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AHMEDABAD FAMILY PHYSICIANS ASSOCIATION

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SALUTE THE CORONA WARRIORS

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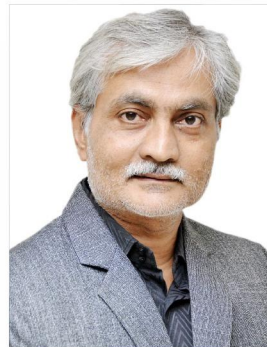
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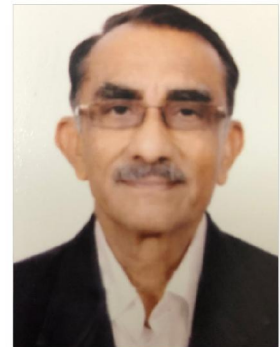
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FROM THE DESK OF **PRESIDENT & SECRETARY**

Dear Colleagues... Members,

Season of routine viral infections and malaria has started already. Corona war is still going on. Corona victims are in higher most number in Ahmedabad city. We all are fighting still on frontline. Some of our AFPA doctors were victims of COVID-19... but by grace of God they recovered well and among them some of family physicians have already started practice again (Great Dedication).

We AFPA doctors are giving marvelous services to COVID patients. Our members provide fulflage services to corona Home Isolated Patients by daily calls to them in collabration with Ahmedabad Municipal Corporation Health Center.

We had webinar, CMEs and also very nice public awarness programme on Facebook- Youtube Live which was watched by more than 3500 people with tremendous appreciation.

Thanks a lot to Home Isolation Patient serving doctors for enlightning AFPA in society and also Ahmedabad Municipal Corporation Health Department for giving opportunity for this noble services to mankind.



JAY AFPA



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REDUCING MORTALITY IN COVID-19

Dr Urman Dhruv MD
Director, Department of Internal Medicine,
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A cluster of patients of novel coronavirus pneumonia (NCP) have been identified in Wuhan in December 2019 and soon this virus spread at a tremendous rate which swept through the whole China and more than 93 countries and regions around the world. Since early January 2020, the world has witnessed unprecedented global scientific and political attention focused on the devastating coronavirus disease 2019 (COVID-19) pandemic, caused by the novel, highly contagious zoonotic pathogen, the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). By July 9th, 2020, there have been 5,58,311 deaths worldwide out of 12,430,029 (7% case fatality) confirmed COVID-19 cases reported from all continents to the World Health Organization (WHO, 2020). As with the two other novel coronavirus zoonotic diseases of humans, SARS and MERS, no specific treatments for reducing mortality or morbidity are yet available. The management of COVID-19 patients remains largely symptomatic and supportive with organ support for severely ill patients. Deaths from COVID-19 will continue to rise globally until effective and appropriate treatments and vaccines are found.





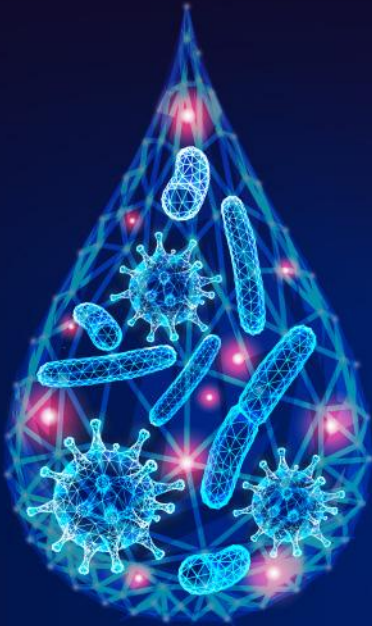
CLINICAL TRIALS OF THERAPEUTIC INTERVENTIONS

With no specific treatments being available for treating COVID-19 patients, the global medical, scientific, pharma and funding communities have rapidly initiated over 500 COVID-19 related trials (https://clinicaltrials.gov/ct2/who_table). These clinical trials have been fast-tracked by ethical committees worldwide and a range of therapeutic interventions registered on clinical trials.gov are taking forward phase 1, 2 and 3 trials of antiviral drug regimens, biologics, repurposed drugs in various combinations, herbal remedies, nutritional supplements, and cellular therapies. A paradigm shift is underway from the current focus of drug treatment combinations targeting the pathogen, to advancing cellular Host-Directed Therapies (HDTs) for tackling the aberrant host immune and inflammatory responses, which underlie the pathogenesis of SARS-CoV-2 and the high COVID-19 death rates. This is an area, which has been eclipsed by the current emphasis the huge number of trials evaluating new anti-viral drugs, repurposed drugs and combinations thereof.





