Review Article

Cancer in corona times

ABSTRACT

Humanity is witnessing an unprecedented tsunami of corona virus disease 2019 (COVID-19) patients. Till date, India houses 10,453 confirmed COVID-19 patients with a death toll of 358 nationwide and the number is steadily rising with each passing day. The capital city of Delhi, harbouring 1510 patients, has the dubious distinction of being the second largest hotspot for COVID positive patients in India, second only to the state of Maharashtra. Being immuno-compromised, cancer patients are first more susceptible to catch this virus and secondly may witness a more devastating course. Having cancer is a bigger risk factor for contracting COVID-19 than even old age. "Death due to untreated cancer is a much bigger reality than death due to COVID-19," is one perspective that advocates continuation of cancer therapy in corona times albeit by converting cancer hospitals into virtual corona-free fortresses with several tiers of barriers against corona. The immediate, short and long term implications of the corona pandemic and a nationwide lockdown to curtail it, on cancer patients and their caregivers is discussed at length here tempered with experience from the largest tertiary care oncology setup of Northern India. Rigorous literature review based on Medline, Google scholar, Embase, Cochrane and Scopus database search was utilized.

Key words: Cancer; chloroquine; corona; personal prophylaxis equipment; triage

Introduction

Corona virus disease 2019 (COVID-19), has placed cancer patients and treating medical-staff in a Catch-22 situation today: To treat cancer or suspend treatment over corona pandemic is a choice between the devil and the deep C. Dedicated cancer institutes maybe better poised and safer for cancer therapy versus multispeciality hospitals where the likelihood of COVID-19 nosocomial cross-exposure is higher. General population statistics show a mild course in 80% of the patients, 14-17% develop adult respiratory distress syndrome and 5% progress to septic shock and renal shutdown.[1-3] Being immuno-compromised, cancer patients are first more susceptible to catch this virus and secondly may witness a more devastating course. In one Italian study, 20% of COVID deaths comprised patients with active cancer.[4] Doctors too, have a 10-12% case-fatality rate as compared to the general public (2-3% case-fatality; fomite exposure transmits less viral load) attributable to the higher virus load (and cytokine storm) in exposed doctors. Viral load determines the infectivity and health workers working for more than 10 h in the wards have higher mortality.[5] While our focus is on age as the major risk factor for contracting corona, cancer maybe an even bigger factor, also being a health care worker, irrespective of age, makes you vulnerable. The COVID-19 pandemic has immediate, short and long term implications for this subset of patients. The disease is known to be extremely contagious with high human-to-human

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transmission.The key safety requirements being hand hygiene and social distancing. To ensure social distancing various steps were undertaken: work in shifts, work from home, online transactions, etc. When these measures proved futile countrywide lockdown was implemented. Lockdown has affected every single individual financially, socially and psychologically with major implications on management of cancer patients including difficulty in reaching the healthcare facility, modifications in the treatment plan and an added apprehension of contracting nosocomial Covid-19 infection. At the time of article submission (13th of April, 20), 10453 confirmed cases with 358 deceased, paints a grim picture in India,[6] but nevertheless better than the developed world.

The article aims to discuss all these key issues of relevance to the anaesthesiologist. It ends with summarising the steps taken by Rajiv Gandhi Cancer Institute and Research Centre (RGCI) to streamline the care of cancer patients during corona times.

Discussion

According to one perspective death due to delay/denial of cancer therapy is a much bigger threat than death due to COVID-19, but at the same time, being a cancer patient or even a health care worker is a much bigger risk factor for corona related morbidity and mortality. It follows that cancer hospitals need to be converted into virtual corona-free fortresses with tiers of barriers against entry of corona virus [Figure 1].

An exhaustive search was performed utilizing several search engines including PubMed, Embase, Cochrane and Google Scholar for manuscripts including prospective/retrospective, randomised/non-randomised, blinded/nonblinded, case control or cohort studies and case reports, case studies, websites, anesthesia, and surgery society guidelines and ahead of print articles published till April 2020. The search terms used for manuscript retrieval were "cancer and corona,' 'COVID-19 and oncosurgery," "chemotherapy, immunosupression and corona" and "anesthesia and corona." Reference crawling was done. In total 7 studies, 7 guidelines and recommendations and 9 website articles were included in the review.

