Diagnosis, referral, and primary treatment decisions in newly diagnosed prostate cancer patients in a multidisciplinary diagnostic assessment program

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Abstract

Introduction: We aimed to report on data from the multidisciplinary diagnostic assessment program (DAP) at the Gale and Graham Wright Prostate Centre (GGWPC) at North York General Hospital (NYGH). We assessed referral, diagnosis, and treatment decisions for newly diagnosed prostate cancer (PCa) patients as seen over time, risk stratification, and clinic type to establish a deeper understanding of current decision-making trends.

Methods: From June 2007 to April 2012, 1277 patients who were diagnosed with PCa at the GGWPC were included in this study. Data was collected and reviewed retrospectively using electronic patient records.

Results: 1031 of 1260 patients (81.8%) were seen in a multidisciplinary clinic (MDC). Over time, a decrease in low-risk (LR) diagnoses and an increase intermediate-risk (IR) diagnoses was observed ($p<0.0001$). With respect to overall treatment decisions 474 (37.1%) of patients received primary radiotherapy, 340 (26.6%) received surgical therapy, and 426 (33.4%) had conservative management; 57% of patients who were candidates for active surveillance were managed this way. No significant treatment trends were observed over time ($p=0.8440$). Significantly, different management decisions were made in those who attended the MDC compared to those who only saw a urologist ($p<0.0001$).

Conclusions: In our DAP, the vast majority of patients presented with screen-detected disease, but there was a gradual shift from low- to intermediate-risk disease over time. Timely multidisciplinary consultation was achievable in over 80% of patients and was associated with different management decisions. We recommend that all patients at risk for prostate cancer be worked up in a multidisciplinary DAP.

Introduction

In 2015, an estimated 24 000 men in Canada will be diagnosed with prostate cancer (PCa) and will need to decide between a variety of management options.[1] For many, this can be distressing and lead to post-treatment regret and worse quality of life.[2,3] Most commonly, a patient diagnosed with PCa will meet with their urologist to learn about management options. Sometimes a referral for consultation with a radiation oncologist is made. The literature has reported that each specialist is more likely to recommend treatment that they provide.[4] In anticipation for an increase in the number of PCa diagnoses in the coming years, an understanding of the decision-making process is exceedingly important.[1,5]

In 2007, the Gale and Graham Wright Prostate Centre (GGWPC), in collaboration with the Odette Cancer Centre (OCC), was established at North York General Hospital (NYGH). As a diagnostic assessment program (DAP), the goal is to improve timely access and the quality of care provided to men with PCa. Our group has already shown that wait times from suspicion to radiation treatment is, on average, two months shorter in the GGWPC vs. standard community practice (183 vs. 138 days, $p=0.046$).[6]

Patients are referred from general practitioners or community urologists if they have an elevated prostate-specific antigen (PSA) in the absence of instrumentation, abnormal digital rectal examination (DRE) or abnormal imaging suggestive of PCa. Patients are seen by one of five urologists and their prostate cancer risk assessed within two weeks of referral. If a biopsy is warranted, this is also done in the clinic within two weeks. Results of the biopsy are given within two weeks of biopsy and if the patient is diagnosed with cancer, the patient seen by both urology and radiation oncology within a week (staging tests are arranged, if appropriate). Throughout the diagnostic journey, the patient

is supported by our expert nurse, clinical coordinator, and Prostate Cancer Canada Network volunteers.

The purpose of this study is to examine data from GGWPC regarding referral, diagnosis, and treatment decisions for newly diagnosed PCa patients. This data was examined over time, risk stratification, and clinic type to establish a deeper understanding of current decision-making trends.

Methods

Patients

From June 2007 to April 2012 at the GGWPC, there were 12 856 patient encounters, 3231 prostate biopsies performed, and 1358 patients newly diagnosed (an additional 63 patients were re-biopsied on an active surveillance protocol). Eighty-one patients were excluded from these analyses due to: lack of followup information (n=75); recurrent disease (n=4); diagnosed before observation window (n=2). This left 1277 patients in the study.

Data collection

Data was collected and reviewed retrospectively using electronic patient records. Information obtained included age at diagnosis, biopsy date, reason for referral, prognostic factors at diagnosis (pre-biopsy PSA level, TNM stage, Gleason Score (GS), and percent core involvement), and initial treatment decision.

