Uro-Oncology: An Evolution of Past Four Decades in India

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During the last 40 years, Uro-oncology as a subspecialty has slowly and steadily evolved and a lot of urologists are getting interested in this superspecialty. At the same time, uro-oncology remains affiliated to Urology – the parent specialty. In the early 1970s, Urology was a part of General Surgery and many general surgeons tackled urological and uro-oncological patients as per concepts of treatment that prevailed then. Urology as a separate specialty also evolved slowly and initially it started as a subsection of ASI around 1960. When Urological Society of India was initiated from the year 1991, there were less than 200 members but with increasing interest in Urology over the years, the number of members practicing solely Urology has increased approximately to 2000 in the year 2010. Today, there is a wider scope for Uro-oncology provided there are adequate numbers of centres to train urologists in this subspecialty, with sufficient number of patients with urological cancers to impart the desired expertise.

Initiation of Uro-oncology as a superspecialty was only possible those days in Cancer Hospitals which were major referral centres. Large numbers of patients with urological cancers were and are still treated at the Cancer Hospitals rather than other general or private hospitals. Around 1970, there were no trained urologists in the cancer centres except at the Tata Memorial Centre (TMC). A separate superspecialty of Uro-oncology was initiated in 1973 at the Tata

Memorial Hospital only, though the expertise for the same was available since 1970.

Prior to 1970, cystoscopes were battery operated and resectoscopes non-existent. Fibreoptic cystoscopes and resectoscopes became available just about the same time improving the diagnostic and therapeutic ability for patients with bladder cancer. For diagnosis of upper urinary tract, IVP and retrograde pyelography were a routine. Transfemoral renal angiogram was a special investigation carried out with the help of a vascular surgeon.

Evolution of newer imaging techniques over the years has not only made early diagnosis of cancer possible but also helped in planning the therapy with improved survivals. Ultrasonography which became available around 1980 was a significant landmark and was of major help to image urinary tract much faster than IVP and slowly replaced it. With improvement of the machines and availability of Doppler, quality of the imaging and consequently the diagnostic ability improved immensely. For Uro-oncology, USG became useful for detecting renal masses, testicular tumours and prostatic lesions at an early age. In fact, because of routine USG of abdomen done for health check ups or any vague abdominal symptoms, incidental renal tumours are being detected when they are small and asymptomatic. This has enabled the urologists to treat these lesions effectively with nephron sparing surgery in many patients, which in turn has resulted in improved survivals in renal cell carcinoma.

USG also became useful for imaging small scrotal swellings to confirm whether they arose from the testis or epididymis. Imaging bilateral inguinal nodes in obese patients with penile carcinoma has also been of a great help. Transrectal ultrasound for prostate imaging has become an important supportive investigation for carcinoma prostate, though its correlation with clinical examination and PSA findings is

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necessary for optimal interpretation. It will be a fair statement to say that ultrasound has offered a sound initial investigation with its simplicity to be followed stepwise with subsequent modalities of imaging for getting more information.

CT scan became available around 1982 which was a major breakthrough in imaging any part of the body since total body could be scanned with thin slices in coronal or sagittal fashion. With the help of contrast enhanced CT, diagnosis of cancer, not only of urinary tract but also regional and distant metastatic disease became possible. Renal, ureteral, bladder cancers could not only be diagnosed but also could be staged to a large extent. Enlarged nodes could be accurately demonstrated by CT scan in renal, bladder and testicular tumours. CT angiography and tridimensional spiral CT scan, when became available (1987), helped in planning nephron sparing surgery for renal tumours especially in difficult anatomical locations.

MR imaging became available around 1986, which has the advantage of avoiding radiation associated with CT scan and added another accurate mode of imaging, especially useful for prostate cancer to define the extent of disease – whether the disease is within or outside the prostatic capsule and for planning appropriate therapy.

Help from Nuclear Medicine which was introduced around 1960, helped to detect skeletal metastases from urological cancers. Positive scan indicated by the increased uptake in the bones needs to be differentiated from conditions other than malignancy.

The latest addition to the armamentarium of imaging modalities – PET-CT, a combination of functional and anatomical imaging to detect distant metastases has been an ultimate investigation to scan the entire body for possible spread. It became available around 2005 with dedicated machine available since 2007. Needless to say that though it has a great potential, it also has certain limitations which need to be recognized and taken into account while interpreting its results.