PATHOLOGY AND AUTOPSY STUDIES OF COVID-19 DEATHS



Defining the underlying pathogenesis and pathology of COVID-19 disease for developing appropriate therapeutic interventions may prevent end organ damage and long-term functional disability in those who survive severe disease. Autopsy and minimally invasive biopsy studies indicate that COVID-19 is a multi-system disease. The lungs in particular manifest significant pathological

lesions, such as alveolar exudative inflammation and interstitial inflammation, alveolar epithelium proliferation and hyaline membrane formation. Significant proliferation of type II alveolar epithelia and focal desquamation of alveolar and bronchial epithelia and hyaline membrane formation are seen; with predominantly macrophage and monocyte immune cell infiltration in alveoli with multinucleated giant cells; lymphocytes (mostly CD4-positive T cells), and some eosinophils and neutrophils. The blood vessels of alveolar septum were congested, edematous and widened, with modest infiltration of monocytes and lymphocytes. Hyaline thrombi in microvessels and focal hemorrhage in lung tissue, organization of exudates, and pulmonary interstitial fibrosis have been observed. Furthermore, degeneration and necrosis of parenchymal cells and formation of hyaline thrombus in small vessels were observed in other organs and tissues. Immunohistochemical staining showed alveolar epithelia and macrophages positive for SARS-CoV-2 antigen. Evidence of SARS-CoV-2 antigens in other organs and tissues has been detected which suggests that host immune responses evoked by SARS-CoV-2 infection are involved in the pathogenesis of multi-organ injury.



COVID-19 PATHOGENESIS AND ABERRANT IMMUNE RESPONSES

SARS-CoV-2 enters the host cells via the cell surface angiotensin converting enzyme 2 (ACE2) receptor on the target cell surface. ACE2 as a cardio-regulator, so there are numerous cells with ACE2 receptors in blood vessels, alveolar type II cells (AT2) in the lungs and several other organs, such as heart, kidneys. It appears that all three lethal zoonotic coronaviruses, MERS-CoV, SARS-CoV and SARS-CoV-2 seem to induce excessive and aberrant host immune responses which are associated with severe lung pathology leading to acute respiratory distress syndrome (ARDS). Characteristic findings on chest imaging in COVID 19 include bilateral ground glass and consolidative changes. An associated cytokine storm may play a role in pathogenesis. Elevated proinflammatory cytokines and chemokines including tumour necrosis factor (TNF) α , interleukin 1 β (IL-1 β), IL-6, granulocyte-colony stimulating factor, interferon gamma-induced protein-10, monocyte chemoattractant protein-1, and macrophage inflammatory proteins 1- α were significantly elevated in COVID-19 patients. Patients with evidence of hyperinflammation have an increased risk of mortality. In those who survive intensive care, the consequences of these aberrant and excessive immune responses may lead to long term pulmonary damage and fibrosis, with functional disability and reduction of quality of life. It is important that therapeutic interventions which can dampen the excess inflammation, thus preventing end organ damage and long-term functional disability in those who survive severe disease.





CELLULAR BASED THERAPIES TO REDUCE EXCESSIVE INFLAMMATION AND IMMUNE-MEDIATED TISSUE DAMAGE

With no specific treatments being available for treating COVID-19 patients, the global medical, scientific, pharma and funding communities have rapidly initiated over 500 COVID-19 related trials (https://clinicaltrials.gov/ct2/who_table). These clinical trials have been fast-tracked by ethical committees worldwide and a range of therapeutic interventions registered on clinicaltrials.gov are taking forward phase 1, 2 and 3 trials of antiviral drug regimens, biologics, repurposed drugs in various combinations, herbal remedies, nutritional supplements, and cellular therapies. A paradigm shift is underway from the current focus of drug treatment combinations targeting the pathogen, to advancing cellular Host-Directed Therapies (HDTs) for tackling the aberrant host immune and inflammatory responses, which underlie the pathogenesis of SARS-CoV-2 and the high COVID-19 death rates. This is an area, which has been eclipsed by the current emphasis the huge number of trials evaluating new anti-viral drugs, repurposed drugs and combinations thereof.