Immediate implications

Should oncosurgery continue in such a situation? The answer is debatable. As per the ISA advisory (April 2020)[7]and IASO guidelines, all elective and semi-urgent surgeries should be postponed and only emergency surgery should continue. But cancer strictly does not qualify as either of these. The assessment and decision for conducting urgent/time-sensitive procedures like cancer surgeries has been left to the concerned hospital and team of caregivers, depending on the available manpower and equipment resources and the individual patient's clinical profile. The goal is conserving manpower, personal protective equipment (PPE) and critical care beds.[7,8]

Personnel and equipment shortage compounded by shortage of even empirical treatment drugs like vitamin-C and hydroxychloroquine necessitates triage of resources.

Triage of cancer patients

- Age: Surgery in all cancer patients above 65 years of age should be deferred since this subsetis most susceptible to COVID-19 and has higher mortality rates[3,4,7-9]
- Co-morbidities: Any patient with uncontrolled diabetes, low left ventricular ejection fraction, prosthetic heart valves, chronic hepatic, pulmonary or renal disease, etc., should not undergo surgery during the epidemic for fear of increased corona-mortality[3,4,7-11]
- Immunosupressants: Postchemotherapy and postradiotherapy patients and those on chronic steroid therapy may not be taken up being highly susceptible to infection[11,12]
- Site of surgery: Breast, thyroid, parotid, renal and basal cell cancer surgery (being slow-growing) can easily be postponed for a month but not a patient with symptomatic brain tumours with raised intracranial pressure or a multiple myeloma patient with pathological fractures or an aggressive carcinoma gall bladder.[8]
- Curative-intent treatment: Highest priority is ascribed to cancer patients aged <60y with life expectancy >5y undergoing curative-intent therapy as against patients undergoing non-curative intent treatment.[13]

Triage of equipment

Ideally COVID-19 tests should routinely be carried out in all patients posted for oncosurgery irrespective of the results of a screening questionnaire on symptoms/foreign travel/contact-history. But paucity of testing-kits limits their use to selected patients postscreening and those with leucopenia, elevated C-reactive protein and normal procalcitonin.[14]

In absence of powered air-purifying respirator (PAPR) sets, N95 respirators[15] are essential for the person performing tracheal intubation and extubation while a surgical mask suffices in non aerosol-generating tasks.[15-17] N95 mask can be reused if dried completely for 72h or heated to a temperature above 65°C for 30 min.[5] Position one high quality heat and moisture exchange filters (HMEFs) at two places: between endotracheal tube and breathing circuit, and between

