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Review Article

Expert Group Consensus Opinion on Prostate Cancer Diagnosis and Management in India: Part 1 of 2

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Purpose: To evaluate Indian literature, clinical practice and develop consensus opinion on various aspects of prostate cancer diagnosis and management in order to assist medical practitioners across India in effectively choosing right treatment option for patients with prostate cancer.
Materials and Methods: At the CAP summit held in Kolkata on 2019, a group of leading experts from across India voted on 42 consensus statements. Final statements were derived on the basis of voting results and subsequent expert panel meeting. Based on the panellists discussion on various areas of prostate cancer and practicability of recommendation in clinical practice, 5 statements were deleted and a draft was prepared. The draft is divided into 2 parts; part 1 covers 16 statements on prostate cancer diagnosis and early prostate cancer.
Results: A total of 37 statements were accepted and finalised by expert panel members based on the voting results. Sixteen statements with varying degrees of support from the panel are described in detail in this article.
Conclusions: The statements derived from several Indian scientific evidences, local clinical experience, and international guidelines will serve as a reference guide for clinicians across India in the management of prostate cancer. **(Korean J Urol Oncol 2020;18:170-182)**

Key Words: Prostate cancer · Guideline · Prostate-specific antigen · Prostatectomy consensus

INTRODUCTION

Prostate cancer (PCa) is predominantly a disease of elderly and more than 3 quarter of cases occurs in men above the age of 65 years.[1] It is the second most common cancer and the sixth leading cause of cancer death amongst men worldwide.[2] The data on true incidence of PCa in India is limited as this entity is not a notifiable disease and there are very few population-based cancer registries.[1] PCa had the fifth highest incidence rate among males in India in 2016 (4.8 per 100,000; 95% uncertainty interval [UI], 3.8–5.8), with 33,000 (26,000–40,000) incident cases and 112,000 (87,000–137,000) prevalent cases. The age-standardized incidence rate of PCa increased significantly by 29.8% (95% UI, 8.5–46.9) from 1990 to 2016.[3] The 5-year survival rate of patients with PCa is much lower in India (58.1%) as compared to Western nations (>90%) with higher incidence.[4] Also, compared to the Western countries it was

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thought that the prevalence of PCa in India is lower but with the increased migration of rural population to the urban areas, increased awareness, changing life style and easy access to medical facility, more cases of PCa are being picked up and this suggests that India is not very far behind from Western countries in the rate of PCa. The cancer projection data reveals that the number of cases will double by the year 2020.[2]

Hence, it is important to have consensus on the issue of PCa – early diagnosis by using latest medical diagnostic tests. The prostate-specific membrane antigen positron emission tomography (PSMA-PET) scan is now rapidly being incorporated to help in staging of the disease. Also, much has been achieved for curing early PCa using radical robotic prostatectomy and radical radiotherapy. Consensus on various issues related to PCa would enable cure and achieve a better quality of care in patients. Also, huge advances have been made in chemotherapy, hormone therapy, and salvage radiotherapy for advanced disease. This would control advanced PCa and provide relief. Consensus on advanced PCa management is also required in order to get optimum control and a better quality of life.

MATERIALS AND METHODS

Experts in the field of urology from all over India were invited to CAP summit and a 2-day consultative meeting was convened under the aegis of Board of Education, Urological Society of India on 24th–25th of May, 2019 at Kolkata, India. As a part of the consensus process (Fig. 1), 4 major areas were defined for discussion, namely prostate cancer diagnosis, early prostate cancer, locally advanced prostate cancer, and metastatic prostate cancer. In each of the sections, the issues were determined according to perceived clinical importance. A total of 42 consensus statements were designed and voting of 28 experts was taken with the help of voting pads. Each major area was discussed on various international guidelines and evidences followed by voting on consensus statements. The grade of the evidence and the level of agreement were based on voting results (Table 1). When the proportion of those who voted was 80% or higher, the statement was regarded as strongly accepted. The result of the consensus and manuscript version one was discussed with the expert panel of 13 members (Table 2) in the consensus board meeting on 29th November 2019 before drafting the final manuscript draft. The meeting resulted in deletion of 5 statements according to the practicability of recommendation. This manuscript is the outcome of the expert group discussion and consensus comprising 16 statements on prostate cancer diagnosis and early prostate cancer.