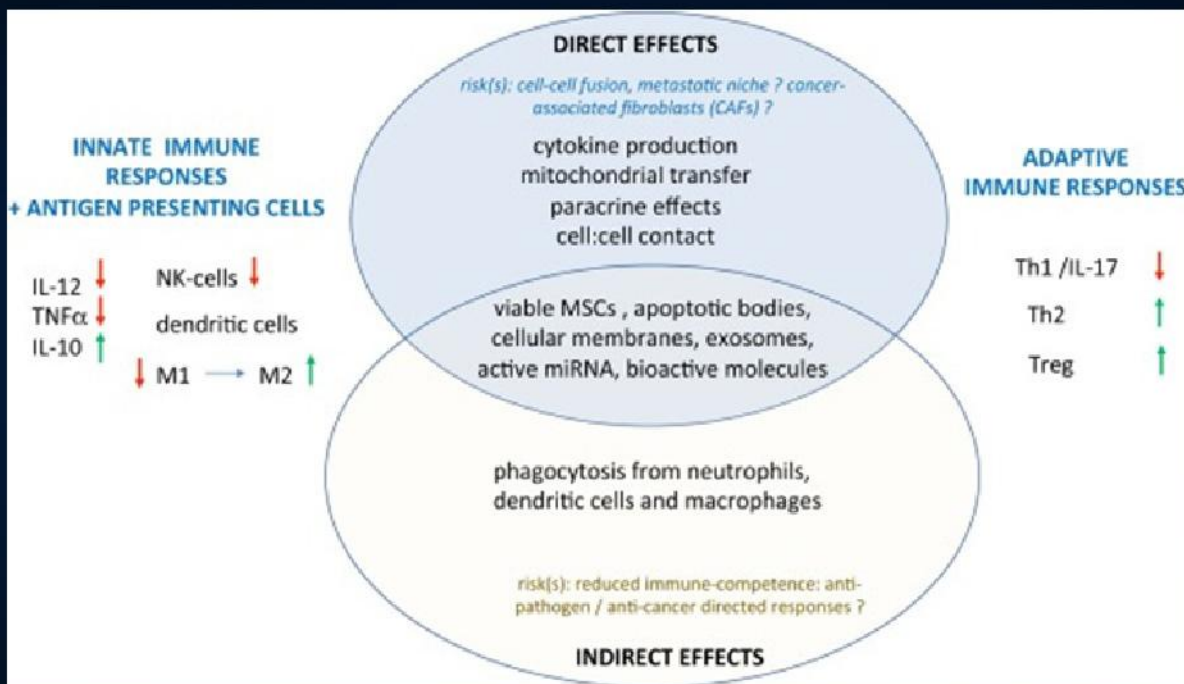


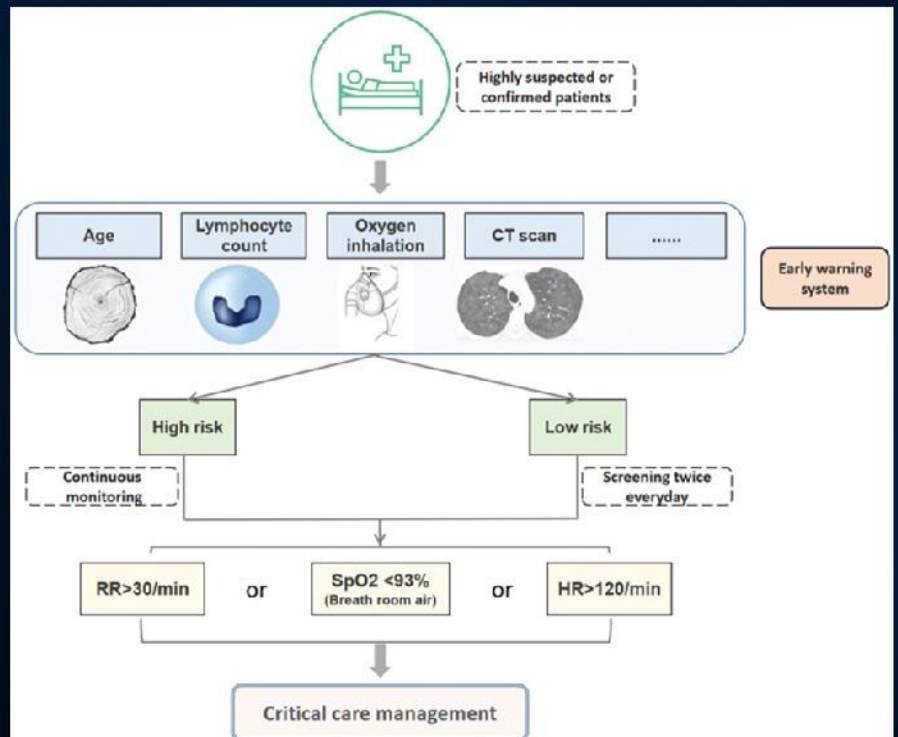
Figure 1. Overview of mechanisms of Action of Mesenchymal Stromal cells.