Though imaging of any kind does not offer histological diagnosis, it is now possible to do USG or CT guided needle biopsy with their help to reach the histological diagnosis.

Oncologists have always hoped for a blood test to detect cancer which would be simple and specific. This dream has never come true as of today. Serum acid phosphatase level was routinely used for carcinoma prostate around the 1960s and 70s but it was neither cancer specific nor could it detect early prostate cancer. Around 1980, PSA became available though in India, it took some time for the laboratories to have it done in a standardized fashion. PSA with its different fractionated components has become an important tool to make early diagnosis possible in prostate cancers. Since then, it is used routine in Western world and increasingly so in India. The great enthusiasm for using PSA values on a

routine basis for early prostate cancer detection from 1980 to 2005 is on the decline in the Western World because over the years, the annual cancer specific mortality has not reduced significantly. With increasing awareness in India, PSA estimation still has a large role to play but at what age we should start advising it for its maximum utility is a matter of debate. This will eventually translate into more patients of prostate cancer being detected early enough to be suitable for potentially curative treatments. Other extremely useful biomarkers alpha-fetoproteins and beta-hCG (though not cancer specific) became available from early 1980s. Although elevated in 80 % of non-seminomatous tumours and not useful in seminomas, they have made a tremendous impact on the management of testicular germ cell tumours. Initial enthusiasm for using NMP 22 as a marker for bladder cancer for initial diagnosis as well as for detecting recurrence has not held its ground over the years.

Presently, a new vista has opened in the field of Genomics. Specific chromosomal alterations in various types of cancers has been demonstrated which hopefully will open the doors for detecting individuals with a high risk of developing cancers and in those who already have diagnosed cancers, will identify those who are likely to have microscopic spread or predict those who will fail primary treatment and develop metastases subsequently.

So far as the treatment strategies are concerned, around 1970, the treatment planning took into consideration the locoregional spread and hence there was a clear consensus about radical nephrectomy and radical cystectomy which included thorough dissection of the draining nodes either retroperitoneal or pelvic. This was implemented in this country around 1970. However, most of the patients with testicular tumours presented with large scrotal masses and most of them were associated with large abdominal node masses. After orchidectomy, they uniformly received radiation to retroperitoneal area, mainly because there was no well defined strategy for its management. With availability of effective chemotherapy in 1982, even large retroperitoneal nodes regressed remarkably. A complete retroperitoneal lymph node dissection was started around 1985 which was accomplished even when the post-chemotherapy residual lymph node masses were large. A definite expertise those days was needed to lift up large residual nodes from the IVC and aorta. It was routinely done at TMC without the backup of a vascular surgeon. Nerve sparing RPLND, a very fine-tuned surgery was started in 1992 at TMC with inspiration from Dr. John Donohue from Indiana University Medical Centre, Indianapolis, USA. This obviously became popular later on all over India. Radical cystectomy with pelvic node dissection was hardly carried out before 1970 and if at all, cystectomy was done for salvage after radiation therapy and the urinary diversion used was ureterosigmoidostomy with all its associated problems. Ileal conduit type of urinary

diversion that was established abroad around 1950 was not practical in India because of non-availability of good urinary collection bags or devices. A Stoma Clinic was established at TMC in the year 1983 which provided total stoma care including pre-operative counseling, stoma marking, providing urinary collection bags as well as post-operative stoma care. Thereafter, the Stoma Clinic trained nurses from across the country in the management of stomas. This was a great relief to all the surgeons who wanted to do radical cystectomies with ileal loop diversion which is still popular. The idea of continent urinary diversion was translated into practice at TMC by doing the first neobladder in India in 1986. The technical innovation of preservation of prostatic apex for anastomosis with the neobladder was introduced and resulted in a better continence and excellent functional outcomes. The acceptance by the patient, of radical cystectomy with neobladder by which the patient continues to pass urine through the natural passage with good control, is undoubtedly superior to that after ileal conduit. Even today, there are not too many centres in India who practice neobladders routinely and this procedure needs to be popularized more in our country.

Though classical node dissection for RCC was being practiced around 1980, its routine role in all patients is now being questioned and the zone of dissection has narrowed to the hilar region unless the nodes are metastatic. Nephron sparing surgery (NSS) those days was practiced mainly for tumours in the solitary kidney. Now NSS is being practiced routinely for tumours <7 cm when suitably located even when the other kidney is normal. The oncological outcomes after NSS are similar to those after radical nephrectomy. Surgery for renal cell carcinoma posed a great challenge when patients presented with tumour extension to IVC with upper limit of the thrombus at varied levels from renal vein to right atrium. This expertise was also brought into this country and first such successful operation was done with the help of cardiovascular surgeon using bifemoroatrial bypass in 1985 when the tumour thrombus was extending along the IVC till its entrance into the right atrium.