PCa risk was divided into five strata based on the Prostate Cancer Risk Stratification (ProCaRS) database.[7] PROCARS is similar to other risk classification schemes[8,9] except that it further subdivides the intermediate- and high-risk groups into low and high tiers, respectively. Classifications are: low-risk disease (LR) (clinical stage ≤T2b, GS≤6 and PSA≤10 ng/mL); low-intermediate-risk disease (LIR) (PSA≤10 ng/mL and [GS=7 or clinical stage=T2c]), high-intermediate-risk disease (HIR) (GS=7 and one or both of PSA 10–20 ng/mL and/or clinical stage=T2c); high-risk disease (HR) (PSA>20 ng/mL or clinical stage=T3-T4 or GS=8-10); and very-high-risk disease (PSA>30 ng/mL or having high-volume disease, defined as >87.5% biopsy core involvement). For patients who were staged, the results of the bone scans and computed tomography (CT) scans for patients were reviewed and men with metastatic disease were documented.

Analyses

The initial treatment choice following diagnosis was examined at each risk stratum. Reasons for referral, quantity of diagnoses, and risk status were examined on an annual basis from June 2007 to April 2012. For time periods less than a year (June 13, 2007 to May 31, 2008 and June 1, 2011 to April 26, 2012), data for the number of diagnosis was prorated for a 12-month year. Treatment decisions among patients who attended a multidisciplinary clinic (MDC) were compared with those in a non-MDC setting using a Chi-square test. A separate analysis was done for patients deciding between surgical therapy (RP) and radiation therapy (RT) treatments alone, as opposed to those also considering conservative management (CM).

The LIR and HIR groups were combined into one intermediate risk (IR) group and generalized linear model[10] was used to test for a significant trend over time between IR and LR groups. Generalized linear model (GENMOD) procedure was applied for this analysis using Statistical Analysis Software (SAS version 9.4 for Windows). The outcome of the model was percent of patients per year; the independent variables were year (2007–2012), risk group (IR vs. LR), and interaction between year and risk group (year × risk). GENMOD was also used to test for a significant difference over time between the proportion of patients choosing between CM, RP, or RT. The outcome of the model was percent of patients per year; the independent variables were year (2007–2012), treatment (RP, RT, or CM), and interaction between year and treatment (year × treatment). For the purposes of these analyses, we defined CM as no therapy, active surveillance, or primary androgen-deprivation therapy (ADT).

Results

From June 2007 to April 2012, 1277 patients were diagnosed with PCa at GGWPC in NYGH. On average, 258 patients were diagnosed per year (range 212–277). The median age of diagnosed patients was 67.2 years old (range 41–93) and was stable over time.

Among newly diagnosed patients, almost all were referred due to an abnormal PSA. Eight hundred twenty-nine men (64.9%) were referred for an elevated PSA alone, 394 (30.9%) for an abnormal PSA and DRE, 13 (1.0%) for an abnormal DRE, and one (0.1%) for benign prostatic hypertrophy (BPH). Suspicious pathological findings were the reason for referral for less than 1% of diagnosed men (typical small acinar proliferation [ASAP] in nine patients [0.7%]; high-grade prostatic intraepithelial neoplasia [HGPIN] in one patient [0.1%]). Data with respect to reason for biopsy was unavailable for 30 men (2.3%). Over time, the proportion of patients with missing data and those referred for an elevated PSA alone decreased slightly (Fig. 1).

Management decisions are summarized in Table 1. Of the 1277 men included in the study, data on management was unavailable for 32 patients (2.5%), leaving 1245 patients. PR was given to 474 (38.1%) patients, of which 203 (42.8%) received primary external beam radiation therapy (EBRT), 107 (22.6%) received brachytherapy (BT) alone, and 48 (10.1%) received EBRT with a BT boost. Additionally, 340 (27.3%)

