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EDITORIAL

HEAD-NECK CANCERS IN ELDERLY – DO WE TREAT THEM DIFFERENTLY ?

Head and neck cancer in elderly patients represents a major health problem because its management provides unique and complex challenges for multidisciplinary teams, such as reduced treatment tolerance, multiple comorbidities, and altered pharmacokinetics and pharmacodynamics. Despite the prominent challenges involved, high-level evidence for the management of this group of patients is scarce. Substantial advances in treatment, such as robotic surgery, dynamic intensity-modulated radiation therapy, immunotherapy, and de-escalation trials, might allow for improved treatment tolerance in this patient population. Advanced age alone does not appear to be a contraindication to curative treatment.

Who is elderly?

There is no universal cutoff age that exists for defining elderly patients. However, the Oxford English Dictionary defines geriatric as relating to old people, especially with regard to their health care. Sixty five years is the accepted age to define elderly individuals in high-income countries. The United Nations defines elderly as 60 years or older to account for shorter life expectancies in low-income countries. The National Institute on Aging at the National Institutes of Health classify elderly patients into three categories: young old (65–74 years), older old (75–85 years), and oldest old (>85 years). The issue of chronological versus biological age is a common dilemma faced by clinicians in the daily care of patients. Although chronological age is an important consideration, biological age is the dominant factor in the selection of the best treatment approach for patients with locoregionally confined head and neck cancer. A clinician is concerned with whether a patient is fit old (ie, likely to withstand curative radical treatment) or frail old (unlikely to withstand such therapy). These categories are somewhat arbitrary, Elderly patients often have a higher number of comorbidities and a lower performance status than do younger patients, which reduces their suitability for the optimal standard of care and probability of cure. Elderly patients are often under-represented in clinical trials and trials are often biased toward the fit-old group. Management of elderly is individualized and tailored to patient preference, symptoms, and institution or clinician preferences, rather than by the use of high-level evidence.

Radical surgical procedures can be performed safely in HNC patients who have no severe co-morbidities; indeed, it is likely that the severity rather than the number of co-morbidities is of greatest relevance in the decision-making process. Co-morbidity as measured by the Adult Comorbidity Evaluation-27 (ACE-27) index is a prognostic factor for overall survival in HNC patients aged >70 years. Sanabria has described a predictive index of postoperative complications in older patients undergoing HNC surgery based on five variables: bilateral neck dissection, two or more comorbidities, reconstruction, male sex and clinical stage IV. Comprehensive geriatric assessment (CGA) describes a multidisciplinary evaluation of an older individual's functional status, co-morbid medical conditions, cognition, psychological state, social support, nutritional status and medications. CGA can predict morbidity and mortality in older patients with cancer.

Conservative surgical techniques appear to be attractive option in elderly. One potential limitation is the lack of compliance with feeding and phonatory rehabilitation observed in older patients. Aspiration pneumonitis is also a major risk. A comparative analysisin patients undergoing reconstructive surgery withflaps showed that there was a major complicationrate of 12% in flaps used in older (aged >70 years) patients, as compared with 8% for those used inyounger (<70 years) patients. Transoral carbon dioxide laser surgery is another attractive option in older patients.

Increasing age does not affect overall survival and locoregional control. However, the occurrence of severe mucosal reactions significantly increasewith increasing age. It is suggested that chronological age is irrelevant for therapeutic decisions. However, it can be argued that subjective acute toxicity and lower tolerance to treatment are more commonly seen in elderly patients. Carotid Artery stenosis is an important cause of stroke.Ultrasound screening of carotids should be done if RT is planned and also during follow up in long term survivors.