Table 1. Grading system for consensus statement

Voting percentage	Recommendation strength
>80%	Strong
60%–80%	Moderate
50%–60%	Weak

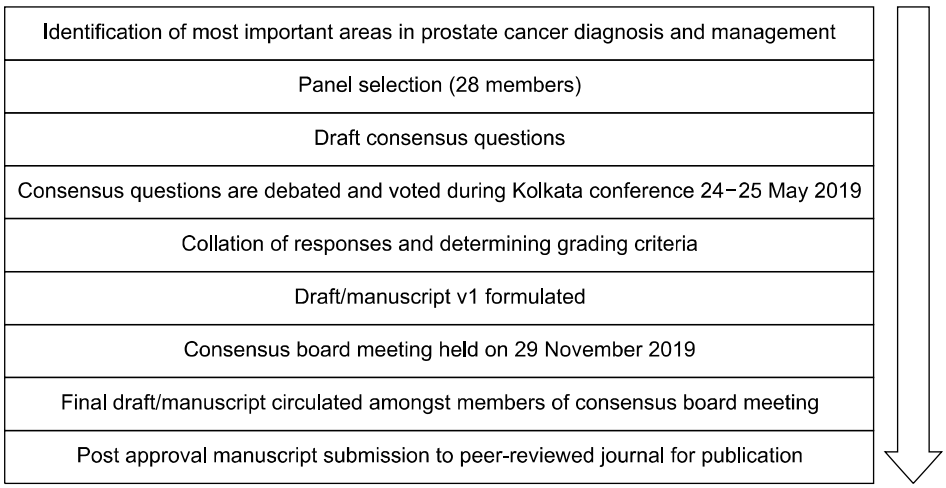

Fig. 1. Consensus process flow.

RESULTS

1. Prostate Cancer Diagnosis

1) Statement No.1.

Is there a role of digital rectal examination (DRE) in prostate cancer diagnosis?

Table 2. Consensus board meeting members and their speciality

Name	Speciality
Dr. Amit Ghose	Urologist
Dr. Ajay Kumar	Urologist
Dr. Anant Kumar	Urologist
Dr. Aneesh Srivastava	Urologist
Dr. C Mallikarjuna	Urologist
Dr. Makarand Khochikar	Urologist
Dr. N P Gupta	Urologist
Dr. Prem Kumar	Urologist
Dr. Rajeev Kumar	Urologist
Dr. Ravindra Sabnis	Urologist
Dr. S K Raghunath	Urologist
Dr. S K Singh	Urologist
Dr. Sudhir Rawal	Urologist

Literature review: In a case series published by Ghagane et al.,[5] 87.5% of 471 PCa cases had abnormal DRE and a significant association was observed between DRE and prostate-specific antigen (PSA) level (p=0.0005).[5] In the study of Jariwala,[6] PSA was not available in 40 cases and PCa was found in 14 cases on prostate biopsy, 35% being positive only on abnormal DRE. In another study, at multiple PSA ranges, suspicious DRE finding significantly increased the cancer detection rates as compared to nonsuspicious DRE.[4] Table 3 shows positive predictive value (PPV) of PSA and DRE in 876 patients who underwent biopsy.[7] In a retrospective study of 922 patients, DRE examination revealed abnormalities in 158 subjects (17.1%). The relationship between the number of subjects with abnormal DRE findings and their PSA levels is shown in Table 4; as the PSA levels increased the number of prostate cancer cases detected by DRE also increased.[8]

Consensus: Is there a role of DRE in prostate cancer diagnosis? (yes: 85.7%, no: 3.5%, no response: 10.7%)

2) Statement No.2.

Is there a role for prostate cancer screening in India?

Literature review: There are no randomized control trials

Table 3. Positive predictive values (PPV) of prostate-specific antigen (PSA) and digital rectal examination (DRE) in patients who underwent prostate biopsy

PSA range (ng/mL)	DRE	Biopsy done	Cancer	PPV (%)
<4	Negative	0	-	-
	Positive	25	5	20.0
4.1-10	Negative	216	33	15.2
	Positive	47	28	59.57
10.1-20	Negative	96	23	24.0
	Positive	60	41	68.3
>20	Negative	115	72	62.60
	Positive	316	301	95.2
Total		875	503	

Table 4. Digital rectal examination findings at varying prostate-specific antigen (PSA) levels

PSA (ng/mL)	No. of subjects with abnormalities on DRE	Detection rate of prostate cancer
<4 (n=490)	14 (2.86)	3 (0.61)
4-10 (n=171)	20 (11.7)	4 (2.34)
10-20 (n=118)	15 (12.71)	3 (2.54)
20-50 (n=41)	35 (85.37)	14 (34.15)
>50 (n=102)	74 (72.55)	56 (54.9)

Values are presented as number (%).

