



Guiding Principles for Cancer Surgery during the COVID-19 Pandemic

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Introduction

COVID-19 pandemic had an unprecedented adverse impact on health care services globally. This pandemic had started in the Wuhan city of China where the first case was reported on 31st December 2019 [1, 2] and on 11th March 2020 the World health organization (WHO) had declared it as a global pandemic and as a public health emergency of international concern [3]. Within a short span of 3 months a significant proportion of different geographic regions of the world are facing the impact of COVID-19 pandemic [4–6]. Government of India has imposed a nationwide lockdown from 24th March 2020 to contain the spread of coronavirus infection. The pandemic has caused major disruption of health care services both in high income and low and middle income countries with limited resources. The challenges faced by health care sector include, caring for critical COVID-19 patients in hospitals resulting in massive diversion of critical hospital resources, caring for non COVID-19 patient population with medical and surgical emergencies and last but not the least - protecting health care providers (HCP) and implement new infection control protocols. In most of the hospitals worldwide, surgeons are operating only on patients with life threatening emergencies and postponing majority of elective surgical cases. The challenges surgical community facing include screening for COVID status, protection of HCP, judicious use of limited personal protective equipment (PPE) and other hospital resources.

Major factors that will guide surgical practice in the current scenario are stage of COVID-19 pandemic in a particular country / region and availability of health care resources. Most of the countries are now reaching the stage of community spread of COVID-19 infection with a huge number of potential asymptomatic carriers and significant number of critical COVID-19 patients.

Based on the COVID-19 status of the region/hospital and availability of health care resources American College of Surgeons (ACS) has proposed 3 different phases that a health care setup can encounter. Phase 1 - Semi-urgent settings (Preparation phase): The disease is not in the rapid escalation phase and institutions have adequate resources such as hospital and ICU beds, ventilators and manpower to cater the services. Phase 2 - Urgent settings: Limited availability of resources due to increased number of COVID-19 patients. Phase 3- Hospitals are over burdened with COVID-19 patients and non-availability of health care facilities like operating rooms, beds, ICU and ventilators.

The challenges faced by surgeons treating cancer are unique, because most of the cancer surgeries are elective but cannot be delayed beyond a certain point of time due to biology of the disease and adverse impact on survival if surgery is delayed. Due to the protracted nature of COVID –19 pandemic surgical oncologists world over are facing ethical and moral dilemmas in day to day practice while taking decisions regarding cancer surgery. In order to overcome these challenges a number of scientific societies and organizations have recommended triaging of surgical patients and proposed guidelines for handling patients waiting for cancer surgeries. These organizations include American college of surgeons (ACS), society of surgical oncology (SSO), European society of surgical oncology (ESSO), National Comprehensive Cancer Network (NCCN), Irish head and neck society, British Association of Surgical Oncology (BASO) and British gynecological cancer society (BGCS) [7–12].

An attempt has been made in this article to summarize various recommendations and propose certain guiding principles which will help the surgeons treating cancer in making

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critical surgical decisions. These guiding principles are not based on any high level of clinical evidence due to the unprecedented nature of COVID-19 pandemic and treating teams should make individualized treatment decisions which are shared and multidisciplinary in nature depending on the local circumstances and status of the patient.