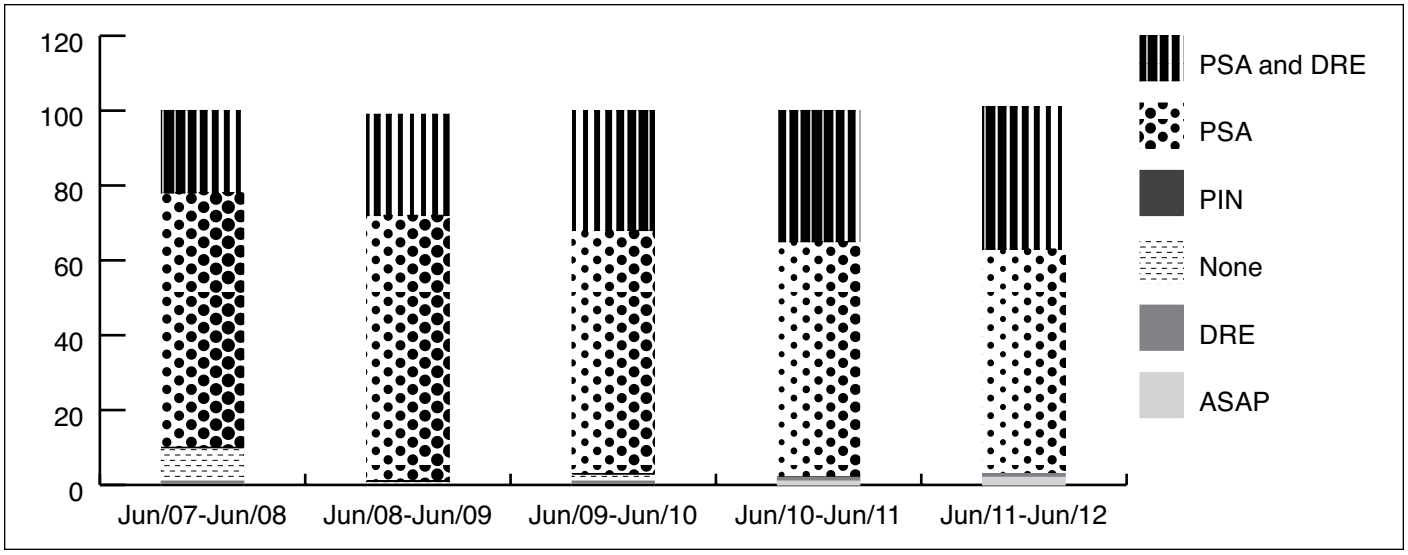

Fig. 1. Annual reason for referral among diagnosed patients over time. ASAP: small acinar proliferation; DRE: digital rectal examination; PIN: prostatic intraepithelial neoplasia; PSA: prostate-specific antigen.

received RP, while 426 (34.2%) were managed conservatively. Of the 426 conservatively managed patients, 353 (82.9%) were managed with active surveillance and 73 (17.1%) were managed with primary ADT. Less than 1% of patients chose high-intensity focused ultrasound (HIFU) or chemotherapy. No significant trend (p=0.8440) was found among proportion of patients choosing active surveillance, RP, and RT over time.

Of the 1277 men with PCa, 41 (3.2%) had metastatic disease. T category, GS, and PSA values were available for 1110 (89.9%) of the patients diagnosed with localized disease. Three-hundred seventy-six (33.9%), 373 (33.6%), 137 (12.3%), 92 (8.3%), and 132 men (11.9%) had low-, low-intermediate-, high-intermediate-, high- and very-high-risk PCa, respectively. This information is summarized in Table 2 and also divided by treatment decision.

Table 1. Primary treatment decision after diagnosis among 1245 patients with management data (32 patients had no data available)

Primary treatment approach	n	% of type of approach	% of total
Radiotherapy	474		38.1%
EBRT	203	42.8%	16.3%
EBRT + ADT	81	17.1%	6.5%
SABR	35	7.4%	2.8%
EBRT + brachytherapy	48	10.1%	3.9%
Brachytherapy alone	107	22.6%	8.6%
Conservative management	426		34.2%
Active surveillance/watchful waiting	353	82.9%	28.4%
Primary ADT	73	17.1%	5.9%
Radical prostatectomy	340		27.3%
Open	36	10.6%	2.9%
Laparoscopic	0	0.0%	0.0%
Robotic	4	1.2%	0.3%
Unknown	300	88.2%	24.1%
Other	5		0.4%
HIFU	3	60.0%	0.2%
Chemotherapy	2	40.0%	0.2%

ADT: androgen-deprivation therapy; EBRT: external beam radiotherapy; HIFU: high-intensity focused ultrasound; SABR: stereotactic ablative radiotherapy.