on population-based PCa screening in India. However, in a study conducted by Agnihotri et al.,[7] of the 4,702 patients, 70.9% had PSA level <4 ng/mL and 29.1% had PSA level >4 ng/mL. Eleven point eight percent had between 4.1−10 ng/mL, 5.4% men had PSA level between 10.1−20 ng/mL, and 11.8% had >20 ng/mL. PSA test positivity rate was 29.1%. In this study, although there was a higher PSA test positivity, the PPV of PSA test in symptomatic men was low. This suggests that an increased number of PSA positive men are unnecessarily put through biopsy.[7] It is now accepted that PSA screening prevents approximately one PCa death per 1,000 men, each screened several times and followed for 10−15 years.[9] Overdiagnosis of prostate cancer (estimated to be 35 overdiagnosed cases per 1,000 men screened), a large majority of which are low-risk cancers that would never progress or metastasize, is the most important harm that outweighs the benefits of screening.[9] Dubey[10] in his review analysed evidences on the usefulness of PSA screening and concluded that there is no scientific rationale to advocate routine use of PSA for early detection of PCa in Indian males. The Government policy in favour of screening for prostate cancer does not exist in India and thus practising population-based screening is difficult.

Consensus: Is there a role for prostate cancer screening in India? (yes: 32.1%, no: 67.9%, no response: 0%)

3) Statement No. 3

Should all men have a multiparametric magnetic resonance imaging (mp-MRI) of the prostate/pelvis prior to making a decision to proceed to biopsy?

Literature review: In one prospective study conducted in India, the diagnostic performance of mp-MRI was analysed in a group of subjects with serum PSA of ≤10 ng/mL. Receiver operating characteristic (ROC) analysis of Prostate Imaging Reporting and Data System (PIRADS-S) score showed area under the curve of 0.93 ($p<0.001$) for the detection of PCa. Youden selected threshold cutoff was 8 (≥ 8) with sensitivity, specificity, PPV, and negative predictive value (NPV) of 85%, 87.88%, 68%, and 95.1%, respectively. Mp-MRI showed high NPV with PIRADS-S score cutoff,[8] which suggest the ability of the test to predict the absence of disease with high confidence. This factor can be used to limit unnecessary biopsy of prostate.[11] In another study conducted in 26 patients, sensitivity, specificity, PPV, and NPV of T2, diffusion-weighted imaging, and magnetic resonance spectroscopy (MRS) in predicting malignancy was calculated after which transrectal ultrasonography (TRUS) guided biopsy was performed; results of which are described in Table 5.[12] Prebiopsy mp-MRI should become standard of care as recommended in 2019 NICE guidelines [NG131]. However, its implementation has proved to be difficult in the United Kingdom and certainly in India.

Consensus: Should all men have a mp-MRI of the prostate/pelvis prior to making a decision to proceed to biopsy? (yes: 25%, no: 67.8%, no response: 7.1%)

4) Statement No. 4

Should transrectal ultrasound-guided biopsies remain the standard approach?

Literature review: Gupta et al.[13] reported a false negative rate of approximately 11% with TRUS-guided sextant biopsy. In symptomatic men with negative DRE, Agnihotri et al.[7] proposed raising the serum PSA cutoff to 5.4 ng/mL for TRUS biopsy in India as this would prevent 10% unnecessary biopsies. This reflects low PCa detection rates of TRUS biopsy in India. It has been observed that compared to other continents, Asian population (including India) have a lower TRUS biopsy yield, especially for serum PSA level

Table 5. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of T2, DWI, and MRS in predicting malignancy

Variable	T2W	MRS	DWI	Combined (T2+DWI+MRS)
Sensitivity	94.7%	84.2%	89.5%	94.7%
Specificity	42.9%	28.6%	85.7%	42.9%
PPV	81.8%	76.2%	74.4%	81.8%
NPV	75%	40%	75%	75%
Diagnostic accuracy	80.8%	69.2%	88.5%	80.8%

DWI: diffusion-weighted imaging, MRS: magnetic resonance spectroscopy, T2W: T2-weighted.

<20 ng/mL. Patil et al.,[4] have confirmed these findings and thus standard serum PSA cutoff of 4 ng/mL followed in Western nations gives lower TRUS biopsy yield for Indian population. Cancer detection rates of TRUS biopsies from Indian studies are shown in Table 6.

Consensus: Should transrectal ultrasound-guided biopsies remain the standard approach? (yes: 85.7%, no: 14.3%, no response: 0%)

5) Statement No. 5

What imaging modalities should be used to complement the mp-MRI of the pelvis/prostate when determining the presence/absence of metastatic disease?