Cancer Surgery - Challenges during COVID-19 Pandemic

1. Apart from oncological emergencies, majority of cancer treatments are planned and elective in nature. However guidelines recommend that elective cancer surgeries should be given priority and should be performed in a time bound fashion due to the biology of the disease and impact on survival if treatment is delayed beyond a certain point of time.
2. Current management approach to cancer is multidisciplinary in nature and a significant proportion of patients receive pre or post-operative radiotherapy or systemic therapy (chemotherapy, targeted therapy or hormonal therapy) based on site, stage and histopathology.
3. In general cancer treatments take relatively long time (few months) to complete and involve multiple visits and admissions to hospital.
4. The field of cancer involves a diverse spectrum of diseases and clinical presentations with varied clinical trajectories.
5. Based on clinical presentation - Cancer patients can be grouped as patients presenting with oncological emergencies, patients presenting with early or locally advanced cancers which are potentially curable and patients presenting with advanced or metastatic disease suitable for palliation only.
6. Based on status of treatment cancer patients can be grouped in to - new patients presenting for workup and diagnosis, patients who have completed diagnosis & staging and waiting for initiation of treatment, patients mid-way through the treatment process and patients coming for post treatment follow-up.
7. Majority of cancer patients are immune compromised and relatively higher fatalities have been reported in cancer patients infected with COVID [13–15].
2. The basic tenets of cancer care – Multi disciplinary treatment approach should be followed using virtual technologies. Involve medical oncology, radiation oncology and palliative care for shared decision making.
3. Involve the patient and family in the decision making and clearly document the shared management decision in the file.
4. Minimize hospital visits of new patients and advise basic necessary diagnostic investigations only.
5. Advise cancer patients who have completed treatments and are disease free to stay at home. Tele consultations can be offered to these patients.
6. Any treatment planning should be made in the context of current and emerging covid situation, facilitating completion of oncologically appropriate treatment protocols in near future.
7. Operate on patients presenting with onco- surgical emergencies with all precautions as recommended for any surgical emergency during covid pandemic.
8. Decisions regarding elective cancer surgeries should be individualized based on type, stage, biology, availability of non-surgical treatment options and status of resources in the treating center.
9. Whenever feasible offer non-surgical treatment options in consultation with medical and radiation oncology (eg. Tamoxifen for hormone receptor positive breast cancer, pre-operative chemo/radiation for rectal or esophageal cancers) to contain or down stage the disease and subsequently plan elective surgery.
10. Offer surgery to patients, when non-surgical treatment options are not available or if the treating team feels that delay of surgery threatens patient's survival chances.
11. Postpone elective cancer surgery in patients with less aggressive and slowly growing cancers (differentiated thyroid cancer, prostate cancer, low grade soft tissue tumors, DCIS, basal cell carcinoma etc.).
12. Avoid aerosol generating procedures whenever feasible including endoscopies and laparoscopies.
13. Involve the anesthesia and critical care teams for surgical, critical care and post op recovery planning.

Proposed Guiding Principles for Cancer Surgeries during COVID Pandemic

1. The key determinants of decision making for cancer surgery during covid pandemic are – status of covid pandemic, availability of resources, patient and tumor related factors.

Key Points

1. All recommendations and safety precautions pertaining to patient screening, preparation of operation theatre, PPE, Intubation protocols, critical care protocols, human resource management, biomedical waste disposal and specimen handling should be strictly followed as described for any emergency or elective cancer surgery during COVID pandemic [16, 17].

2. These guiding principles are not based on high level evidence and can be considered as advisories to overcome the challenges posed by unprecedented COVID-19 pandemic affecting health care sector. Due to rapidly evolving nature of the pandemic these guidelines should not be considered as standard of care in the long term. Due to anticipated breakthroughs and advances related to understanding of COVID-19 management further modifications to the guidelines related to cancer surgery field are anticipated and surgical oncologists are recommended to access resources related to COVID-19 and cancer management on a regular basis for updates.

Proposed Organ Specific Guiding Principles for Cancer Surgery Decision Making during the COVID-19 Pandemic for Common Cancers

(ACS- American College of Surgeons, SSO-Society of Surgical Oncology, NCCN – National Comprehensive Cancer Network, BASO- British Association of Surgical Oncology, AHNS- American Head & Neck Society, IASLC – International Society for study of lung cancer)

Breast Cancer

SL	No	Subtypes	Recommendations by <u>(ACS, SSO, NCCN)</u>	Suggested non-surgical options
				Suggested surgical options
1.	Benign/premalignant lesions	Defer surgery for 3 months		Defer surgery for 3 months
2	ER +ve DCIS Premenopausal	Tamoxifen versus aromatase inhibitor (at the discretion of medical oncology) for 3-5 months.	Tamoxifen/Aromatase Inhibitors	Defer Surgery for 3 months
3	ER-ve DCIS	Low volume disease & low clinical suspicion of invasion – Defer surgery & reassessment Large volume disease – Reassessment 4 weekly for progression , if progressed then plan for Surgery		Defer surgery & reassessment 4weekly Reassessment 4 weekly for progression , if progressed then plan for Surgery
4	Her+ or TNBC	≥T2 and any N – NACT T1N0 – Can consider for surgery, Else NACT (as per local resources)	NACT& Reassess Complete NACT if Stable disease, PR or CR	Progression on or after chemotherapy – Consider for surgery
5	ER+/PR+	All Stages – Consider endocrine therapy for at least 3-5 months (Tamoxifen/AI) Reassessment 4 weekly Can also start chemotherapy (If indicated)	All stages- Tamoxifen/AI and response assessment Continue HT till progression	Surgery only if progression during HT
6	Post-neoadjuvant chemotherapy	Consider endocrine therapy (if PR/CR and ER+) and delay surgery versus surgery in 4-8 weeks. Can add anti-HER2 therapy along with endocrine therapy if HER2+	Consider HT (for luminal subtypes) and Anti - HER2 therapy for HER2+	Delay surgery as long as possible
7	Special cases – Malignant phylloides, Angiosarcoma	If TNBCdelay surgery for 4-8 weeks Consider for surgery		Consider for surgery