Although randomized controlled trials have demonstrated superiority for concurrent chemoradiotherapy compared with radiotherapy alone, data about the benefit of chemoradiotherapy in elderly patients is conflicting. Decreasing benefit of concomitant chemotherapy has been found on survival with increasing age. Recent advances in systemic therapy for head and neck cancer have focused on the role of checkpoint inhibitors in the treatment of recurrent and metastatic disease. Early indications point to promising activity in patients who have progressed on platinum-based therapy, with a response rate of 10–20%. Nivolumab and pembrolizumab are two drugs that have been studied in the platinum refractory setting. These drugs appear to be well tolerated by elderly patients. No data currently support the incorporation of these drugs into the curative setting.

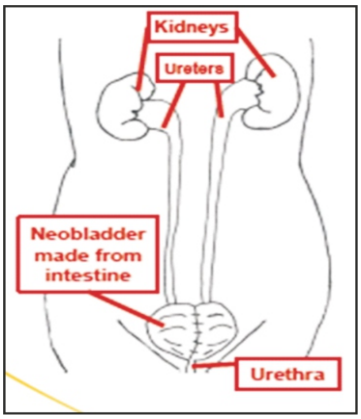
In nutshell assessment of elderly patients includes the evaluation of clinicopathological and age-specific factors. A clinicopathological assessment involves routine multidisciplinary assessment, as is done for newly diagnosed head and neck cancer. Age-specific assessment involves life expectancy estimation and evaluation of comorbidities, performance and functional status and psychosocial support. After correction of physiological and biological risk factors, a large proportion of geriatric patients can and should be offered the same cancer treatment as that offered to younger patients.

Dr. A. K. Dewan
Director - Surgical Oncology

INCHING TOWARDS A NORMAL LIFE POST CYSTECTOMY WITH PITCHER'S POT ILEAL NEOBLADDER

Bladder cancer is the ninth most common cancer accounting for 3.9% of all cancer cases as per the Indian Cancer Registry data. It is the second most common urological cancer among patients presenting to Uro-oncology Disease Management Group at our hospital. Increasing use of tobacco and increasing risk of exposure to industrial chemicals are the likely causes for Bladder cancer. In Muscle invasive bladder cancer (MIBC) tumour cells invade into the detrusor metastasis, the negativity of urethral biopsy. muscle of the bladder. The detrusor muscle is the thick muscle deep in the bladder wall. This cancer is more likely to spread to other parts of the body.

Radical cystectomy and urinary diversion have been the mainstay of treatment for muscle-invasive urothelial (transitional cell) bladder cancer for decades and remain the standard by which other treatments are judged. Radical cystectomy and urinary diversion has high morbidity (20-50% short term and up to 90% long-term morbidity) and mortality rate (0-5%), Therefore it is advisable to get these surgeries done by high-volume surgeons and hospitals to achieve improved outcomes for cystectomy when measured by perioperative mortality, recurrence rates, complications, duration of hospital stay, and cost. After radical cystectomy (RC), several techniques of urinary diversions (UD) are possible: ureterostomy, ileal conduit (IC), orthotopic neobladder (ONB) etc.



Picture 1: Diagrammatic description of orthotopic neo bladder

The two most commonly practised techniques are IC and ONB. Patient and surgeon preferences, health status, diseasestage, and targeted QoL should all be considered in the selectionof UD. With advancements in robotic surgery, the morbidity associated with RC+ neobladder has been reduced in terms of short hospital stay, lesser blood loss, lesser pain & return to regular activities. With these advancements now more patients prefer to undergo neobladder during adical cystectomy.

Neobladder

Orthotopic neobladders are internal reservoirs connected to the native urethra that rely upon the external striated sphincter and a high-capacity, low-pressure reservoir for continence. Because this approach facilitates the restoration of normal self-image by approximating normal voiding, orthotopic neobladders have become the procedure of choice for many patients requiring reconstruction following cystectomy for bladder cancer. We at Rajiv Gandhi Cancer Institute and Research Centre have started Pitcher pot bladder in the early 2000s & have seen successful outcomes with this procedure.