Risk status at time of diagnosis is summarized annually in Fig. 2. The graph shows that over time, IR disease diagnoses increased and LR disease diagnoses decreased. Significant time trends (p=0.0203) and a highly significant difference (p<0.0001) between the IR and LR groups was found. Additionally, the interaction term between year and risk group was highly significant, indicating LR and IR have completely different time trends. The HR disease rates remained stable.

Of the 1277 patients, there were no data regarding attendance in a MDC for 17 men (1.3%), leaving 1260 patients; 1024 (81.3%) were seen in a MDC. The differences in treatment decisions in a MDC compared to a non-MDC are presented in Fig. 3. Of the 1024 patients seen in a MDC, the majority opted for RT, followed by CM, and lastly RP. Of the 236 patients not seen in a MDC, the majority opted for CM, followed by RP, then RT. This difference was highly significant (p<0.0001). Additionally, a highly significant difference (p<0.0001) was found in the proportion of patients choosing either RT or RP with more patients opting for RT in a MDC setting.

Discussion

This study reports the diagnostic and treatment results over time from a large Canadian DAP for prostate cancer from 2007–2012. We are not aware of any similar data from other Canadian centres.

Table 2. Primary treatment by risk category

Initial treatment	Risk category									
	LR		LIR		HIR		HR		VHR	
	n	%	n	%	n	%	n	%	n	%
AS/WW	222	59.0	58	15.5	12	8.8	6	6.5	7	5.3
BT	52	13.8	33	8.8	9	6.6	1	1.1	5	3.8
EBRT	20	5.3	95	25.5	49	35.8	14	15.2	16	12.1
EBRT & BT	1	0.2	31	8.3	4	2.9	2	2.2	4	3.0
EBRT & ADT	0	0	8	2.1	12	8.8	23	25.0	27	20.5
HIFU	2	0.5	1	0.3	0	0	0	0	0	0
Primary ADT	0	0	0	0	2	1.5	10	10.9	32	24.2
SABR	8	2.1	6	1.6	4	2.9	5	5.4	9	6.8
RP	63	8	136	36.5	43	31.4	28	30.4	24	18.2
Unknown	8	2.1	5	1.3	2	1.5	3	3.3	8	6.1
Total	376	100	373	100	137	100	92	100	132	100

ADT: androgen-deprivation therapy; AS: active surveillance; BT: brachytherapy; EBRT: external beam radiotherapy; HIFU: high-intensity focused ultrasound; HIR: high-intermediate-risk; HR: high-risk; LIR: low-intermediate-risk; LR: low-risk; RP: radical prostatectomy; SABR: stereotactic ablative radiotherapy; VHR: very-high-risk; WW: watchful waiting.

Between 2007 and 2012, the proportion of patients diagnosed with LR disease decreased, while the proportion of patients with IR disease increased ($p<0.0001$). This was likely due to grade migration after the International Society of Urologic Pathologists' 2005 recommendations where poorly formed glands and any cribiform pattern (Gleason pattern 3b and 3c) were reassigned pattern 4.[11]

We were encouraged by the high proportional use of active surveillance in LR patients (59%), which seems to be higher than other jurisdictions in Canada or the U.S.[12,13] This may reflect a comfort level stemming from Sunnybrook's and others' seminal work in the region.[14,15] We noted that 16% of LIR and 9% of HIR patients were managed by active surveillance. While both the National Institute for Heath and Care Excellence (NICE) and Cancer Care Ontario (CCO) active surveillance guidelines allow the use of active surveillance for selected IR patients,[16,17] further data is calling this practice into question. Data from the Sunnybrook cohort presented at the 2015 Genitourinary Cancers Symposium reported that IR patients at baseline managed with active surveillance have an increased risk of PCa death (hazard ratio 3.74, $p=0.01$) compared to patients with LR disease.[18]

Interestingly, there were significantly different management choices made by the approximately 20% of patients who did not attend a MDC consult. Patients not attending were more likely to choose active surveillance (64% vs.

