Controversies in the management of localized prostate cancer: consensus development by Canadian urologists

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This consensus statement emerged from the 2nd Canadian Uro-Oncology Congress, held January 16–20, 2002. The attendees at this meeting comprised approximately 125 urologists from across Canada, representing both community and academic perspectives. The group heard presentations by experts in the field addressing the spectrum of controversies in prostate cancer. After each session, the meeting broke into workshop sessions where attendees discussed the controversies raised by the speakers. Present in each workshop was a reporter who summarized the consensus of the group. These summaries were collected and integrated into a set of questions. At the end of the congress, the attendees voted on the questions and controversies identified through the workshop process.

Key Words: localized prostate cancer, consensus statement, risk stratification

Introduction

This consensus development process represented a unique opportunity to determine the range of approaches to prostate cancer by the urological community in Canada, and to identify areas of agreement and disagreement. The questions were deliberately constructed to reflect the range of opinion expressed in the workshops, and to identify the clinical scenarios in which the greatest differences of opinion exist.

Consensus questions and discussion

1. An appropriate 'risk of death' stratification scheme prior to definitive therapy, based on prostate-specific antigen (PSA), grade, and stage, is as follows:
Low risk: PSA <10 ng/mL, Gleason Score (GS) of 6 or less, stage T2a or less.

1.	Agree	92% (87)
2.	Disagree	6% (6)
3.	Undecided	2% (2)
	Total 95	

A remarkable degree of consensus existed on the definition of good risk prostate cancer. This reflects the substantial amount of recent data incorporated into nomograms which clearly support the favorable outcome in patients in this category. The emphasis on 'risk of death' underscored the importance of survival, rather than surrogate end points such as PSA progression, in evaluating the value of different therapies. Importantly, this risk stratification for favorable disease is identical to that of the Canadian Genito-Urinary Radiation Oncology Group (CGUROG).

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2. An appropriate 'risk of death' stratification scheme prior to definitive therapy, based on PSA, grade, and stage, is as follows:
Alternative: Low risk: PSA <10 ng/mL, GS of 6 or less, stage T2a or less.

1. Agree	32% (28)
2. Disagree	63% (55)
3. Undecided	6% (5)
Total 88	

A minority view was that the cut-off for favorable risk should be for Gleason score 5 or less.

3. An appropriate 'risk of death' stratification scheme prior to definitive therapy, based on PSA, grade, and stage, is as follows:
Intermediate risk: PSA 10–20 ng/mL, or GS of 7, stage T1–T2.

1. Agree	94% (88)
2. Disagree	5% (5)
3. Undecided	1% (1)
Total 94	

Again, a clear consensus regarding intermediate risk disease. This result is also consistent with the CGUROG perspective.

4. An appropriate 'risk of death' stratification scheme prior to definitive therapy, based on PSA, grade, and stage, is as follows:
High risk: PSA >20 ng/mL, or GS of 8, 9, or 10, or stage T3a and greater.

1. Agree	99% (95)
2. Disagree	1% (1)
3. Undecided	0% (0)
Total 96	

A clear consensus. This consensus regarding risk groupings is an important building block towards establishing agreement on the role of various interventions for prostate cancer.

5. Age and co-morbidity should be incorporated into a risk assessment strategy.

1. Agree	93% (93)
2. Disagree	6% (6)
3. Undecided	1% (1)
Total 100	

There was widespread agreement that patient age and co-morbidity, the two crucial determinants of average life expectancy, are critical components of decision-making and risk assessment.

6. Decision-making should be based on estimated average life expectancy rather than chronological age.

1. Agree	88% (85)
2. Disagree	8% (8)
3. Undecided	4% (4)
Total 97	

While most participants felt that estimated life expectancy should be the basis for decisions as to aggressiveness of therapy, a small subset believed that age was the most reliable determinant of life expectancy.

7. Tools to predict life expectancy should be incorporated into individual patient treatment decisions.

1. Agree	87% (83)
2. Disagree	7% (7)
3. Undecided	5% (5)
Total 95	

This response is similar to question 6. Tools for the accurate estimation of life expectancy based on age and co-morbidity are freely available in the published literature, and include the Index of Co-Existent Morbidity (ICED) and the Charlson Comorbidity Index. While many are aware of these tools, they are used by relatively few. Most attendees agreed that facilitating the widespread use of these tools was an important goal in improving the quality of treatment decisions.

