

Round Up

ROLE OF EXTENDED PELVIC LYMPH NODE DISSECTION IN THE MANAGEMENT OF PROSTATE CANCER

The role of extended pelvic lymph node dissection in the management of prostate cancer is controversial. A single-center, phase 3, prospective randomized control trial was performed between limited (obturator only) or extended pelvic lymphadenectomy in patients with intermediate- or high-risk localized cancer prostate.^[1] Biochemical recurrence-free survival (BRFS) was the primary endpoint, and secondary outcomes were metastasis-free survival (MFS) and cancer-specific survival. Median BRFS was 61.4 months in the LPLND group and not achieved in the EPLND group (hazard ratio [HR] 0.91). Secondary endpoints with regard to median MFS were not achieved in either group and there was no death to calculate the cancer-specific survival. On subgroup analysis, those with ISUP grade 3–5 who had EPLND had better BRFS (HR 0.33, 95% confidence interval 0.14–0.74, $P = 0.007$). The study suggests that EPLND may be offered to patients with aggressive histology. The major limitation of the study is the short follow-up and small sample size. It could act as baseline data to start a large multi-institutional study to verify the findings.

COMPARISON OF LONG-TERM EFFICACY OF CONTEMPORARY TREATMENT OF BLADDER OUTFLOW OBSTRUCTION FOR BENIGN PROSTATIC HYPERTROPHY

TURP and open prostatectomy are the accepted gold standards for the treatment of bladder outflow obstruction due to benign prostatic hyperplasia. Photoselective vaporization and laser enucleation of the prostate are used frequently. There are limited head to head data on comparison of long-term efficacy of these treatments. In a study from the German Local Healthcare Fund Registry involving a total of 43,041 patients undergoing these procedures, 5-year efficacy defined as the need for reintervention was studied.^[2] About 12.5% of patients required reinterventions. Photoselective vaporization carried an increased hazard of reintervention (HR 1.31, $P < 0.001$) compared to TURP while open prostatectomy had the lowest risk (HR 0.43, $P < 0.001$). Laser enucleation was at par with TURP with regard to reintervention. Reintervention rate is a good indicator of long-term efficacy of surgery for relief of bladder outflow obstruction. The strength of the study is the large

number of patients and multiple institutions with different levels of care and a 5-year follow-up. Limitations include non-inclusion of immediate complication rates and an early learning curve with laser enucleation of the prostate.

LENVATINIB IN COMBINATION WITH PEMBROLIZUMAB OR EVEROLIMUS VERSUS SUNITINIB IN ADVANCED RENAL CELL CARCINOMA

The treatment of metastatic renal cell cancer (RCC) has been rapidly changing in the last few years. A multicenter randomized control trial was conducted on 1069 subjects to assess the efficacy of lenvatinib in combination with pembrolizumab or everolimus versus sunitinib in advanced RCC.^[3] The primary endpoint was progression-free survival (PFS). The median follow-up was 26.6 months. PFS was longer with lenvatinib plus pembrolizumab than sunitinib (median 23.9 vs. 9.2 months, HR 0.39; $P < 0.001$) and also longer with lenvatinib plus everolimus than with sunitinib (median, 14.7 vs. 9.2 months; HR 0.65; $P < 0.001$). Median overall survival (OS) was not reached in any treatment arm. OS was longer with lenvatinib plus pembrolizumab than with sunitinib (HR 0.66; $P = 0.005$). Complete response was 16.1% in the lenvatinib-plus-pembrolizumab group, 9.8% in the lenvatinib-plus-everolimus group, and 4.2% in the sunitinib group. The median duration of treatment was 17.0 versus 11.0 versus 7.8 months in the lenvatinib-plus-pembrolizumab group, lenvatinib-plus-everolimus group, and sunitinib group, respectively. Grade 3 or higher adverse events were very high in these patients. Tumor progression followed by toxicity was the main reason for discontinuation of treatment in most patients. With the whole range of agents now available for the treatment of metastatic RCC, a combination of agents with differing modes of action will be the future of standard of care for these patients. These treatments will increase PFS, and hopefully OS, but at an added cost and toxicity.

INDICATIONS OF RADIATION IN OLIGOMETASTATIC PROSTATE CANCER

Radiation to the prostate improves survival in oligometastatic carcinoma prostate (PCa). However, the definition of the oligometastatic disease varies and it is not certain what number or sites of metastatic disease would benefit. Patients with newly diagnosed metastatic PCa, using conventional imaging (computed tomography/magnetic resonance imaging/bone scan), from the STAMPEDE M1 radiotherapy (RT) arm were included for this study.^[4] The association between the number of metastasis and OS and failure-free survival (FFS) was the primary endpoint. Treatment was randomized

between the standard of care versus standard of care with RT to the prostate. 1939 men were included in the study and 89% of them had bone metastasis. Survival decreased as the number of bone metastasis increased with the greatest benefit accruing to those with 3 or fewer metastasis. Maximum benefit was in those with M1a (nonregional lymph node) or 3 or fewer bone metastasis without visceral metastasis (HR for OS 1.62 and FFS 0.57) compared to those with four or more bone metastases or visceral or other metastasis (HR for OS 1.08; $P = 0.003$ and FFS 0.87; $P = 1.002$). Radiation to the prostate should be carefully chosen according to the above criteria to attain maximal benefit in patients with oligometastatic carcinoma prostate.

SURGICAL SKILLS AND OUTCOMES – AN OFTEN MISSED LINK

Surgical skills of individual surgeons are often unaccounted for and unreported when looking into the results of common surgeries performed. Most surgical reports are from high volume and specialized centers, and are used to set up standards but cannot often be matched by smaller centers with fewer patients. There is no doubt that there is heterogeneity in the surgical skills of individual surgeons and this affects results. Surgical volume indirectly relates to the development of surgical skills. Laparoscopic Prostatectomy Robot Open (LAPPRO) trial was a prospective, controlled, nonrandomized multicenter trial to see the functional and oncological outcome after retropubic or robot-assisted radical prostatectomy for localized PCa.^[5] This study focused on the heterogeneity of all operating surgeons with relation to functional and oncological results at 24 months of follow-up. The variation in results was significant for incontinence, erectile function, and rate of recurrence of the disease. Only 42% of this variation could be explained by the volume of surgeries done by the surgeon. Surgical skills have a role to play apart from the surgical approach chosen.

INTERMEDIATE MARKERS OF SURVIVAL IN PCA-HOW VALID?

OS is the best endpoint in the evaluation of treatment for malignant diseases. However, in certain slow-growing cancers like PCa, the OS may be too distant and difficult to study. Intermediate markers such as biochemical failure, local failure, distant metastases, biochemical FFS, PFS, and MFS are used as surrogate markers. The International Intermediate Clinical Endpoints in Cancer of the Prostate working group assessed the performance of commonly used intermediate clinical endpoints across all randomized controlled trials (RCTs) in localized PCa.^[6] They looked at 75 RCTs (53,631 patients) on localized or biochemically recurrent PCa between 1970 and 2020 with at least 70 participants. Only MFS correlated strongly and PFS showed modest correlation with OS. They validated that for PCa, MFS is the only appropriate surrogate endpoint for OS. This

finding could have a significant impact on the assessment of outcomes of intervention for PCa.

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Financial support and sponsorship: Nil.

Conflicts of interest: There are no conflicts of interest.

Access this article online	
Quick Response Code:	Website: www.indianjurol.com
	DOI: 10.4103/iju.IJU_98_21

How to cite this article: Kumar S. Round Up. *Indian J Urol* 2021;37:111-2.

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