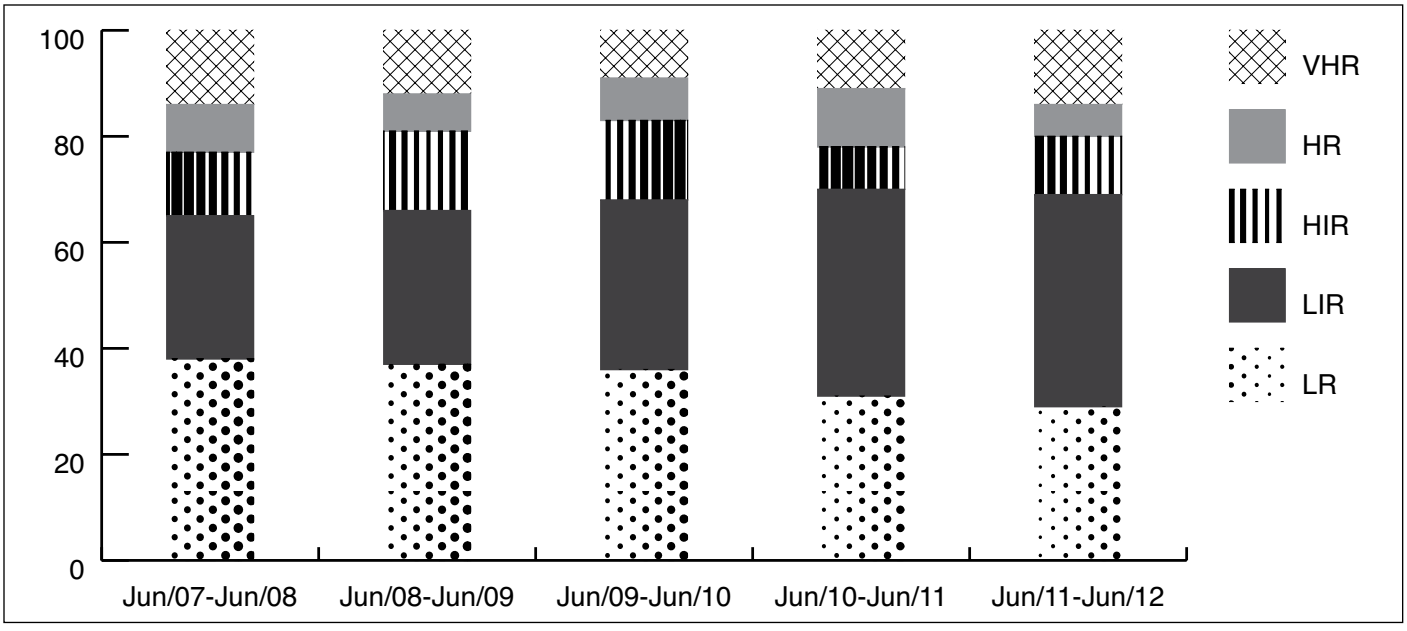

Fig. 2. Annual risk category of diagnosed patients. HIR: high-intermediate-risk; HR: high-risk; LIR: low-intermediate-risk; LR: low-risk; VHR: very-high-risk.