The studies across the world have suggested that critical care-dominated treatment patterns might be the core in reducing mortality.

1. EARLY RECOGNITION OF HIGH-RISK AND CRITICALLY ILL PATIENTS

Since the severity of disease is closely related to the prognosis, the basic and essential strategies to improve outcomes that we should adhere to remain the early detection of high-risk and critically ill patients. Most of the studies suggested that mortality reduced when critical care was shifted forward and early screening was measured. All NCP patients were screened twice every day and respiratory rate (RR), heart rate (HR), SpO₂ (room air) were monitored regularly. Once SpO₂ < 93%, RR > 30/min, HR > 120/min or any signs of organ failure were observed, patients would be transferred to intensive care unit (ICU) and ICU physicians and nurses would take over their treatment. From available data, age, lymphocyte count, oxygen supplementation and aggressive pulmonary radiographic infiltrations are independent risk factors for NCP progressing to a critical condition. We should establish an early warning system combining these four factors to identify high-risk patients and then kept them under continuous close monitoring. The sensitivity of this warning system was 0.955 (95% CI [0.772–0.999]), the specificity was 0.899 (95% CI [0.863–0.928]). Following line of action is recommended for high-risk patients recognition and all patients' screening to make it possible for early intervention (Fig. 2).



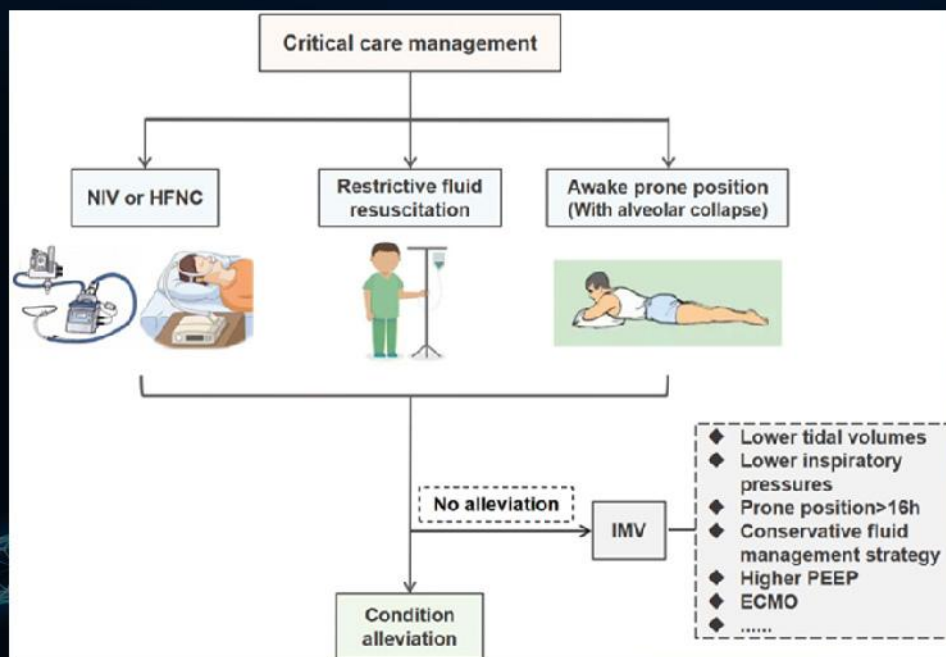
Early warning system and screening procedures for NCP patients



2. EARLY INTERVENTION GUIDED BY INTENSIVISTS

Since there have been no effective antiviral treatments for COVID-19, the vital way to reduce mortality is early and strong intervention to prevent the progression of disease. Following three points which showed valid evidence in reversing the disease and preventing tracheal intubation rate were summarized.