Literature review: There are no Indian studies on direct comparison of PSMA-PET-computed tomography (CT) and Isotope bone scan-CT. In the study of Gupta et al.,[14] in their experience of 97 staging prostate cancer patients, PSMA-PET-CT showed 57.41% with only sclerotic metastasis. 33.33% mixed, 7.14% marrow, and 2.3% lytic types of lesions constitute the rest; therefore, bone scan alone in these patients may result in underestimation of bony disease burden.[14] In another study, ^{68}Ga-PSMA PET CT and MRI diagnostic sensitivity, specificity, PPV, NPV, and accuracy for detection of lymph node metastasis in high-risk cases were 66.67%, 98.61%, 85.71%, 95.95%, 95.06%, and 25.93%, 98.61%, 70%, 91.42%, 90.53%, respectively.[15] In a retrospective study of 262 patients having PCa or suspected recurrent PCa, ^{68}Ga-PSMA scan detected extra-prostatic disease in 53.2% of subjects when done at baseline prior to starting any treatment. In this study, the sensitivity of ^{68}Ga-PSMA at baseline with histopathological diagnosis was 95% and the PPV was 98%.[16] PSMA-PET-CT is a suitable replacement for conventional imaging as it provides superior accuracy than CT scan and bone scan.

Consensus: What imaging modalities should be used to complement the mp-MRI of the pelvis/prostate when determining the presence/absence of metastatic disease? (PSMA-PET-CT: 57.1%, isotope bone scan+CT scan: 39.2%, no response: 3.57%)

6) Statement No. 6

Should all prostate cancer biopsies be reviewed by a pathologist with specific experience in the interpretation of prostate cancer histology?

Literature review: In the study of Singh et al.,[17] general pathologists scored PCa cases using Gleason grade. For Gleason score (GS) groups (2–4, 5–6, 7, and 8–10) overall agreement with consensus score was 68%. For primary grade 60% of readings were in fair to moderate agreement range; for secondary grade 78% of readings were in slight to fair agreement range. For GS, 80% of readings were in slight to fair agreement range; and for GS groups 68.5% of the readings were in fair to moderate agreement range. In practice, it has been seen that general pathologists often underscore than overscore. In the same study, overscoring was observed in 33.7% and underscoring in 23%.[17] In another study, after attending a web-based tutorial, pathologist scored PCa cases independently using the Gleason scoring system. Pathologist overgraded 15% cases of score 7 and 12.5% cases of scores 5–6 in the pretutorial round. In post-tutorial round, this score was reduced to 11.25% and 10.6, respectively.[18]

Consensus: Should all prostate cancer biopsies be reviewed by a pathologist with specific experience in the interpretation of prostate cancer histology? (yes: 89.2%, no: 10.7%, no response: 0%)

Table 6. Comparison with cancer detection rates of transrectal ultrasonography biopsy reported in India

Study	No. of patients	Cancer detection rate (%)						
		Overall	PSA<4	PSA 4–10	PSA 10–20	PSA 20–50	PSA 50–100	PSA>100
Agnihotri et al.[7]	875	57.5	20†	15.2* 59.57†	24* 68.3†	62.6* 95.2†		
Sinha et al.[40]	119	24.37	-	7.14	6.67	52.17		
Patil et al.[4]	235	25.53	-	5.95	13.16	32.26	100	100

PSA: prostate-specific antigen, DRE: digital rectal examination.
*Normal DRE. †Abnormal DRE.

SUMMARY OF RECOMMENDATIONS ON PROSTATE CANCER DIAGNOSIS

S/N	Statement	Strength of recommendation
1	Is there a role of DRE in prostate cancer diagnosis? Yes: 85.7%, no: 3.5%, no response: 10.7% There is a role of DRE in prostate cancer diagnosis	Strong
2	Is there a role for prostate cancer screening in India? Yes: 32.1%, no: 67.9%, no response: 0% There is no role for prostate cancer screening in India	Moderate
3	Should all men have a mp-MRI of the prostate/pelvis prior to making a decision to proceed to biopsy? Yes: 25%, no: 67.8%, no response: 7.1% All men should not have a mp-MRI of the prostate/pelvis prior to making a decision to proceed to biopsy	Moderate
4	Should transrectal ultrasound-guided biopsies remain the standard approach? Yes: 85.7%, no: 14.3%, no response: 0% Transrectal ultrasound-guided biopsies should remain the standard approach	Strong
5	What imaging modalities should be used to complement the mp-MRI of the pelvis/prostate when determining the presence/absence of metastatic disease? PSMA-PET-CT: 57.1%, isotope bone scan+CT scan: 39.2%, no response: 0% PSMA-PET-CT should be used to complement the mp-MRI of the pelvis/prostate when determining the presence /absence of metastatic disease	Weak
6	Should all prostate cancer biopsies be reviewed by a pathologist with specific experience in the interpretation of prostate cancer histology? Yes: 89.2%, no: 10.7%, no response: 0% All prostate cancer biopsies should be reviewed by a pathologist with specific experience in the interpretation of prostate cancer histology	Strong

2. Early Prostate Cancer

1) Statement No. 1

Is active surveillance (AS) a viable management option for low-risk prostate cancer in the Indian context?