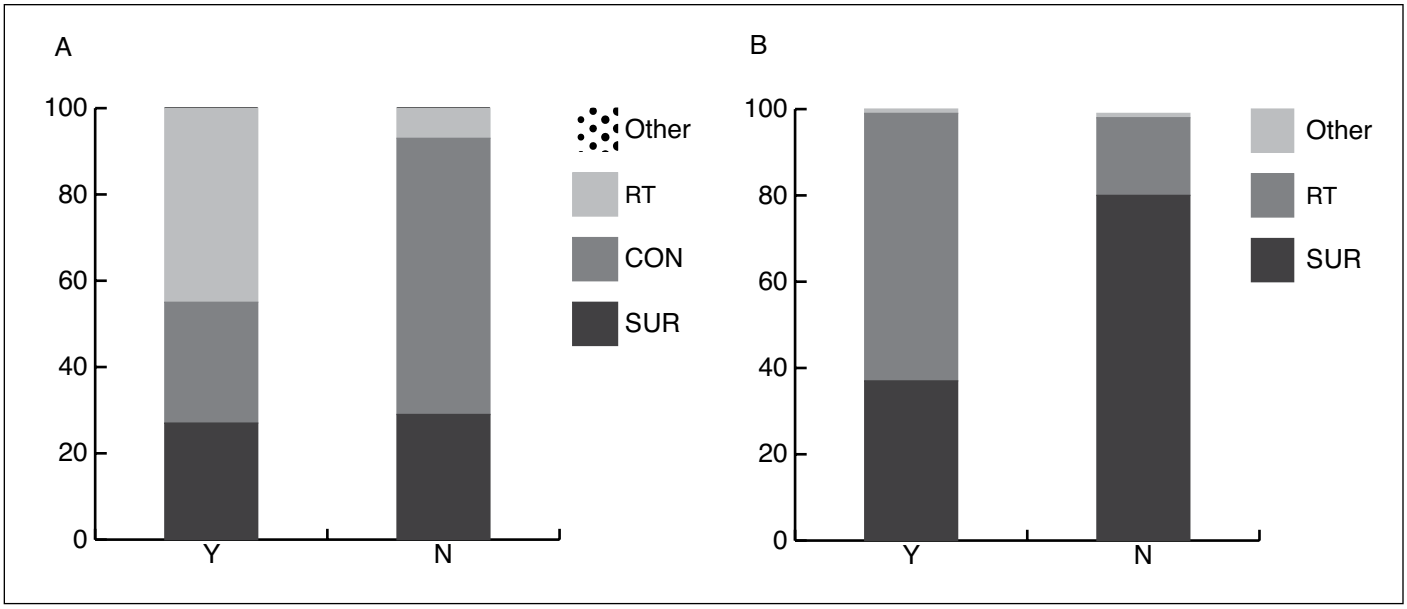

Fig. 3. Patient management stratified by attendance in multidisciplinary clinic: (A) all treatments; (B) active treatments. CON: conservative therapy; RT: radiation therapy; SUR: surveillance.

28%); of those choosing treatment, more chose RP than RT (81% vs. 19%, p<0.0001). The clinic's mandate is to ensure all of the patients diagnosed with PCa have a MDC appointment, regardless of how clear they are on their choice of treatment to ensure they make a fully informed decision. We could not force them to attend, but arranged their MDC appointment so all the disciplines are readily available for them to take advantage of this unique opportunity. Therefore, caution should be taken when interpreting these differences, as MDC consult was not a random process (i.e., is associational not causational) and we didn't collect age and comorbidity data. It may well be that patients chose not to attend a MDC because they were comfortable with their decision (i.e., they knew they didn't want radiation) or had limited life expectancy based on comorbidities. However, based on previous studies[19] and our experience, patients often have preconceived misconceptions about radiation and benefit from hearing about the logistics, success rates, and side effects from a specialist trained in radiation oncology, preferably one sub-specialized in PCa care. A similar study found that patient preferences had little effect on treatment decisions. Rather, they were associated with the specialty of the counseling physician.[20] The GGWPC aims to provide balanced information surrounding management options in an open and interactive manner. It is important for quality of life after treatment that patients receive balanced information to make an informed decision and avoid post-treatment regret.[2,21] In addition, reports from other MDCs indicate high patient satisfaction with this approach.[22]

Of the 224 patients with high or very high risk, 13 (5.8%) and 42 (18.8%) were also managed conservatively or with primary ADT. While these numbers are not large, multiple randomized, controlled trials have shown that compared to RT and ADT, patients have an increased risk of PCa-related and overall mortality[23-25] and combined modality treatment should be offered. Obviously, some patients will have such limited life expectancy that they would not benefit from this approach, but in our experience these patients are usually not offered prostate screening.

Conclusions

In this large, Canadian, multidisciplinary DAP, the vast majority of patients presented with screen-detected disease. Over the observation window, there was a gradual shift from LR to IR disease. Over 50% of patients who were candidates for active surveillance were managed this way. Timely multidisciplinary consult was achievable in over 80% of patients and was associated with different management decisions. We recommend that all patients at risk for PCa be worked up in a multidisciplinary DAP.

Competing interests: The authors declare no competing financial or personal interests.

This paper has been peer-reviewed.

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