8. 70 years of age is the 'hard' cut-off age for radical surgery.

1. Agree	32% (32)
2. Disagree	68% (67)
3. Undecided	0% (0)
Total 99	

Consistent with the previous views, most felt that an age cut-off for radical prostatectomy should be based on the best assessment of life expectancy rather than a hard age cut-off. However, a significant minority believed that a hard cut-off was appropriate.

9. At all stages of prostate cancer, different treatment options exist. None is clearly superior. Options should be discussed in the process of individual patient decision-making.

1.	Agree	87% (76)
2.	Disagree	13% (11)
3.	Undecided	0% (0)
	Total 87	

Remarkably, the vast majority of urologists in the audience supported the view that a single 'best' treatment could not be clearly identified for any stage of prostate cancer. This is consistent with the published data, which consists largely of non-comparative studies, ongoing stage migration, and is bedeviled by confounding issues. It is likely that the ongoing randomized trials comparing different treatment options for localized prostate cancer will shed light on this important question.

10. For low-risk disease, curative therapy is unlikely to be necessary or beneficial where the patient's estimated average life expectancy is less than 10 years.

1.	Agree	79% (70)
2.	Disagree	20% (18)
3.	Undecided	1% (1)
	Total 89	

Most responders supported the concept of a conservative, expectant approach for patients with a life expectancy less than 10 years.

A minority opinion was that patients with low risk disease with a life expectancy of 5 to 10 years stand to benefit from local therapy, particularly radiation. The benefit was primarily one of improved local control, rather than a survival benefit. Another concern was that some patients in whom a short life expectancy is predicted go on to survive considerably more than 10 years, and that these patients might lose the opportunity for cure.

11. For intermediate-risk disease, curative therapy is unlikely to be necessary or beneficial where the patient's estimated average life expectancy is less than 10 years.

1.	Agree	18% (17)
2.	Disagree	79% (75)
3.	Undecided	3% (3)
	Total 95	

In sharp contrast, the consensus for intermediate disease was that treatment should be offered with curative intent, even when life expectancy was less than 10 years. These patients are clearly at higher risk for early progression.

A minority opinion was that, for patients with life expectancy less than 10 years, a survival benefit of radical therapy was unlikely, and conservative management, including delayed androgen ablation, would in most cases produce sufficient disease control.

12. Watchful waiting with delayed palliative therapy is the preferred option in low-risk disease in patients with estimated average life expectancy of less than 10 years.

1.	Agree	86% (69)
2.	Disagree	11% (9)
3.	Undecided	3% (2)
	Total 80	

A remarkable degree of consensus on watchful waiting for favorable disease in patients with a limited life expectancy (less than 10 years).

13. Watchful waiting with delayed palliative therapy is the preferred option in low-risk disease in patients with estimated average life expectancy of less than 15 years.

1.	Agree	30% (27)
2.	Disagree	62% (56)
3.	Undecided	9% (8)
	Total 91	

Substantial concern exists, based on data from Sweden, that after 10 years, the risk of prostate cancer death rises substantially. Thus, in patients with 10–15-year life expectancy (ie, healthy men age < 73), definitive intervention was thought to be required. A minority opinion held that, based on the data from Albertsen and others, many patients with a 15-year life expectancy were still destined not to die of their low-risk disease.

14. Watchful waiting with delayed palliative therapy is the preferred option in low-risk disease in patients older than 70 years of age.

1.	Agree	56% (53)
2.	Disagree	41% (39)
3.	Undecided	2% (2)
	Total 94	

There was no consensus with respect to a hard cut-off for watchful waiting. Some felt that watchful waiting was preferred for patients with low risk disease and limited life expectancy; a similar proportion believe that definite therapy is preferred for patients with limited life expectancy due to age. There was a range of opinion with regard to the age/life expectancy cut-off at which palliative therapy alone was warranted. This cut-off ranged from 5 to 10 years.

15. Watchful waiting with delayed palliative therapy is the preferred option in intermediate-risk disease in patients with estimated average life expectancy of less than 10 years.