Literature review: There are no Indian guidelines or studies on the role of AS in prostate cancer. Data of AS in more than 4,000 PCa patients with median follow-up of 4.5 years has been shown in Table 7.[19] In Indian setting, patients generally have insufficient medical knowledge and their treatment outcome expectation is high. In addition, the large Indian population is not regular for AS follow-up. Medical violence is also quite common, thus it is difficult for urologists in India to face the medical disputes caused by PCa progression during AS. Implementing AS in India is therefore difficult. Even conditions in China are similar to India, which is why radical prostatectomy is still the primary choice of Chinese urologist in low-risk prostate cancer, followed by AS.[20]

Consensus: Is AS a viable management option for low-risk prostate cancer in the Indian context? (yes: 42.9%, no: 57.1%, no response: 0%)

2) Statement No. 2

Should Gleason Grade Grouping (GG) be adopted across India as a standard for reporting histological grade?

Literature review: In a retrospective study comparing the GS of 2005 and 2015 criteria, there was a marked decrease (80%) in GS 6; among these cases, 80% cases were graded as score 7, and 20% cases were graded as score 8. There was also a 28.57% decrease in GS 8 and 60% increase in GS 9 due to the new criteria for pattern 4. The GG 1, 2, 3, 4, and 5 constituted 3.03%, 18.18%, 15.15%, 15.15%, and 48.49% of cases respectively.[21] In another Indian study, applying World Health Organization 2016 modified Gleason scoring system and prognostic grade grouping criteria to PCa biopsies, there was upgradation of prognostic groups in 7.69% patients. There was also an increase in GS 4+3 from 19.6% to 23.8% and a decrease in GS 3+4 from 13.9% to 9%; After follow-up of 2 years poor prognoses was observed in those patients who were upgraded to the higher prognostic group.[22]

Table 7. Studies of active surveillance in prostate cancer

Study	Patients (n)	Median follow-up (yr)	Freedom from treatment	Prostate cancer death
PRIAS 2013[41]	2,494	1.6	77% at 2 yr	0
Selvadurai et al.[42]	471	5.7	70% at 5 yr	0.40%
Tosoian et al.[43]	769	2.7	59% at 5 yr	0
Dall'Era et al.[44]	321	3.6	67% at 5 yr	0
Thomsen et al.[45]	167	3.4	NA	0
SAMS* 2013[46]	148	NA	NA	NA
Klotz et al.[47]	450	6.8	70% at 5 yr	3% at 15 yr
Total	4,820			

NA: not applicable, PRIAS: Prostate Cancer Research International Active Surveillance, SAMS: Study of Active Monitoring in Sweden.
*Prospective and randomized.

Consensus: Should Gleason Grade Grouping be adopted across India as a standard for reporting histological grade? (yes: 100%, no: 0%, no response: 0%)

3) Statement No. 3

Does the management and prognosis for high-risk localized and locally advanced prostate cancer differ?

Literature review: The current standard of care in management of high-risk and locally advanced disease is external beam radiotherapy (EBRT) in combination with long-term androgen deprivation therapy (ADT); specifically, a 3-dimensional conformal radiation therapy or intensity-modulated radiation therapy (IMRT) radiation therapy technique with a dose of 75–80 Gy in conjunction with long-term ADT in a neoadjuvant, concurrent, or adjuvant setting for 2–3 years. In general, brachytherapy is not considered for treatment in high-risk patients; however, in certain scenario brachytherapy boost could be used in conjunction with EBRT, along with consideration of short-term ADT. In addition, surgery could be considered in selected high-risk patients, even though, it is not a popular approach because of it is invasive in nature compared to EBRT. Also, surgery has it's complication which is long-term sexual dysfunction, urinary incontinence etc. It's highly likely that postoperative radiotherapy would be required which will expose patients to toxicities of radiotherapy as well as surgery.[23]

Consensus: Does the management and prognosis for high-risk localized and locally advanced prostate cancer differ? (yes: 75%, no: 17.8%, no response: 7.1%)

4) Statement No. 4

Should hypo fractionated radiotherapy (60 Gy in 20 fractions) be considered the standard radiotherapy regimen for low-to-intermediate risk prostate cancer?

