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Perspectives and View Points

Prostate Cancer Management During the COVID-19 Pandemic

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The COVID-19 pandemic has derailed the management of many cancers. Prostate cancer although a disease known for good response to treatment has posed unique challenges in this pandemic in view of the co-morbidities associated with these elderly patients. A pandemic specific treatment approach following the RADS (Remote, Avoid, Defer, Shorten) principle is required while dealing with these patients. Very low, low and favourable intermediate risk cancers may be kept on active surveillance rather than active treatment. Unfavourable intermediate, high and very high risk cases may follow the 'defer' policy by initiating hormonal therapy for 6-8 months to defer radiotherapy. When radiation is planned for these patients extreme or moderate hypo fractionation may be used to follow the 'shorten' policy. Metastatic hormone sensitive cancers may be initiated on hormonal therapy avoiding antiandrogens like Abiraterone and chemotherapy upfront. In the castration resistant phase the antiandrogens like Abiraterone or Enzalutamide may be given preference over chemotherapy. In the post operative settings early salvage may be preferred over adjuvant that too, using hypofractionation. Symptomatic patients require prompt attention and radiation should not be delayed for palliation of impending spinal compression or fracture or for local symptoms. Aggressive histologies like small cell types also need prompt treatment. Other general measures like universal masking, hand hygiene, physical distancing, respiratory etiquettes, etc., must also be emphasised keeping in mind the vulnerability of these patients.

Introduction

The unprecedented pandemic of recent times caused by the SARS-CoV2 virus aka the COVID-19 has undoubtedly disrupted lives of all to monumental proportions. At the time of writing this, there has been a total of 672,940 diagnosed COVID-19 cases in India, and a staggering 1,10,72,276 cases confirmed worldwide. And among those who required medical attention, cancer patients may have been among the most affected, although there may be no objective evidence for the same [1]. Prostate cancer has historically been considered to be associated with good response to treatment reflecting the long-term survival with reasonably good quality of life in majority of the patients. Known to be a disease of the elderly, this poses an unique threat in this pandemic in view of their age and associated co-morbidities. In general the RADS (Remote, Avoid, Defer and Shorten) principle in general is to be followed. They should be encouraged to access the health system by remote access and tele-consultation; avoid or defer active intervention when possible; and if treatment is planned, make it as short as possible. The rising evidence that ADT might have a protective effect from COVID-19 is opening up a new pandora's box for debate [2].

It often becomes a big dilemma whether to treat a prostate cancer patient or not during this pandemic. Calling the patient to the hospital for treatment puts them at risk of infection from COVID-19 and its associated morbidities and mortalities. It is all the more important as we know that the testing strategy is not infallible. The false negative rate of the standard RT-PCR is about

20%, if tested on day 8 of infection and may be even up to 100% depending on the day of testing [3]. The 30 day mortality rate for a covid positive patient who undergo surgery is to the tune of 24 percent [4]. Rather treating a positive patient also risks other fellow patients and healthcare workers and will jeopardise the whole health care system. On the other hand, if we avoid treating all prostate patients during this period it can be a real tragedy for some patients. Rapidly growing cancers can cause avoidable miseries and a deterioration in quality of life with urinary obstruction, gross hematuria and renal failure. Patients with spinal metastases can develop paraplegia and will have to lead a dependent life with poor quality till the end if not addressed promptly. So it is of utmost importance to stratify the patients and differentiate those who require urgent attention from those who can wait for treatment and for those the treatment can be avoided. Treatment of prostate cancer during this pandemic has become a real test for a clinician to use his clinical judgement for decision making.

Ordinarily the treatment of prostate cancer depends on the stage of the disease, risk group, life expectancy, performance status and the co-morbidities that the patient has. Localised prostate cancers are grouped into various risk groups based on their T stage, PSA level, Gleason score, number of core involvement, percentage of cores involved, PSA Density. Accordingly we have very low, low, favourable intermediate, unfavourable intermediate, high and very high risk groups.

Very low and low risk group are very slow growing cancers. There are studies which compared the options of radical prostatectomy, radical radiotherapy and active monitoring for these patients. The PROTEC-T trial which had randomized patients into these three treatment approaches has very clearly demonstrated that all the approaches yield equal results. So there is no controversy regarding the management of this sub-group of patients during this pandemic, as active surveillance alone was already a standard of care for this sub-group [5]. Active Surveillance is the standard of care and no staging investigation or imaging should be advised at present during this pandemic.