Four decades ago, patients with prostate cancer were diagnosed in advanced stages – majority of them with skeletal spread. For them, bilateral orchiectomy was the standard uniform treatment. For patients with bone pains, focused radiation therapy was being given and suprapubic cystostomy was done for urinary obstruction. With the availability of PSA as a marker, and with the use of suitable imaging studies, it became possible to better evaluate and stage prostate cancer to plan appropriate therapy. LH-RH analogues became available around 1990 thereby providing a substitute to orchiectomy. Thereafter, the concept of total (maximal) androgen blockade came with the research work done by Labrie et al. (1989), claiming superior cancer

related outcomes. However, with limited benefit and increased morbidity and cost, treatment option of total androgen blockade for metastatic prostate cancer is still a debated issue.

With the help of PSA assays, transrectal ultrasound and increased awareness in the population, it became possible to diagnosed prostate cancer in the organ-confined stage. This picked up quickly in the western world, with the result that the number of radical prostatectomies done in USA galloped from 1982 onwards. The first reports of high volume radical prostatectomies came from Johns Hopkins and Mayo Clinic. Since then, radical prostatectomy for patients with organ confined prostate cancer became a routine procedure. In our country, the necessary awareness presently exists only at the city level but in future, increasing number of patients will be diagnosed at an early stage and radical prostatectomies will be done routinely at many more centres. Radiation therapy for early prostate cancer has also emerged as an optional competitive treatment with certain limitations. Presently, it is being offered to a patient as an alternative treatment, after explaining all its advantages and disadvantages for the patient to select. The first radical prostatectomy was carried out in TMC in 1987. Although suitable patients for this surgery were very few in those days, more and more patients are now being diagnosed with organ confined disease and are suitable for this surgery at present.

Penile cancer was very commonly seen in cancer centres in the 60s and 70s. Though with improving penile hygiene, the incidence of penile cancer now seems to be on the decline, a significant number of patients still come on the records of cancer hospitals. Surgery in the form of partial or total penectomy with or without groin node dissection was advocated in those days and still remains the surgical standard today. The problem of skin flap necrosis producing wound dehiscence and increased lymphorrhoea was solved in 1990 with the help of plastic surgeons who primarily covered the defect with the tensor fascia lata myocutaneous flap which allowed the wound to heal primary and also reduced the incidence of lymphoedema of the scrotum and lower extremities. Today, the major morbidity of wound problems traditionally associated with groin node dissection is seen uncommonly with the use of flaps and the plastic surgeons have a number of different flaps to choose from to suit individual patients.

Radiation therapy was another modality to treat cancer patients with conventional machines available in those days, which resulted in severe reaction in the surrounding tissues and skin. Muscle invasive bladder cancers and large retroperitoneal metastatic node masses were then treated with radiation therapy merely for palliative purpose. Those days, a lot of urological cancers were in the category of palliative treatment and hence radiation therapy was a chosen modality in many patients. With the availability of linear accelerators

and technical innovations, it has now become possible to deliver large doses of radiation in a precise manner thereby reducing morbidity. Radiation therapy, however, plays a limited role in urologic oncology and is preferred in selected patients with seminoma, as a part of bladder preservation protocols for muscle invasive bladder cancer and for locally advanced T3 prostate cancer.

The concept of combination therapy with radiation therapy followed by surgery was initiated at TMC around 1980 for muscle invasive bladder cancer, with improvement in survival. The concept at that time was control of the primary disease in the pelvis and to prevent pelvic recurrences. With availability of effective systemic chemotherapy, however, the role of radiation therapy has narrowed down.