1. Agree	26% (21)
2. Disagree	70% (56)
3. Undecided	4% (3)
Total 80	

As the risk of progression increased, the attraction of expectant management diminished. Most believed that with intermediate risk disease, patients with a life expectancy in the range of 5-10 years still warranted definitive therapy.

16. Would you consider radical surgery and radiation therapy on the same treatment level?

1. Yes	21% (16)
2. No	78% (60)
3. Undecided	1% (3)
Total 77	

Differences in acute and chronic morbidity, and long-term disease control are clearly perceived to differentiate between radiation and surgery.

17. Watchful waiting with delayed palliative therapy is the preferred option in intermediate-risk disease in patients with estimated average life expectancy of less than 5 years.

1. Agree	76% (65)
2. Disagree	21% (18)
3. Undecided	2% (2)
Total 85	

There was a consensus that intermediate risk patients have a high likelihood of short term progression. These patients were likely to require palliative therapy. However, in those with a life expectancy of 5 years or less, most responders would not offer definitive therapy.

18. Watchful waiting with delayed palliative therapy is the preferred option in intermediate-risk disease in patients aged 75 years and older.

1. Agree	50% (39)
2. Disagree	42% (33)
3. Undecided	8% (6)
Total 78	

Cases falling into the borderline zones with respect to age and life expectancy sharpened the differences in management approach. For patients over 75 years of age, many felt that expectant management was warranted. Others believed that definitive therapy, usually with radiation, still had a role. A small percentage would offer surgery to selected patients over 75 years of age in excellent health, believing that an advantage accrued to those destined to live for more than 10 years.

19. Watchful waiting with selective deferred curative therapy is an appropriate option in patients with low-risk disease and a slow rate of PSA and clinical progression.

1. Agree	73% (59)
2. Disagree	26% (21)
3. Undecided	1% (1)
Total 81	

A surprisingly high proportion of attendees supported the approach of using the rate of clinical or biochemical progression as a trigger for definitive therapy in favorable-risk patients, who otherwise would remain on a course of active surveillance.

20. Radical prostatectomy and conformal external beam irradiation therapy are effective treatment options for cure in patients with low- and intermediate-risk prostate cancer and a 10- to 15-year life expectancy.

1. Agree	88% (72)
2. Disagree	10% (8)
3. Undecided	2% (2)
Total 82	

Most attendees supported the view that both therapies were effective; a small group was firmly committed to surgery over radiation in patients with a longer life expectancy and intermediate-risk disease.

21. Brachytherapy, performed in experienced centres, is a reasonable curative treatment for low-risk prostate cancer in a patient over 60 years of age with minimal voiding symptoms and a prostate volume < 50 cc.

1.	Agree	85% (66)
2.	Disagree	5% (4)
3.	Undecided	10% (8)
	Total 78	

Strong support for brachytherapy in selected patients. Due to concerns about long-term outcome and morbidity, brachytherapy received strong support only in the context of careful patient selection according to age, risk, and lack of voiding symptoms.

22. Brachytherapy, performed in experienced centres, is a reasonable curative treatment for low-risk prostate cancer in a patient over 55 years of age with minimal voiding symptoms and a prostate volume < 50 cc.

1.	Agree	46% (38)
2.	Disagree	41% (34)
3.	Undecided	13% (11)
	Total 83	

There was clear concern over the use of brachytherapy in men under age 60. Many attendees felt that the lack of long-term follow up data (i.e., 10-15 years), made the use of brachytherapy in these patients overly risky.

23. In the face of uncertainty regarding the optimal therapy for low-risk localized prostate cancer, clinical trials comparing treatment options should be strongly supported by the Canadian urological community.

1.	Agree	95% (79)
2.	Disagree	2% (2)
3.	Undecided	2% (2)
	Total 83	

There was strong support for accrual to clinical trials in prostate cancer. This reflects the commitment and success that the Canadian urology community has demonstrated in accruing to trials in prostate cancer over the last decade. This also reflects a recognition that many unanswered questions exist, and that clinical trials represent the only viable solution to resolve these uncertainties.