The behaviour of the favourable intermediate risk group patients is similar to the low risk group. For this group too, active surveillance may be offered, although there are no randomised trials comparing active surveillance versus definitive treatment in this group. Large prospective analysis does not show an inferior outcome [6]. Conventionally definitive therapy in the form of Radiation therapy or Surgery without ADT has been the standard of care for this group. Staging investigations may be delayed. It is advisable to put these patients on active surveillance during this pandemic. If at all there is any need to treat this sub-group of patients, it may be delayed till it is deemed safe.

Unfavourable intermediate risk group, high risk group and very high risk group will require some form of treatment. Staging investigation in the form of CECT Abdomen and Pelvis, MRI Pelvis and bone scan may be considered from patient to patient basis for unfavourable intermediate risk cases. For the high risk and very high risk cases, staging investigations should be done, even during the pandemic, as this would significantly affect further management and prognosis. The standard of care for unfavourable intermediate risk group is definitive therapy with radiation or surgery, with 4 to 6 months of ADT. [7]. However, neoadjuvant ADT may be given for longer duration (say for 6 to 8 months) during this pandemic, with 3 or 6 monthly regimens for obvious reasons. If radiation therapy is to be planned, the RADS principle is to be followed. High and very high risk cases merit treatment initiation as early as possible, especially due to impeding local symptoms and risk of metastasis. They should be started on neoadjuvant hormonal therapy. A little longer duration of hormonal therapy for say 6 to 8 months can be given to these patients without much impact on the overall treatment results. They should be promptly considered for definitive local therapy following this period. Radiation therapy should be preferred over surgery in these patients. In those considered for surgery, delaying surgery for up to 6 months have no major detriment in the outcome of these patients [8].

In patients considered for radiotherapy, the shortest hypo-fractionated regimen is the best one

during this pandemic. If logistics and facilities permit, these patients should be considered for stereotactic ablative regimes using 5 fractions. A dose of 36.25Gy/5 fractions is widely recommended. Some institutions including ours are following a dose of 40 Gy/5 fractions [9-10].

The SBRT protocol can be two fractions a week, every other day or one fraction per week all with equivalent results. If possible one should avoid interventions like fiducial placement and spacer placement during the pandemic. Image guidance is crucial while performing SBRT. We use realtime trans perineal ultrasound guidance and gating system (CLARITY TPUS) which do not require any fiducial placement for tracking at our institute. If facility for SBRT is not available patient may be considered for moderate hypo fractionated regimens like that of the CHHiP protocol of 60Gy in 20 fractions over 4 weeks [11]. Brachytherapy, although an important component in the management of this sub-group of patients, [12] may be avoided during the pandemic in view of it being an invasive procedure, requiring longer time to execute treatment and in-patient admissions. We may avoid prophylactically treating the pelvic nodes in those cases without an enlarged node during this pandemic.

For metastatic disease, ADT should be the standard of care. Antiandrogens like Abiraterone and Enzalutamide may be reserved for the castration resistant phase. Chemotherapy should be reserved for hormone refractory prostate cancer, after exhaustion of other 2nd line treatment options. Agents like Abiraterone and Enzalutamide may be preferred over chemotherapy in indicated patients. If at all chemotherapy is considered prophylactic G-CSF Should be given. Patients with low volume metastatic disease can be considered for SBRT 36 Gy/ 6 fractions.

Palliative radiation therapy for local symptoms (Urinary obstruction, haematuria etc) or metastatic sites (Spinal metastasis, spinal cord compression etc) should not be delayed by any means, as this would lead to further burden on the present delicate health care system, if they do present to the emergency department with these symptoms.

For patients who have indications for postoperative radiotherapy, we are fortunate to have the results of the RADICALS and RAVES last year which has shown that early salvage approach may be preferred over adjuvant. In fact it is all the more pertinent now to use this early salvage approach instead of the adjuvant approach during this pandemic. In these cases we should adopt hypo fractionated regimens like 52.5 Gy/20 fractions to cut short the patient visits during the pandemic.

Treatment of rare histologies other than adenocarcinoma, like small cell variant, which has an aggressive course, must not be delayed by any means, in view of the immediate risk to the life of the patient, and systemic chemotherapy must be initiated at the earliest.

Like all other cancers, prostate cancer too, require a “pandemic specific” modification of treatment approach, more so, considering the elderly age group and associated co-morbidities. Communication with the patient, is of utmost importance, regarding the evolving protocols of treatment and its impact on the outcome of treatment.

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