Literature review: In an Indian study, patients with organ-confined PCa received hypofractionated IMRT. Dose prescribed to the prostate was 77 Gy/35 fractions or 60 Gy/20 fractions. After a median follow-up of 26 months, there were 6 biochemical relapses, 1 in intermediate and 5 in high-risk group, of whom 3 deaths occurred due to distant metastasis. In this study, the 2-year biochemical recurrence-free survival (bRFS), prostate cancer-specific survival (pCSS), and overall survival (OS) were 92.3%, 93.9%, and 91.5% respectively. Twenty percent and 13.3% developed acute and late Radiation Therapy Oncology Group (RTOG) grade 2 or worse gastrointestinal (GI) toxicities respectively. Eight point nine percent and 11.1% developed RTOG grade 2 or worse genitourinary (GU) toxicity respectively. One patient developed grade 3 rectal toxicity, and none developed bladder toxicity.[24] In another Indian study, no significant difference was observed in the incidence of grade 2 GI and GU toxicities between the 2 schedules of 60 Gy in 20 fractions and 65 Gy in 25 fractions.[25]

Consensus: Should hypo fractionated radiotherapy (60 Gy in 20 fractions) be considered the standard radiotherapy regimen for low-to-intermediate risk prostate cancer? (yes: 57.1%, no: 35.7%, no response: 7.1%)

5) Statement No. 5

Should radical prostatectomy be considered as a management option for men with high-risk (D'Amico) cN0 cM0

prostate cancer?

Literature review: Most patients in India present with locally advanced disease or metastatic disease due to lack of medical education and awareness. Even those patients presenting with localized disease who could be managed with RP, are in the high-risk group. In an Indian study, patients underwent robotic-assisted radical prostatectomy (RARP) and it was observed that 39.6% were in high-risk group. After a follow-up of 12 months post-RARP, 27.8% had biochemical recurrence (BCR), and 92% patients were continent.[26] Kulkarni et al.[27] studied the outcome of upfront RP in Indian patients with high risk PCa. From 1996 to 2010, 208 PCa patients (high-risk category D'Amico's criteria) underwent open RP with bilateral pelvic lymphadenectomy. At 7 and 10 years, pCSS was found to be 79.7% and 65%, respectively, bRFS was 42.4% and 36.7%, respectively and the metastasis-free survival (MFS) was 71.1% and 64.4% respectively.[27] In another study, out of 192 patients who underwent RP 109 had D'Amico high-risk (HR) disease. The 2- and 5-year bRFSs were 45% and 35%, respectively. It was also observed that the 2-year bRFS was 63%, 23%, and 22%, for 1HR, 2HR, and 3HR respectively (log rank, $p<0.0001$).[28] In the study of Mishra et al.,[29] after undergoing laparoscopic radical prostatectomy for a clinical T2 localized disease, patient's 5-year progression-free probability with low-, intermediate-, and high-risk PCa was 91%, 82%, and 58%, respectively.[29]

Consensus: Should radical prostatectomy be considered as a management option for men with high-risk (D'Amico) cN0 cM0 prostate cancer? (yes: 85.7, no: 7.1%, no response: 7.1%)

6) Statement No. 6

Should lymph node dissection be recommended in all men with high-risk (D'Amico) cN0 cM0 prostate cancer undergoing a radical prostatectomy?

Literature review: Lymph node positivity is detected in 5%–6%, 20%–25%, and 30%–40% of low-, intermediate-, and high-risk PCa patients respectively who undergo RP and extended pelvic lymph node dissection (ePLND).[30] In contrast to the Western countries, most Indian patients are detected with higher stage of PCa and with greater probability of lymph node involvement. Results of the study of Batra et al.[31] showed that 7% and 45% of patients had low-risk and high-risk disease respectively and positive lymph node was found in 20% of these high-risk patients on ePLND. This demonstrates how much important pelvic lymphadenectomy is in patients undergoing RARP in the Indian subcontinent. Abdollah et al.[32] studied the practice patterns in the utilization of pelvic lymph node dissection in Indian and United States (US) practices. Even this study confirmed that Indian patients had a higher risk distribution compared to US (53.4% in India vs. 27% in the US; $p<0.001$). It was also observed that Indian patients with low risk more frequently underwent PLND (81.0% vs. 41.4%). In addition, the study showed that the probability of Indian patients undergoing PLND was 2.57-fold higher than their US counterparts.[32]

Consensus: Should lymph node dissection be recommended in all men with high-risk (D'Amico) cN0 cM0 prostate cancer undergoing a radical prostatectomy? (yes: 92.8, no: 0%, no response: 7.1%)

7) Statement No. 7

In men undergoing lymph node dissection during radical prostatectomy for high-risk (D'Amico) cN0 cM0 prostate cancer, which lymph node regions should be dissected?