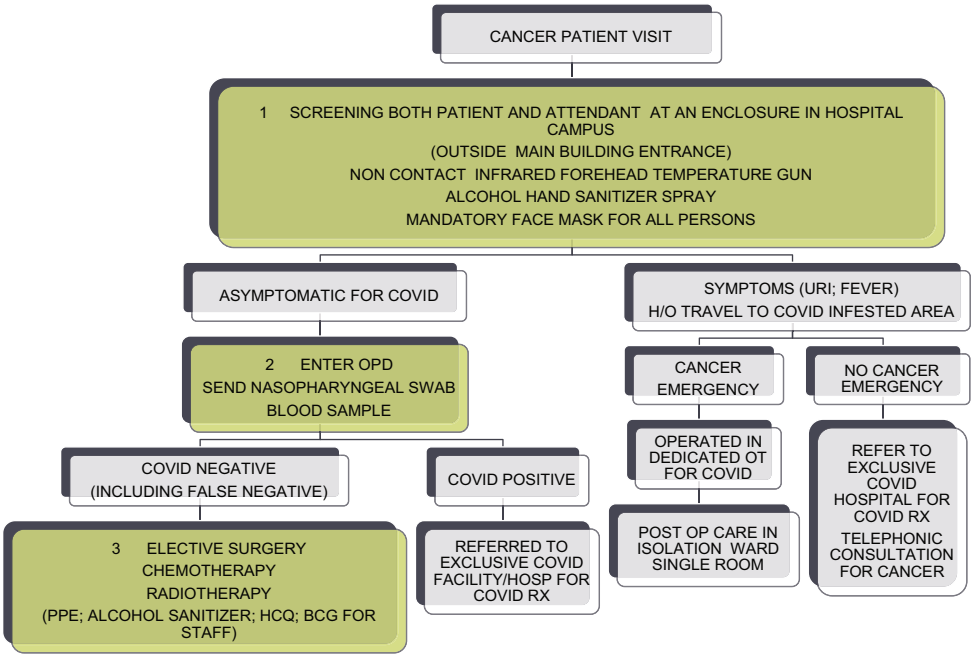

Figure 1: Three tiers of COVID barriers in cancer hospitals

Figure 2: An indigenous technique for personal protective wear for intubating cancer patients in Corona pandemic; Left: Double surgical mask, gown, double gloves (surgical gloves atop working gloves) and a transparent polythene bag with a breathing hole on the posterior aspect (repurposing the plastic bag holding the fresh disposable circuit) adorning the head and shoulders of the intubating anaesthesiologist; Right: C-Mac D-blade video laryngocope being used for tracheal intubation

expiratory limb and anaesthesia machine.[3,7,9,10] These HMEFs remove upto 99% of airborne particles sized above 0.3 μm, thus reducing OT-contamination.[7,9] Most Indian OTs lacking negative pressurization, it necessitates the positive pressure system and air-conditioning to be turned off.[7,9] Laminar flow and functional high-efficiency filters are preferable.

PPE-kits need to be reserved for symptomatic, suspected or known COVID-positive patients. An indigenous technique is suggested for the remaining patients. A double surgical mask, gown, double gloves (surgical gloves atop working gloves), and a transparent polythene bag with a breathing hole on the posterior aspect (repurposing the plastic bag holding the fresh disposable circuit) adorning the head and shoulders should be worn by the intubating anaesthesiologist both at tracheal intubation and extubation [Figure 2]. The impervious plastic sheet routinely used under instrument-trolleys maybe repurposed to serve as a barrier for droplets and aerosols released at extubation.

Triage of personnel

Pregnant ladies, anaesthesiologists above 60 years of age and those with multiple co-morbidities should not attempt tracheal intubation, extubation and other aerosol generating procedureslike suctioning, nebulization, fiberoptic bronchoscopy, CPAP, BiPAP or high-flow nasal oxygen therapy.[3,7] The most experienced/skilled anaesthesiologist must perform tracheal intubation.[7,9,10] Not exceeding three anaesthesiologists should remain in the OT during tracheal intubation/extubation.[3] The OT-staff can be segregated into two or more non-intermixing teams working on alternate days/alternate weeks/alternate fortnight to reduce hours of exposure, cross-infection and stress.

Modification of anaesthesia technique

Out of available airway-securing devices endotracheal intubation is preferred over bag-masking or supraglottic airway devices (SAD) owing to a better seal and reduced leakage of potentially contaminated aerosols. A vice (VE) grip requiring both hands is advisable during preoxygenation, leaving the bagging and PEEP-adjustments to an assistant.[3] Suspected/proven COVID patients may be asked to remove all facial hair to facilitate bag-masking.

Rapid sequence induction using generous doses of muscle relaxant (IV rocuronium >1.5mg/kg ideal body weight and IV

succinylcholine 1.5 mg/kg total body weight)[3,17] to hasten onset of neuromuscular block and reduce risk of coughing on airway instrumentation is advisable. Sellicks-manoeuvre can be omitted due to dubious utility and heightened exposure–risk of the performing assistant. Low tidal volume breaths maybe given if required. Video laryngoscope is preferable to direct laryngoscopy and ditto with low flow and closed-circuit anaesthesia.[3,7,9,10] Avoid fiberoptic bronchoscopy.[9] PPE may hinder auscultatory confirmation of ETT placement necessitating end-tidal carbon dioxide detection.[18] Total intravenous anaesthesia is preferable to volatile anaesthetics to curtail spread of aerosol.[18]

Dedicated COVID-19 intubation tray[3] should be available containing a hyperangulated video laryngoscope blade, Macintosh direct laryngoscope, endotracheal tubes, bougie/stylet, tube-securing tapes, oropharyngeal and nasopharyngeal airways, second-generation SAD, emergency tracheostomy/needle cricothyrotomy scalpel and blade, and large-bore nasogastric tube. Sachet lubricant, viral filters and inline suction catheter are essential.