Picture 2: Open Pitcher pot neobladder

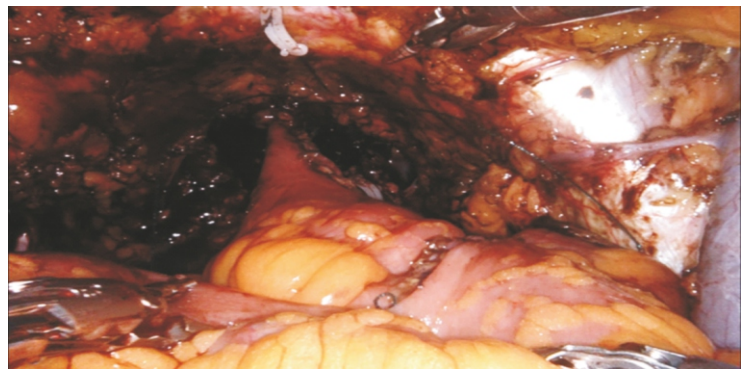
The usual oncological indications are: the same as for radical cystectomy (clinical stage T2, T3a, T3b, T1 high grade uncontrolled endoscopically), with the absence of metastasis, absence of nodal metastasis, the negativity of urethral biopsy.

The advantages of ONB (orthotopic neo-bladder) are

1. Orthotopic position of bladder resembling the original bladder in location and function, providing the most physiological form of voiding,
2. Maintenance of self-image,
3. Maintenance of interpersonal relationships and,
4. The QOL (Quality of Life) is preserved to a higher degree than ileal conduit urinary diversion. The patient voids with the relaxation of the pelvic floor muscles and Valsalva manoeuvre.
5. The cost effectiveness on the long run for the patient is lesser in neo-bladder compared to ileal conduit owing to maintenance cost of stoma.

A meta-analysis of various comparative studies on the impact of different types of urinary diversions on quality of life showed a significant advantage of ONB compared to IC.

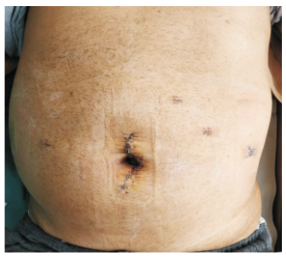
Our hospital data shows the median time to achieve day and night time continence was 9 and 12 months respectively. Less than 2% of patients did not achieve continence. Robotic cystectomy patients had lower median blood loss compared to open cystectomy patients (220 vs 310 ml) and hospital stay (eight vs nine days). Urinary health-related QOL reached levels similar to preoperative values for almost all patients. Open surgery was associated with significantly higher 'any' complication (40% vs 27%) and 'major' complication rate (15% vs 11%). Less than 2% of patients developed the need for long term intermittent self-catheterisation.



Picture 3: Intra-operative picture of Robotic orthotopic pitcher pot neobladder

Despite being better it's not done frequently in India because:

1. Late presentation due to ignorance, low literacy rate and poverty giving rise to the high-stage disease or renal impairment not suitable for ONB.
2. A large number of patients first present to a general practitioner who try to control the disease with some medicinal means and hence, delaying the proper treatment.
3. Lack of training, expertise and facilities to reconstruct ONB.
4. The low acceptance rate for ONB due to nature of job and need of intermittent self-catheterization.
5. Some centres reported a slightly higher incidence of early and late surgical and metabolic complications in the continent diversion as compared to ileal conduit.
6. Poor compliance and follow-up due to lack of education and resources.



Picture 4: Robotic surgery done with small incisions

Conclusion: The decision about which urinary diversion will be best suited to the individual patient is a complex one and depends on multiple factors relating to the patient and tumour, as well as a clear understanding about the risks and benefits of each diversion. ONB reconstruction is better than IC urinary diversion in terms of physical, role and social functioning, and global health status / QoL and financial burden. So, hopefully, in future the neobladder is performed more than ileal conduit by understanding its pros & cons.

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THE RACE FOR COVID - 19 VACCINE

As someone rightly said:

"Developing a vaccine against COVID-19 is the most pressing challenge of our time - and nobody wins the race until everyone wins".