Literature review: With the absence of Indian literature, evidences from international studies have been evaluated. In high-risk men with lymph node positive disease after RP and ePLND, Bader et al.[33] found that the common sites for metastasis in patients were obturator fossa (60%) followed by internal iliac (hypogastric) (58%) and external iliac nodal areas (36%). Nineteen percent of the patients had metastasis in the hypogastric region alone. In another study, 470 lymph nodes were detected scintigraphically and 46% positive nodes were found in patients during ePLND. If ePLND went only up to the common iliac chain, 94% would have been correctly staged, but only 77% would have had all their metastasised sites removed.[30] A recent study of PLND versus ePLND evaluated bPFS outcomes in localized PCa patients undergoing open RP. The 5-year bPFS in low risk, intermediate-risk, and high-risk patients undergoing PLND and ePLND were found out to be 90.1% and 91.3%, 73.1% and 85.7%, 51.1%, and 71.4% respectively.[34]

Consensus: In men undergoing lymph node dissection during radical prostatectomy for high-risk (D'Amico) cN0 cM0 prostate cancer, which lymph node regions should be

dissected? (below common illiac bifurcation: 64.2%, above common iliac bifurcation: 32.1%, no response: 3.5%). In the discussion during Consensus Board Meeting (CBM), expert committee was of the opinion that the statement derived from this question should have a strong recommendation.

8) Statement No. 8

Which staging investigations should be performed in a man with high-risk (D'Amico) cN0 cM0 prostate cancer prior to confirming suitability for surgery?

Literature review: There are no Indian studies on comparison of various investigations in high-risk (D'Amico) cN0 cM0 prostate cancer prior to confirming suitability for surgery. However, Indian data on different investigations in prostate cancer are mentioned in statement No. 5 under the diagnosis section of consensus opinion. Due to lack of Indian data, evidences from other literature were assessed. In a study conducted in Jordan, ^{68}Ga PSMA PET/CT scan in high-risk disease patients showed a higher concordance rate of 90% as compared to the bone scan (75%) followed by MRI scan (73%), and CT scan (60%). The study also demonstrated that ^{68}Ga PSMA PET/CT was more accurate in detecting suspicious pelvic lymph nodes than MRI scan (95.2% vs. 80%) but it had almost same accuracy to MRI in detecting PCa lesions. In this study ^{68}Ga PSMA PET/CT also performed better than CT scan in identifying suspicious lymph nodes (95.2% vs. 75%) and extrapelvic nodes (100% vs. 75%), as well as bone lesions via bone scan (100% vs. 62.5%). Intriguingly the management of PCa was changed by ^{68}Ga PSMA PET/CT in 52% patients.[35]

Consensus: Which staging investigations should be performed in a man with high-risk (D'Amico) cN0 cM0 prostate cancer prior to confirming suitability for surgery? (multiparameteric MRI+bone scan: 35.7%, PSMA-PET: 60.7%, no response: 3.5%)

9) Statement No. 9

Should neoadjuvant ADT be considered for men with high-risk (D'Amico) cN0 cM0 prostate cancer prior to radical prostatectomy?

Literature review: Indian studies are lacking on this subject, thus other available literature was reviewed for this statement. Narita et al.[36] studied the outcomes in patients having high-risk disease treated with neoadjuvant chemohormonal therapy (NCHT) with RP alone. In this study, 10% patients had pathologic complete response and 3.3% had positive surgical margins. The BCR-free survival rates for 2 years and 5 years were 69.2% and 60.1%, respectively. After propensity score matching, it was observed that the BCR rate in patients remained significantly lower in the NCHT+RP group than RP group alone.[36] In 2006 a Cochrane review published that neoadjuvant ADT improved pathological outcomes but not overall or disease-free survival.[37]

Consensus: Should neoadjuvant ADT be considered for men with high-risk (D'Amico) cN0 cM0 prostate cancer prior to radical prostatectomy? (yes: 28.5%, no: 64.2%, no response: 7.1%)

10) Statement No. 10

Is there a role for trimodality therapy (ADT+radical prostatectomy+adjuvant radiotherapy [ART]) for men with high-risk (D'Amico) cN0 cM0 prostate cancer?