Regional anaesthesia is preferable wherever feasible,[19] since tracheal intubation and extubation (essential parts of delivering general anaesthesia) generate aerosols and should be performed in a negative pressure operation theatre (OT).[17]

Closed loop communication is to be practised among caregivers.

Modification of surgical technique

Pertaining to the mode of surgery (open versus laparoscopic/robotic surgery), paradoxical as it may seem, conventional/open techniques are a better option due to apprehensions of CO_2 release from the ports showering corona viruses in the OT.[17] Monopolar devices, advanced bipolar cautery and ultrasonic dissectors should be minimally employed, apprehending particle-aerosolization.[17] Smoke-evacuator fitted monopolar diathermy pencils at lowest possible settings are advocated.[17] Oral and gut surgeries pose a greater threat to the operating surgeons, COVID-19 being transmitted by the respiratory tract and gut secretions.[8]

Emergency surgery (tracheostomy, obstruction, bleeding, perforation, sepsis, tension pneumothorax, massive pleural effusion with respiratory distress) and terminal care treatment must be attended to and surgeries with high probability of cure with early treatment must be performed.[8] Simple, short surgeries with minimal blood loss may be performed as against extensive liver resection, microvascular and cosmetic breast reconstructive surgeries or those requiring post operative ventilatory support.[8]

Training for donning and doffing technique of PPE-kit as per WHO-guidelines[20] should be arranged and hospital-grade antiviral wipes maybe used for cleaning the exposed areas/neck after doffing.[3]

Chemotherapyradiotherapy and immunosupression

Should chemotherapy be discontinued? Chemotherapy is known to precipitate profound immunosuppression[11,12] and building up a strong immunity is the best bet against any virus Corona being no exception. ICMR has advised empirical therapy with hydroxychloroquine (side effects: immunosuppression, prolonged QT-interval) for all caregivers,[21] but has met with limited compliance. Neo-adjuvant chemotherapy for breast, oesophagus, gastric and lung malignancies is preferable over surgery in COVID times.[8] Keeping radiotherapy, medical and surgical oncology departments as corona free-sanctuaries is the goal.[13]

Social distancing and shielding

There should be a single-entry point constantly manned by a security guard who screens all persons entering with a non-contact infrared forehead-temperature gun and sprays alcohol hand rub on their palms. Wearing a face mask must be made mandatory for any person entering the hospital complex. Trips to OPD-clinics multiply exposure and follow-up patients can safely take the telephonic route.[22] At a time of acute shortage of PPE-kits for caregivers the patients cannot hope to get any of these and remain in constant danger of corona cross-infection nosocomially. Social distancing (masked patients minimum 1 m apart) needs to be followed in any queues at the OPD, PAC-clinic, billing centres or hospital mess and dietary services. In the waiting area, individual stools/seats should be arranged with 1m radius of free space between them allowing only say 20 patients/attendants at any given time. An invigilating staff should be in charge of allowing only that many fresh people to enter as the number exiting the enclosure. Minimal staffing in the OTs and postoperative wards to reduce cross-infection is advised.

Short term implications

Psychologically and emotionally drained out cancer patients and their caregivers may become paranoid about COVID-19 and corona-counselling clinics and digital bridges may have to be setup.

Backlog of cancer patients will need to be tackled on a war-footing once the pandemic subsides.

Long term implications

Clinical trials on new cancer drugs have come to a grinding halt because researchers are in a madrush to launch clinical

trials of experimental vaccines, drug treatments and testing-kits against the COVID-19.[23]

Mortality from cancer in the months following the corona outbreak may spike due to two reasons. First, sudden spurt in the number of oncosurgeries to clear the backlog of patients deferred due to the nonurgent nature of their surgery. There is more likely to be an absolute increase in in-hospital complications and mortality, but the proportion of patients with complications/mortality out of the numbers being treated maybe the same as that in the precorona days. Second, in some cancer patients, the tumor, node, metastasis (TNM) staging would have progressed to the next higher inoperable levels. Chemotherapy, palliative surgery and empirical modes like HIPEC and PIPAC may be the new line of therapy in such patients with advanced disease. A retrospective comparison of cancer mortality in corresponding months of previous years will paint the true picture.