(1) For patients with ARDS or pulmonary extensive effusion in CT scan, high-flow nasal cannula oxygen therapy (HFNC) or non-invasive mechanical ventilation (NIV) was used to maintain positive end expiratory pressure (PEEP) to prevent alveolar collapse even if some of these patients did not have refractory hypoxemia. (2) Restrictive fluid resuscitation under the premise of adequate tissue perfusion is performed to relieve pulmonary edema. (3) Although previous study proved prone position's benefit in moderate-to-severe ARDS patients with invasive mechanical ventilation (IMV), even awake prone position in NCP patients which showed significant effects in improving oxygenation and pulmonary heterogeneity (Fig. 2). With all these measurements, mortality has been shown to reduced dramatically.

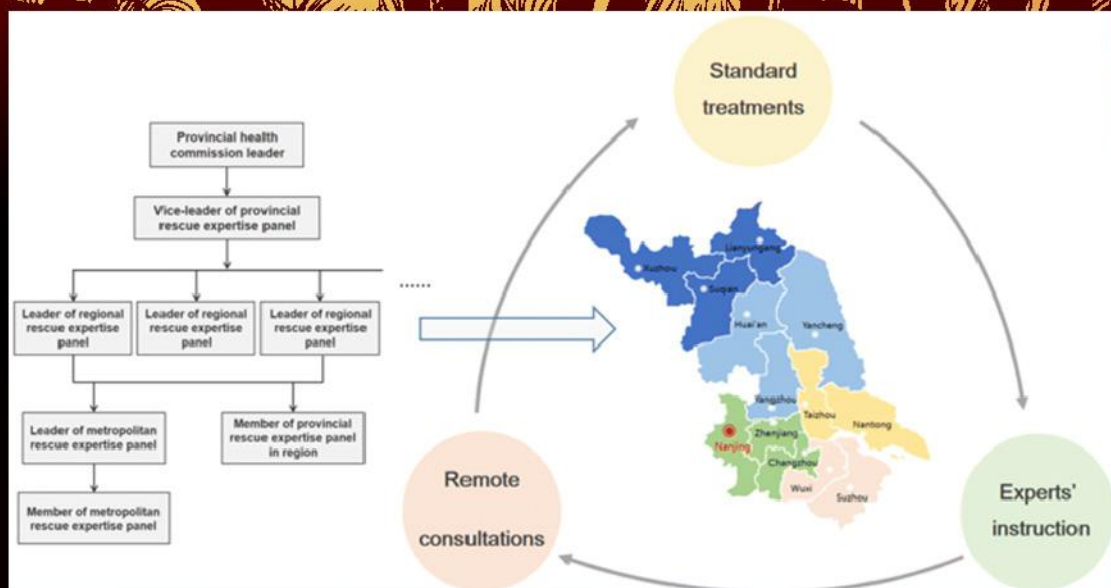


Early intervention for patients with critical condition



3. CLINICAL EXPERTS-GUIDED HIERARCHICAL MANAGEMENT STRATEGY

At the outset of epidemic situation, a clinical experts-guided, multidisciplinary, province-wide hierarchical management group should be established to provide medical guidance for all NCP patients. The members of this panel should be mainly critical care specialists and respiratory specialists from tertiary hospitals. This kind of regional responsibility, timely feedback communication management makes it possible for effective medical interventions (Fig. 3).



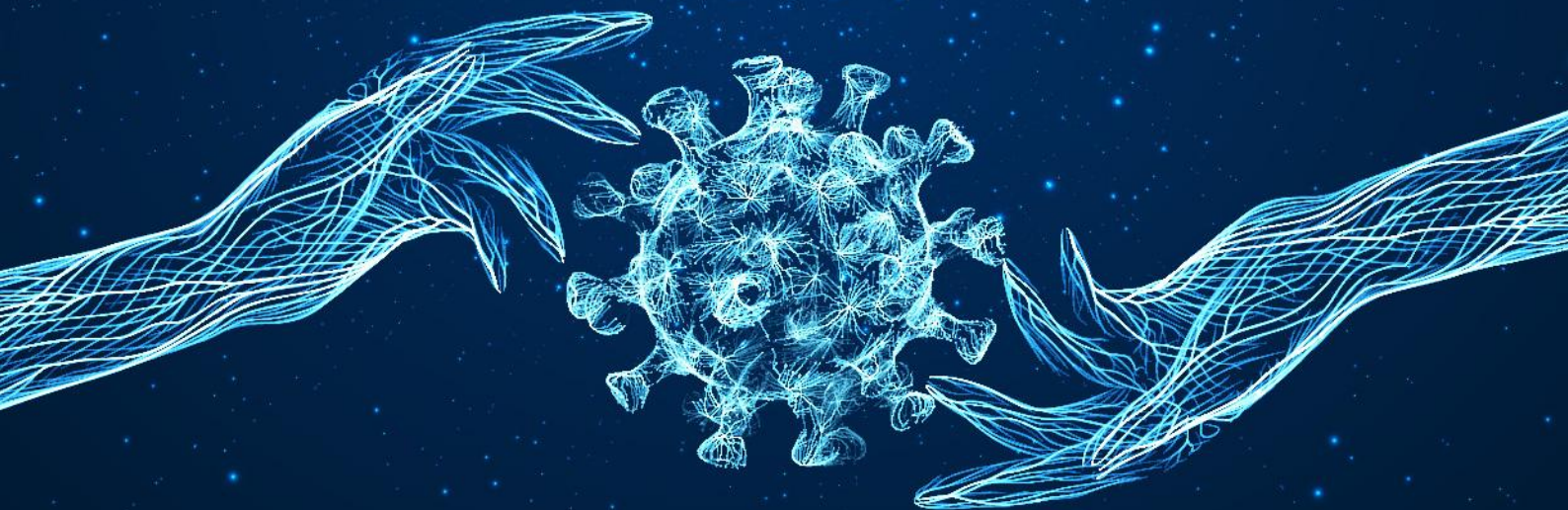
Organization chart of hierarchical management strategy