CR complete response, PR partial response, SD stable disease, HT hormonal therapy, AI aromatase inhibitors, NACT neo-adjuvant chemotherapy

Colo-Rectal Cancer

SL No	Subtypes	Recommendations by - ACS, SSO.	Suggested non-surgical options	Suggested surgical options
1.	Benign/premalignant lesions (polyps)	Defer surgery		Defer surgery/consider surgery if progression
2	Early stage colon cancer	Defer surgery		Defer surgery/consider surgery if progression
3	Locally advanced colon and Metastatic colon Cancer	Neoadjuvant therapy	Neoadjuvant therapy/ Oral capecitabine only	Defer surgery until progression or emergency indications
4	Rectal cancer (all stages)	Neoadjuvant CT+ RT (Prefer short course radiotherapy over long course radiotherapy) Delay surgery for 12–16 weeks post neoadjuvant therapy	Neoadjuvant therapy/ Oral capecitabine Post neoadjuvant treatment – can consider oral capecitabine	Defer surgery until progression or emergency indications
5	Emergency indications (Obstruction/perforation/bleeding)	Emergency surgery (Diversion stoma or resection of primary depending on intraoperative findings and hospital resources)		Emergency surgery (Diversion stoma or resection of primary depending on intraoperative findings)

Gastro - Esophageal Cancers

SL No	Subtypes	Recommendations by - ACS, SSO.	Suggested non-surgical options	Suggested surgical options
1.	Very early & superficial screen detected cancers.	Prefer endoscopic procedures		Defer Surgery
2	Early stage operable Cancers	Surgery	Esophageal cancer -NACT/ NACT+RT Gastric cancer - NACT	Prefer surgery/consider surgery if progression during neoadjuvant treatment
3	Locally Advanced Cancer	Neoadjuvant therapy (On completion of NACT and responding to it, patients can continue to stay on chemotherapy till surgery)	Neoadjuvant therapy (On completion of NACT and responding to it, patients can continue to stay on chemotherapy till surgery)	Defer surgery until progression or emergency indications
4	Emergency indication- Absolute dysphagia/ GOO	Prefer endoscopic procedures, if fails consider for surgery		Prefer endoscopic procedures, if fails consider for surgery

Hepato Pancreatico Biliary Cancers

SL No	Subtypes	Recommendations by - ACS, SSO.	Suggested non-surgical options	Suggested surgical options
1.	Early stage tumors	Consider surgery		Consider surgery if resources are available
2	Borderline resectable or locally advanced inoperable	Neoadjuvant treatment	Consider for neoadjuvant chemotherapy	Defer surgery until progression or emergency indications
4	Emergency indication- Obstructive jaundice/ GOO	Prefer endoscopic procedures, if fails consider for surgery		Prefer endoscopic procedures, if fails consider for surgery
5	Asymptomatic PNET, GIST, high risk IPMN's	Defer surgery	Consider systemic or targeted therapy	Defer surgery

Peritoneal Surface Malignancies

SL No	Subtypes	Recommendations by - ACS, SSO.	Suggested non-surgical options	Suggested surgical options
1.	Pseudomyxomaperitonei and colorectal tumors			
	Low grade appendiceal tumors	Defer Surgery		Defer surgery
	High grade appendiceal tumors and Colorectal tumors	Defer Surgery	Neoadjuvant chemotherapy	Defer Surgery
2	Mesothelioma	Consider systemic therapy. Defer Surgery	Consider systemic therapy	Defer Surgery
3	Ovarian Cancer	Consider systemic therapy. Defer Surgery	Consider systemic therapy/ Metronomic chemotherapy (Pazopanib/Endoxan/Etoposide)	Defer Surgery

Thoracic Malignancies

SL No	Subtypes	Recommendations by -ACS, IASLC.	Suggested non-surgical options	Suggested surgical options
1.	Ground glass nodules Pulmonary metastases	Defer surgery		Defer surgery
2	Carcinoids	Defer surgery		Defer surgery
3	Mediastinal tumors- Thymoma	Defer surgery unless symptomatic		Defer surgery
4	NSCLC T1a/T1b and node negative	Defer surgery	Defer surgery In adenocarcinoma- consider oral targeted therapy if suggested by mutational analysis	Defer surgery
5	NSCLC T1c or above and cN0, cN1	Consider early surgery for operable tumors	Neoadjuvant chemotherapy In adenocarcinoma- consider oral targeted therapy if suggested by mutational analysis	Defer surgery until progression
6	Emergency indication- Bleeding/hemoptysis, obstructed airway	Consider non-invasive intervention procedures, if fails surgery		Consider non-invasive intervention procedures, if fails surgery

