Hospital encounters and associated costs of prostate evaluation for clinically important disease

MRI vs. standard evaluation procedures (PRECISE) study from a provincial-payer perspective

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ABSTRACT

INTRODUCTION: Systematic transrectal ultrasonography (TRUS) biopsy has been the standard diagnostic tool for prostate cancer (PCa) but is subject to limitations, such as a high false-negative rate of cancer detection. Multiparametric magnetic resonance imaging (mpMRI) prior to biopsy is emerging as an alternative diagnostic procedure for PCa. The PRECISE study found that MRI followed by a targeted biopsy was more accurately able to identify clinically significant cancer than TRUS biopsy.

METHODS: PRECISE study patients recruited in Ontario between January 2017 and November 2019 were linked to various Ontario provincial administrative databases available at the Institute for Clinical and Evaluative Sciences (ICES) to determine health resources used, associated costs, and hospitalizations in the 14 days after biopsy. Costs are presented in 2021 CAD.

RESULTS: A total of 281 males were included in this study, with 48.4% of the patients in the TRUS biopsy group, 28.1% in the MRI+, and 23.5% in the MRI- group. Twenty-one patients (15%) from the TRUS biopsy group were seen at a hospital in the 14 days after their biopsy compared to fewer than five patients (6%) from the MRI+ group. The mean per person per year (PPPY) costs for the TRUS and all MRI groups (MRI- and MRI+) were $7828 and $8525, respectively.

CONCLUSIONS: Patients in the TRUS biopsy group experienced more hospital encounters compared to patients who received an MRI prior to their biopsy. This economic analysis suggests that MRI imaging prior to biopsy is not associated with a significant increase in costs.

INTRODUCTION

Systematic transrectal ultrasonography biopsy (TRUS biopsy) has been the standard approach to the diagnosis of prostate cancer (PCa). Systematic TRUS biopsy requires 10–12 samples in the peripheral zone, where it is thought that most prostate cancer can be found. Conventional TRUS biopsy has a low sensitivity for discriminating actual tumor from normal tissue, and has a high false-negative rate of 30–45%, which means that many cancer diagnoses are missed.[1-3]

Multiparametric magnetic resonance imaging (mpMRI) prior to a targeted biopsy is emerging as an alternative diagnostic procedure for PCa. MRI prior to a biopsy allows for the accurate identification of cancerous tissue, meaning less biopsy samples need to be taken, which is why it is called a 'targeted' biopsy. This not only improves cancer detection rates, but MRI visibility is also associated with the identification of higher cancer grades, that is many patients can avoid unnecessary biopsies and, therefore, avoid overdiagnosis of clinically insignificant cancer.[4,5]

The PRECISE (PRostate Evaluation for Clinically Important disease: MRI vs. Standard Evaluation procedures) study aimed to determine whether MRI prior to targeted biopsy was non-inferior to systematic TRUS biopsy in the detection of clin-

KEY MESSAGES

- 15% of patients who received a TRUS biopsy had a hospital encounter within 14 days of their procedure compared to <5% in the MRI+ group.
- MRI imaging prior to biopsy did not lead to a significant increase in costs.

ically significant and clinically insignificant PCa.[6] In this trial, men referred with clinical suspicion of PCa who had no prior biopsy were randomized to either the control arm of receiving a transrectal TRUS-guided systematic biopsy or to the investigational arm of receiving an MRI followed by a transrectal targeted biopsy.[6] The trial found that targeted biopsy was better able to identify clinically significant cancer than the systematic TRUS biopsy, with 35% of men in the targeted biopsy arm being diagnosed with clinically significant cancer compared to 30% of men in the systematic biopsy arm. Forty percent of patients in the targeted biopsy arm were able to avoid a biopsy, and the rate of insignificant cancer diagnosis dropped by 50%.[6]

Although the PRECISE trial showed that there was merit to using MRI prior to targeted biopsy in determining a patient's PCa diagnosis, a comparison between these diagnostic procedures and associated outcomes and costs was needed. The objective of this study was to compare healthcare resource utilization (HCRU), costs, and post-biopsy hospitalizations between men who received either a TRUS biopsy (systematic biopsy), an MRI scan and a targeted biopsy (MRI+), or an MRI scan only with no subsequent biopsy (MRI-).

METHODS

The PRECISE study enrolled males aged 18 years and older from five Canadian centers. Specific study methodology and findings were published by Klotz and colleagues in 2021.[6] For this study, only the PRECISE study patients recruited in Ontario between January 2017 and November 2019 were analyzed. These patients were linked to various Ontario provincial databases available at the Institute for Clinical and Evaluative Sciences (ICES) to determine health resources used, associated costs, and post-biopsy hospitalizations from the date of their diagnostic procedure (index date) up to March 31, 2020.