4. RATIONAL ALLOCATION OF MATERIALS AND HUMAN RESOURCES

Health authorities should attach great importance to epidemic and deploy disease prevention and control measures effectively . All kinds of resources, including frontline medical staff and medical protective materials, should be mobilized and deployed uniformly to guarantee patients' medical care. Adequate material and human resources are important cornerstones for controlling this epidemic.

From our experience, early screening of critically ill patients and critical care-guided early intervention are prominent in reducing NCP patients' mortality. At this critical moment in the global outbreak of NCP, we hope our valid management and treatment bundles can help us achieve the victory in the battle against COVID-19.





5. CONTROL OF RISK FACTORS

Controlling the risk factors like hypertension and Diabetes with suitable agents is of paramount importance early in the course of disease. Withdrawing SGLT 2 Inhibitors, Diuretics at the earliest and posting patient on Insulin especially when steroids are on will be useful in reducing mortality.



Ultimately, one should remember that prevention is the best way to reduce mortality.

Suggested Readings:

1. Lower mortality of COVID-19 by early recognition and intervention: experience from Jiangsu Province Qin Sun¹ , Haibo Qiu¹ , Mao Huang^{2*} and Yi Yang^{1*}Sun et al. *Ann. Intensive Care* (2020) 10:33
2. Reducing mortality and morbidity in patients with severe COVID-19 disease by advancing ongoing trials of Mesenchymal Stromal (stem) Cell (MSC) therapy — Achieving global consensus and visibility for cellular host-directed therapies. *International Journal of Infectious Diseases* <https://doi.org/10.1016/j.ijid.2020.05.040>



Invasive Tests Procedures

- Coronary Angiography (CAG)
- 4 Vessel Angiography
- Peripheral Angiography & Renal Angiography
- Coronary Angioplasty (PTCA) & Stenting
- Robotic Stenting
- Peripheral Angioplasty & Stenting
- Renal Angioplasty & Stenting
- Pacemaker Implantation
- AICD, CRT & Combo Device Implantation
- IVUS, OCT, FFR Evaluation
- Rotablation
- EP Study & RF Ablation
- Cath-interventions for Congenital Heart Defects

Non-Invasive Tests

- ECG
- 2D ECHO with Colour Doppler
- Stress Test (TMT)
- 24 Hour Holter Monitoring
- 24 Hour BP Monitoring
- Ankle brachial index

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Stenting**

Surgical Procedures

- Coronary Artery Bypass Graft (CABG)
- Congenital Heart Surgery
- Valve Surgery, Replacement & Repair
- Aortic Aneurysm Surgery
- Coronary Bypass Combined With Valvular Surgery
- Bentall's Operation
- Surgery For Tetralogy of Fallot
- Carotid Surgery
- Peripheral Artery Reconstruction

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- 24x7 Pharmacy
- 24x7 Pathology Lab
- Physiotherapist
- Dietician

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- Dr. Rajni Patel
- Dr. Kalpesh Patel
- Dr. Bonny Gajjar
- Dr. Keith Fonseca
- Dr. Biren Gandhi
- Dr. Haroon Khatumbara

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- Dr. Mehul Shah & Team
- Dr. S. Bhattacharya & Team

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