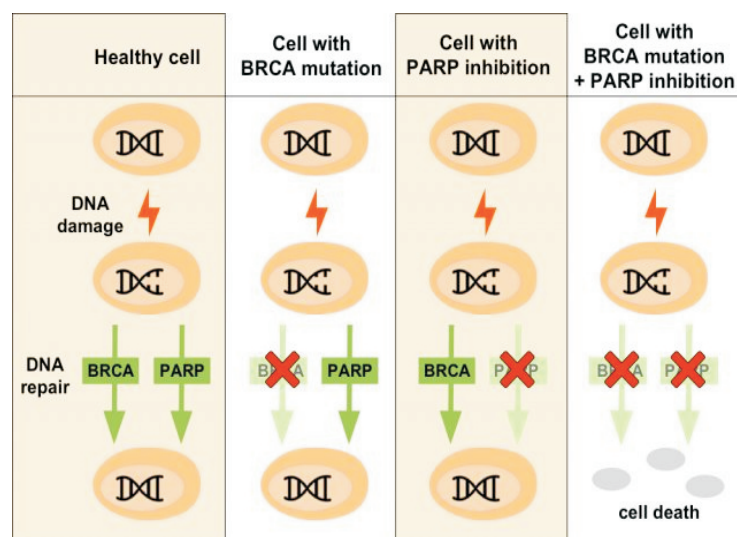


Fig. 2

Based upon this concept since the inception of various human clinical trials the earliest success was achieved by the PARP inhibitor olaparib. It got accelerated approval in 2014 for treatment of relapsed BRCA-mutated advanced ovarian cancer. As of today olaparib is used in germline/somatic BRCA mutated breast, ovarian, pancreatic and prostate cancer either as a maintenance or palliative treatment. There are number of other PARP inhibitors which are under clinical development, few of these are already approved for various other indications. Other PARP inhibitors approved in various indications are rucaparib, niraparib, velaparib and talazoparib. These newer agents have drastically changed the outlook of these BRCA mutated cancers significantly increasing either overall survival or progression free survival. Apart from BRCA mutated cancers some of these agents are also active in homologous recombination deficient cancers (HRD) which is an enzyme system analogous to BRCA. PARP inhibitors show promise as a powerful therapeutic tool, where these genes may be dysfunctional clearly signifying a new era in personalized medicine.

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and after 2-3 weeks develop severe febrile illness with rashes and inflammation of skin and mucus membranes and myocarditis. Recent reports have described a hyper inflammatory response to the novel, pandemic coronavirus, COVID-19. The first reports came from the United Kingdom, these features have been described to resemble Kawasaki Disease as some of them displayed characteristic coronary artery changes.

Although the aetiology of Kawasaki Disease remains unclear, there is substantial data pointing to a likely viral aetiology. Many investigators have hypothesized that some children may be genetically predisposed to a more robust inflammatory response to specific viruses. Once exposed to the specific virus, children then mount an exaggerated inflammatory response which clinically manifests as what is now defined to be Kawasaki Disease (KD). As the prevalence of KD in Asian countries is more than western countries, clinicians in Asian countries need to be especially alert to the possible occurrence of this disease in the time of viral pandemics.

Furthermore, hyperinflammatory response to COVID-19 has been reported in adults as well. This is supported by the presence of elevated inflammatory and reactive markers like C-reactive protein, procalcitonin, ferritin, and D-dimer among these patients. These markers also have prognostic significance as those whose illness is more severe have higher values. Based on evidence in adult patients, we now know that a subset of patients with severe COVID-19 have a

"cytokine storm syndrome" in which a cascade of activated cytokines leads to harmful auto-amplifying hyperinflammatory cytokine production. Adult patients with worse illness and greater evidence of inflammation also had a higher incidence of cardiac findings such as troponin leak and ventricular dysfunction. Thus, these findings also may simply be inherent to more severe COVID-19 secondary to overall inflammatory response. Both Kawasaki Disease and adult multi system inflammatory syndrome can have cardiovascular involvement. Similar findings have also been observed in viremia from other organisms as well.

Long-term complications of Covid-19, whether caused by the virus itself or the inflammation it triggers, appear to cover a wide range of chronic health conditions, although some of these are speculative. Nevertheless, in view of the large numbers of people who are affected by COVID-19, even rare complications can have important implications at the population level. Hence individuals as well as Institutions need to plan rehabilitation for the COVID-19 survivors, to improve their quality of life and nurse them back to health.



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