Literature review: Trials have demonstrated that combination therapies improve survival and cancer outcomes when compared to monotherapy for men with high-risk PCa. To date, only one prospective randomized trial comparing RP plus ADT with EBRT plus ADT in the treatment of patients with high-risk PCa has been published; men with T2b–3N0M0 tumours were included in this trial, regardless of serum PSA level. After a follow-up of 102 months, the 10-year OS rate in the patients who underwent surgery tended to be better than the rate observed in the radiation group (76.2% vs. 71.1%). Furthermore, other outcomes were improved in the surgery cohort compared to radiotherapy cohort: bPFS was 83.5% versus 66.1%, clinical progression-free survival rates were 85.7% versus 77.1%, and disease-specific survival (DSS) rates was 67.9% versus 60.9%. However, none of these survival advantages reached statistical significance.[38] In another retrospective study, the outcome in PCa patients receiving combination of ART and ADT after RP was evaluated. After a median follow-up of 61 months, the 5- and 7-year bRFS rates were 90.5 and 77.2%, respectively. Distant relapse occurred in 5 patients, resulting in 5- and 7-year MFS of 95.9% and 81.7%, respectively. During follow-up, 7 patients died (2 PCa deaths), resulting in 5- and 7-year DSS and OS rates of 100% and 94.7% and 90.6 and 81.5%, respectively.[39]

Consensus: Is there a role for trimodality therapy

SUMMARY OF RECOMMENDATIONS ON EARLY PROSTATE CANCER

S/N	Statement	Strength of recommendation
1	Is AS a viable management option for low-risk prostate cancer in the Indian context? Yes: 42.9%, no: 57.1%, no response: 0% AS is not a viable management option for low-risk prostate cancer in the Indian context	Weak
2	Should Gleason Grade Grouping be adopted across India as a standard for reporting histological grade? Yes: 100%, no: 0%, no response: 0% Gleason Grade Grouping should be adopted across India as a standard for reporting histological grade	Strong
3	Does the management and prognosis for high-risk localized and locally advanced prostate cancer differ? Yes: 75%, no: 17.8%, no response: 7.1% The management and prognosis for high-risk localized and locally advanced prostate cancer should differ	Moderate
4	Should hypo fractionated radiotherapy (60 Gy in 20 fractions) be considered the standard radiotherapy regimen for low-to-intermediate risk prostate cancer? Yes: 57.1%, no: 35.7%, no response: 7.1%	Weak
ss	Hypo fractionated radiotherapy (60 Gy in 20 fractions) should be considered the standard radiotherapy regimen for low-to-intermediate risk prostate cancer	
5	Should radical prostatectomy be considered as a management option for men with high-risk (D'Amico) cN0 cM0 prostate cancer? Yes: 85.7%, no: 7.1%, no response: 7.1% Radical prostatectomy should be considered as a management option for men with high-risk (D'Amico) cN0 cM0 prostate cancer	Strong
6	Should lymph node dissection be recommended in all men with high-risk (D'Amico) cN0 cM0 prostate cancer undergoing a radical prostatectomy? Yes: 92.8%, no: 0%, no response: 7.1% Lymph node dissection should be recommended in all men with high-risk (D'Amico) cN0 cM0 prostate cancer undergoing a radical prostatectomy	Strong
7	In men undergoing lymph node dissection during radical prostatectomy for high-risk (D'Amico) cN0 cM0 prostate cancer, which lymph node regions should be dissected? Below common iliac bifurcation: 64.2%, above common iliac bifurcation: 32.1%, no response: 3.5% In men undergoing lymph node dissection during radical prostatectomy for high-risk (D'Amico) cN0 cM0 prostate cancer the lymph node regions below common iliac bifurcations should be dissected	Moderate
8	Which staging investigations should be performed in a man with high-risk (D'Amico) cN0 cM0 prostate cancer prior to confirming suitability for surgery? Multiparameteric MRI+bone scan: 35.7%, PSMA-PET: 60.7%, no response: 3.5% PSMA-PET should be performed in a man with high-risk (D'Amico) cN0 cM0 prostate cancer prior to confirming suitability for surgery	Moderate
9	Should neoadjuvant ADT be considered for men with high-risk (D'Amico) cN0 cM0 prostate cancer prior to radical prostatectomy? Yes: 28.5%, no: 64.2%, no response: 7.1% Neoadjuvant ADT should not be considered for men with high-risk (D'Amico) cN0 cM0 prostate cancer prior to radical prostatectomy	Moderate
10	Is there a role for trimodality therapy (ADT+radical prostatectomy+ART) for men with high-risk (D'Amico) cN0 cM0 prostate cancer? Yes: 53.5%, no: 42.8%, no response: 3.5% There is a role for trimodality therapy (ADT+radical prostatectomy+ART) for men with high-risk (D'Amico) cN0 cM0 prostate cancer	Weak

(ADT+radical prostatectomy+ART) for men with high-risk (D'Amico) cN0 cM0 prostate cancer? (yes: 53.5%, no: 42.8%, no response: 3.5%). During CBM, the expert committee was of the opinion that the statement derived from this question should have a strong recommendation and the terminology trimodality is to be replaced with multimodality.

CONFLICT OF INTEREST

The authors claim no conflicts of interest.

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