The SARS-CoV-2 pandemic has led to worldwide devastation in terms of infections, deaths and economic damage. Unfortunately the maximally impacted are, the elderly, the immunocompromised, those with cardiopulmonary comorbidities as well as the economically underprivileged. It has caused more than 7.5 crore infections and 15 lakh deaths globally and disrupted the lives of billions of people. It is clear that a vaccine is urgently needed to prevent the spread of this pandemic.

An unprecedented effort is under way to rapidly develop Covid-19 vaccines, with pharmaceutical companies, academic researchers, and government agencies aiming to compress into several months a process that typically requires at least several years. This work is supported by extraordinary public and private investments. Concurrent with clinical testing of vaccine candidates, new mechanisms are being established to expedite manufacturing and distribution ahead of a future vaccination campaign. As per WHO there are more than 50 candidate vaccines under clinical trials of which about 8 are in advanced stages of testing. It is supporting the building of manufacturing capabilities, and buying supply, ahead of time so that 2 billion doses can be distributed worldwide by the end of 2021.It is believed that India too, has tied up with various indigenous and foreign manufacturers to secure 1.6 billion doses of the vaccine for its citizens.

The world reached a historic point in the fight against covid pandemic when UK announced mass vaccination drive early in the second week of December. India which is the worlds largest vaccine producer and second largest country hit by covid, is likely to roll out a vaccine in the next few weeks. Although Pfizer is the frontrunner in the race, it is an mRNA vaccine and requires storage at very low temperatures (-70^{0}C), therefore it is not suitable for widespread use in India due to logistic reasons. Hence India is considering two indigenous vaccine candidates, one being developed by the Serum Institute of India in partnership with AstraZeneca and Oxford University and the second one by Hyderabad-based Bharat Biotech (Covaxin, in collaboration with ICMR). Both these are conventional vaccines somewhat similar to the flu vaccine.

Recent updates reveal that the Pfizer vaccine has an efficacy of 95%, and the Company has sought permission from Central Drug Controller to import the vaccine for sale and distribution in India. The two India based vaccines, AstraZeneca's, Covishield, with a 65% efficacy, and Bharat Biotech's Covaxin (60% efficacy) have applied for emergency use authorisation of the vaccine. India's first homemade mRNA vaccine (HGCO19), being developed by Gennova in Pune, has received permission for human trials. It is believed to be stable at 2-8 degrees for2 months and will be a boon for India. The Russian Sputnik vaccine in collaboration with Dr Reddy's Laboratories is also doing human clinical trials in India. There are a few other candidate vaccines in advanced phase two clinical trials.

What is interesting is that two doses will be required for most of these vaccines. Although the acute side effects of these vaccines are similar to other viral vaccines, like pain at injection site, headache, fever, fatigue etc, one will have to wait and see what is the exact nature and incidence of late side effects.

Who will be the first to get vaccinated?

Initially the availability of the vaccine will be quite tight. As per the Health Ministry, GOI, health care workers, frontline workers of other departments, senior citizens and those with co-morbidities will be prioritized to receive the first supplies of the vaccine.

Logistics

Although India runs a massive immunisation programme, has a track record of immunizing nearly 55 million people each year, these are newborns, children and pregnant women, most of whom receive free doses through government run agencies. However it is clearly going to be a challenge to vaccinate millions of adults. Furthermore almost all vaccines are cold chain vaccines ie need to be transported and distributed between 2C and 8C. So, India does have about 27,000 "cold chain" stores from where stocked vaccines can reach more than eight million locations. We will also require a billion disposable syringes and other supplies. One will also need to track the vaccinees, and IT inputs and co-ordination with state health programs will be much needed.

Hence we can see that critical decisions will need to be made, not only regarding scientific evaluations of data on vaccine safety and efficacy, but also regarding issues related to prioritization, distribution, logistics, tracking deployment and co-ordination.

As someone rightly said, "Developing a vaccine against COVID-19 is the most pressing challenge of our time - and nobody wins the race until everyone wins".

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