The brunt of financial losses to the hospitals may have to be borne by hike in healthcare charges in private institutions.

An already physically and mentally exhausted healthcare worker team maybe deprived of a well deserved holiday. Obsessive compulsive disorder in healthcare workers as a legacy of repeated hand washing and alcohol rub sanitization, and various stress-related health problems like depression may materialize.

Coping with cancer patients during COVID-19 pandemic at RGCI: Our experience

Rajiv Gandhi Cancer Institute and Research Centre is a premiere tertiary care institution of North India dedicated to comprehensive cancer care under one roof. Several administrative and engineering controls [Table 1] have been undertaken here in an effort to serve cancer patients in corona times taking adequate safety precautions in a resource-constrained setting. The same have been tabulated for the benefit of readers.

Table 1: Administrative and engineering controls undertaken for patients and staff at Rajiv Gandhi Cancer Institute

Controlling element	Description
Preliminary assessment in dedicated fever/flu clinic	Set up near the main entrance gate Every patient screened for temperature, history of cough, cold, travel to a COVID affected area All suspected cases referred to designated government hospital
Liberal use of hand sanitizers	Every person entering/exiting the hospital is required to wipe hands with alcohol hand sanitizers provided by security guard
Face masks	All healthcare providers, patients and attendants required to wear face mask for self-protection and preventing spread of aerosol borne infection. Majority of patients have personal masks (surgical/cloth/N95) Surgical masks are provide to every hospital staff member In high risk areas (OT, ICU, Emergency) N95 masks are provided with guidelines for reuse due to limited availability
Hydroxychloroquine	Prophylaxis for healthcare workers offered as per ICMR guidelines (two 400 mgdoses <12h apart, followed by 400 mg weekly for 7 weeks)
Crowd restriction in hospital (both patients and staff)	Restriction of one attendant per patient is strictly followed Consultants of various departments advised to devise a roster requiring alternate day presence in the hospital. Consultants are being rotated in the OPDs with postponement of appointments and advocating telephonic consultations based on a robust electronic medical records system. Follow-up of patients on telephonic advice Consultants ≥60 y, co-morbid persons requested to be extra cautious. Secretarial-staff given an off Medical staff segregated into non-intermixing groups and placed on rotation duty
Modification in operation theatre working	Number of operational major OTs curtailed to 8 from the existing 14 (with closure of one OT-block) with systematic staff rotation. All suspected in-patients kept in single isolated rooms in a segregated area with PPE supply and linen stored in a trolley outside the door. Nurses and paramedics posted to isolation facility and non-critical patient care equipment (stethoscope, thermometer, sphygmo manometer) are dedicated to the patient and not allowed elsewhere. 12 air changes/hour and filtering of exhaust air is ensured. These areas are not a part of central air conditioning.
Covid-19 Consent form	A new consent form has been designed wherein patient is informed that he/she stands the risk of infection
Chemotherapy and radiotherapy units	Taking up only those patients with time-sensitive issues as decided by treating units
Resource Constraints	Limited availability of PET-scan isotopes, blood-donors, PPE kits, N95 masks
Stress on each health care worker in present situation	Fear of getting infected and carrying infection home Resources, reading material and a helpline, for helping staff cope with COVID-19-related anxiety and burnout provided by hospital Stress in view of lockdown Road blocks and closure, repeated checking by law enforcing agencies making it at times difficult reaching hospital; Specific passes issued to staff to enable ease in commuting to and from the hospital. Domestic front: with all helping staff not available, the daily chores (washing, cleaning cooking, purchase) have also to be undertaken.

COVID: Corona virus disease; OT: Operation theatre; ICU: Intensive care unit; ICMR: Indian council of medical research; OPD: Out-patient department; PPE Personal prophylaxis equipment

Summary

The COVID 19 pandemic has multiple immediate, short and long term implications for the cancer patient and their caregivers.

Triage of patients, triage of equipment and triage of personnel is important.

The choice between cancer and corona is that between the devil and the deep C. An intentional postponement of adjuvant chemotherapy and elective surgery for stable cancer is advisable in Corona hotspots.

Mortality from cancer in the months following the corona outbreak may show a spike.

For healthcare workers the message is clear: use PPE, stay apart, stay safe, and do not bring it home.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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