24. Adjuvant therapy is not warranted for patients with pT1–2 disease, negative surgical margins, GS equal to or less than 7, and undetectable post-operative PSA.

1.	Agree	99% (81)
2.	Disagree	0% (0)
3.	Undecided	1% (1)
	Total 82	

The role of adjuvant therapy after surgery is clearly evolving. There was unanimity, however, that there was no current role for adjuvant treatment—either radiation or androgen deprivation—for low-risk patients.

25. For patients with positive surgical margins, no firm evidence supports the use of adjuvant radiation over radiation administered at the time of biochemical progression.

1.	Agree	79% (65)
2.	Disagree	17% (14)
3.	Undecided	4% (3)
	Total 82	

While radiation is widely used for salvage of biochemical failure after surgery, there was relatively little support for the use of radiation in the truly adjuvant setting, i.e., for patients with undetectable PSA at high risk of biochemical progression. The common practice is to reserve radiation therapy until biochemical progression occurs, reasoning that progression cannot be predicted with certainty.

26. In node-negative patients at high risk for systemic progression (i.e., GS of 8–10, seminal vesicle infiltration), the evidence supports a role for adjuvant hormone therapy irrespective of post-operative PSA.

1.	Agree	40% (34)
2.	Disagree	53% (46)
3.	Undecided	7% (6)
	Total 86	

The use of adjuvant hormone therapy for high-risk patients is becoming more widely accepted. Taking the response to this question in conjunction with the response to question 25 for low-risk disease, those who use adjuvant hormone therapy believe this should be restricted to high-risk patients.

27. For node-positive patients, adjuvant hormone therapy is warranted.

1.	Agree	93% (77)
2.	Disagree	6% (5)
3.	Undecided	1% (1)
	Total 83	

This reflects the Messing data, which clearly demonstrated a survival and progression benefit to early hormone therapy for node-positive patients. A small percentage remain unconvinced by this data, which are drawn from a single, relatively small clinical trial.

28. Neoadjuvant hormone therapy is warranted prior to surgery in selected high-risk patients.

1.	Agree	20% (17)
2.	Disagree	68% (59)
3.	Undecided	13% (11)
	Total 87	

Most attendees have abandoned the use of neoadjuvant therapy prior to surgery, believing that the randomized trials have failed to demonstrate a benefit in terms of progression rates, in spite of the apparent downstaging. Twenty percent continue to use NHT in the high-risk setting. Of these, most felt that longer term NHT, i.e. 8 months, offered a benefit in the high-risk setting, and that the results of the CUOG trial comparing 3 to 8 months of therapy would be critical in determining their future practice in this regard.

29. Neoadjuvant hormone therapy is warranted prior to radiation in all high-risk patients.

1.	Agree	81% (67)
2.	Disagree	16% (13)
3.	Undecided	4% (3)
	Total 83	

In contrast, there was a clear majority opinion that neoadjuvant hormone therapy prior to radiation therapy had a demonstrated benefit in terms of radiation response and progression rates. There was a considerable variation in practice between the use of neoadjuvant and adjuvant therapy in conjunction with radiation, however.

30. The workshop format provided an opportunity for effective discussion with my peers.

1.	Strongly agree	46% (37)
2.	Agree	42% (34)
3.	Undecided	4% (3)
4.	Disagree	7% (6)
5.	Strongly disagree	1% (1)
	Total 81	

31. The workshop format should be continued in future meetings.

1.	Strongly agree	44% (35)
2.	Agree	44% (35)
3.	Undecided	6% (5)
4.	Disagree	3% (2)
5.	Strongly disagree	3% (2)
	Total 79	

Conclusions

In conclusion, this exercise provided a unique opportunity to examine the range of opinion on the management of localized prostate cancer. Approximately 20% of Canadian urologists were present for these discussions, which have enabled us to identify areas where leading opinions converge, as well as those subjects on which consensus has not yet been reached.

How best to treat patients remains open for discussion, but despite uncertainties regarding optimal treatment strategies, this exercise revealed broad agreement on the idea that proper stratification of patients is crucial. Good consensus also exists with regard to the definition of risk categories under which to stratify patients.

We hope this exercise will spur Canadian urologists to explore further means of generating consensus on these and other topics of significant clinical interest. □