Chemotherapy – the third modality to treat cancer, was in its infancy around 1970 when only a few drugs were available and was hardly used in Urologic Oncology. After availability of platinum compounds and trials with its combinations with other drugs, the scenario of treatment strategies in uro-oncology changed immensely. The prime objective of cancer control shifted from control of locoregional disease to subclinical or evident systemic control. Effective combination chemotherapy brought testicular cancers even when advanced, under the purview of potentially curative tumours – a major breakthrough indeed and as of today, it remains a model of result oriented treatment for rest of the cancers. Advanced bladder cancer also did not have any hope those days, except radiation therapy for palliation. With the introduction of M-VAC regimen by MSKCC group, even patients with advanced disease responded well and could be palliated effectively. This brought muscle invasive bladder cancer with its subclinical or clinical metastases under the umbrella of chemotherapy responsive cancers. With further trials with less toxic combinations of drugs, improved survival rates were reported when used in the neoadjuvant or adjuvant fashion along with surgery or radiation therapy. Around 1965, recurrent superficial bladder tumours were treated with intravesical instillation of thiotepa after TUR-BT, with favourable outcomes. Over subsequent years, thiotepa was replaced by various more effective chemotherapy agents till intravesical BCG immunotherapy became the gold standard of instillatory treatment from the year 1987 and remains so today. Following availability of many more effective chemotherapy agents over the years, multiple trials using these for the treatment of testicular, bladder and even prostate cancer are currently ongoing. Advanced castration resistant prostate cancer which hardly responded to any therapy can be effectively treated today with docetaxel chemotherapy, with fairly good response rates and encouraging survival results. New agents like cabazitaxel in docetaxel-failure group and Cytochrome P-450 inhibitor abiraterone have shown encouraging responses. Prostate Cancer Working Group has embarked

on testing many more agents to treat HRPC patients. Such a breakthrough is awaited with a great hope.

In recent years, the concept of molecular targeted therapy has evolved with many agents available for various cancers. These glycoproteins essentially block the cytokines which promote the growth of cancer cells or block the angiogenesis which is associated with the disease. In short, they arrest the growth of cancer cells by blocking various pathways and their downstream events. The tyrosine kinase inhibitors and angiogenesis inhibitors for renal cell carcinoma have given encouraging results. Such targeted therapies are likely to be evolved for all cancer with ongoing research and their use either alone or in combination with chemotherapy seems to be on the horizon.

Oncopathology is the backbone for planning therapy and needless to say that the pathology expertise available for a surgeon profoundly influences dispensation of optimal therapy. Oncopathology has progressed with innovations like immunohistochemistry, which identifies variety of cancers. It can also identify markers which can predict biological behaviour of cancer to offer help in selecting chemotherapeutic or targeted therapies.

Lastly, 4 decades ago, we were depending upon personal experience based on the data available with us or relied on published reports of retrospective analysis from the western world, to decide treatment strategies in a given patient. At that time, even such analysis was lacking in this country for multiple reasons. After 1975, it was possible to carry out a randomized study comparing two treatment approaches to evaluate which of the two was better. Today, the treatment approach is completely evidence-based based on results of randomized controlled multicentre trials which have statistical validity. This has enabled us to draft treatment guidelines for a given patient. While these are the best guides to optimal therapy, the clinician must decide the best treatment for an individual patient based on guidelines and his own clinical judgment considering all aspects under our own circumstances in India. Cost-benefit ratio, side reactions of therapy, additional survival benefit at the cost of impaired quality of life are extremely important factors that must be taken into consideration while embarking on treatment.

I have not gone into the details or merits of surgical approaches of open, laparoscopic or robotic surgery. In recent years, there has been a progressive shift towards the minimally invasive approaches, with their inherent advantages and some limitations. Needless to say that minimally invasive surgery should be the approach of choice only if it meets all the principles of cancer surgery and more importantly, if performed by an adequately trained surgeon. All those who perform either laparoscopic or robotic surgery should have the basic foundation of performing open surgical procedures. Also, it has been clearly and scientifically reported that by doing only a few surgical cases a year by any methodology, even after one has learnt the basic

surgical techniques, the surgeon remaining in the learning curve are high, resulting in poor surgical, oncological and functional outcomes. Every surgeon involved in the practice of uro-oncology needs to keep this aspect in mind.

Uro-oncology has an open horizon like any other super specialty. Those trained uro-oncosurgeons who concentrate on a narrow zone with deep understanding of cancer biology, are likely to deliver optimal and high quality treatment with improved outcomes as opposed to those who are treating a wide spectrum of urological diseases.

It is most essential at this stage that we carry out randomized clinical trials in our patients since the patient population from the western world may be far different from the one in India. I am sure that the Departments of Urologic Oncology at large institutions can take up this challenge to script the management guidelines for our patients.

I am confident that the eminent contributors of articles in this journal are well experienced and the topics covered by them will be very informative for a sound practice in Uro-oncology.