Sarcomas

SL No	Subtypes	Recommendations by -SSO.	Suggested non-surgical options	Suggested surgical options
1.	Truncal/extremity low grade sarcomas (ALT, classic DFSP, desmoids)	Defer surgery		Defer surgery and assessment for progression 4–6 weekly
2.	High grade or recurrent sarcomas	Consider for neoadjuvant treatment (Chemo/radiotherapy)	NACT or NART	Defer surgery until progression
3.	GIST	Consider Imatinib	Consider Imatinib	Defer surgery until progression
4.	Emergency indications- Bleeding or obstruction	Consider for palliative surgery	Consider palliative radiotherapy for bleeding	Consider for palliative surgery

NART neoadjuvant radiotherapy, NACT neoadjuvant chemotherapy

Oral and Endocrine Tumors

SL No	Subtypes	Recommendations by -SSO, AHNS, Irish head and neck society.	Suggested non-surgical options	Suggested surgical options
1.	Thyroid cancer	Defer surgery		Defer surgery
2.	Parathyroid	Defer surgery unless life threatening hypercalcemia		Defer surgery unless life threatening hypercalcemia
3.	Adrenal tumors	Defer surgery unless medically uncontrolled		Defer surgery unless medically uncontrolled
4.	Oral Cancers Early & Locally advanced	Defer Surgery for T1 slow growing tumors involving low risk sub sites with node negative neck. Operable Locally Advanced Oral cancer	Consider for neoadjuvant chemotherapy /Chemoradiation/Oral metronomic chemotherapy	Defer surgery until progression
5.	Emergency indication- Bleeding/hemoptysis, obstructed airway	Consider non-invasive intervention procedures, if fails surgery	Consider non surgical options (RT/ embolization)	Surgery if non surgical options fail

Gynaecologic Cancers

SL No	Subtypes	Recommendations by - ACS, British gynecological cancer society.	Suggested non-surgical options	Suggested surgical options
1.	Ovarian Cancer	Consider systemic therapy. (Defer Surgery except pelvic confined suspected masses of ovarian cancer)	Consider systemic therapy Metronomic chemotherapy (Pazopanib/Endoxan/Etoposide)	Defer Surgery
2	Endometrium Ca (high grade/high risk uterine)	Consider for surgery within 4 weeks based on the urgency of symptoms	Consider for alternative treatment Radiotherapy/chemotherapy/Hormonal therapy	Consider for surgery
3	Early stage, low grade endometrial cancers	Defer surgery for 10–12 weeks		Defer surgery/ Consider surgery if progression
4	Cervical cancer	Defer surgery for CIN	Palliative radiotherapy for bleeding	Consider surgery for early stage cancer
		Consider surgery for early stage operable cancer Locally advanced cancers	Consider CT+ RT CT + RT	
5	Emergency indications – Bleeding, bowel perforation, peritonitis, torsion, rupture of suspected malignant pelvic masses	Surgery		Surgery

MELANOMA

SL No	Subtypes	Recommendations by (NCCN, SSO)	Suggested non-surgical options	Suggested surgical options
1.	Melanoma in situ	Defer surgery for upto 3 months		Defer surgery and assessment for progression 4–6 weekly
2	T1 melanomas (≤ 1 mm)	Defer surgery for upto 3 months even if positive margin on biopsy		Defer surgery and assessment for progression 4–6 weekly
3	Melanomas >2 mm thick (T3/T4)	Surgery should take priority over ≤ 2 mm (T1/T2)		Surgery should take priority over ≤ 2 mm (T1/T2)
4	Stage III disease (Clinically palpable regional nodes)	Defer lymphadenectomy and offer neoadjuvant systemic therapy immune blockade or BRAF/MEK inhibitors (Exception-if node encroaching vital structures eg., carotid artery, skull base). Surgery should be performed 8–9 weeks after initiation of neoadjuvant therapy	Neoadjuvant systemic therapy	Defer surgery
5	Metastatic resections (Stages III and IV)	Defer surgery and continue systemic therapy (as per hospital resources)	Continue systemic therapy	Defer surgery

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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