Patients were excluded if they were unable to be linked to ICES administrative data, if they had erroneous dates (i.e., invalid death date [e.g., died before index date date], invalid birth date [e.g., missing or after index date]), if they were a non-Ontario resident at index date, or if they had gaps in Ontario Health Insurance Plan (OHIP) coverage over 90 days between index date and end of followup. Ethics approval was obtained from the Ontario Cancer Research Ethics Board (CTO Project ID: 1263).

Databases

Data were accessed using data available from the ICES, which collects data on public coverage via the OHIP and other population-level health information to generate real-world data. To determine the HCRU, costs, and outcomes for our cohort, health information on each individual patient was linked to applicable datasets. For this study, linkages were made to the following data sets: Activity Level Reporting (ALR), Continuing Care Reporting System (CCRS), Home Care Database (HCD), Ontario Home Care Administrative System (OHCAS), ICES Physician Database (IPDB), Hospital Discharge Abstract Database (DAD), Local Health Integration Network (LHIN), National Ambulatory Care Reporting System (NACRS), National Rehabilitation Reporting System (NRS), Ontario Mental Health Reporting System (OMHRS) Ontario Cancer Registry (OCR), Ontario Drug Benefit (ODB) Program, New Drug Funding Program (NDFP), OHIP, Ontario Case Costing Initiative (OCCI), Postal Code Conversion File (PCCF), Registered Persons Database (RPDB), Standard Price (STDPRICE), and Same Day Surgery (SDS). The Registered Persons Database contains demographic information on all individuals with OHIP coverage (e.g., date of birth, date of death). The OCR database was used to identify patients who were eventually diagnosed with PCa. The DAD and NACRS databases were used to identify any inpatient and outpatient hospital clinic visits, respectively. The OHIP database captures physician visits and fees for health professionals, including general practitioners, medical oncologists, radiation oncologists, and other specialists. All datasets are linked using unique, encoded patient identifiers, and housed at ICES.

Statistical analysis

Statistical analyses were conducted at ICES and performed in SAS Enterprise Guide 7.1. Baseline characteristics were summarized by number and percentage for categorical variables and by mean and standard deviation (SD) and median and interquartile range (IQR) for continuous variables. Comorbidity data was recorded via the Charlson Comorbidity Index.[7]

Table 1. Baseline characteristics for Ontario PRECISE study patients

		MRI- n=66	MRI+ n=79	TRUS n=136	Total n=281	p
Age at index date	Mean ± SD	63.3±7.2	66.0±7.5	64.7±7.4	64.7±7.4	0.0915
	Median (IQR)	63 (59–67)	67 (60–73)	65 (60–69)	65 (60–70)	0.0823
Rural	No, n (%)	61–65*	74–78*	121 (89.0%)	257 (91.5%)	0.3042
	Yes, n (%)	1–5*	1–5*	15 (11.0%)	24 (8.5%)	
Neighbourhood income quintile	1, n (%)	7 (10.6%)	7 (8.9%)	14 (10.3%)	28 (10.0%)	0.7821
	2, n (%)	10 (15.2%)	15 (19.0%)	25 (18.4%)	50 (17.8%)	
	3, n (%)	9 (13.6%)	19 (24.1%)	22 (16.2%)	50 (17.8%)	
	4, n (%)	17 (25.8%)	13 (16.5%)	31 (22.8%)	61 (21.7%)	
	5, n (%)	23 (34.8%)	25 (31.6%)	44 (32.4%)	92 (32.7%)	
Local Health Integration Network (LHIN)	Central, n (%)	11 (16.7%)	12 (15.2%)	31 (22.8%)	54 (19.2%)	0.127
	Central East, n (%)	2–6*	1–5*	(6.6%)	18 (6.4%)	
	Central West, n (%)	1–5*	1–5*	1–5*	6 (2.1%)	
	Champlain, n (%)	0 (0.0%)	0 (0.0%)	1–5*	1–5*	
	Erie St. Clair, n (%)	1–5*	1–5*	10–14*	15 (5.3%)	
	Hamilton Niagara Haldimand Brant, n (%)	0 (0.0%)	1–5*	1–5*	6 (2.1%)	
	Mississauga Halton, n (%)	1–5*	1–5*	1–5*	6 (2.1%)	
	North Simcoe Muskoka, n (%)	0 (0.0%)	1–5*	3–7*	1–5*	
	Southeast, n (%)	1–5*	0 (0.0%)	1–5*	1–5*	
	Southwest, n (%)	27 (40.9%)	19 (24.1%)	37 (27.2%)	83 (29.5%)	
	Toronto Central, n (%)	13 (19.7%)	35 (44.3%)	34 (25.0%)	82 (29.2%)	
	Waterloo Wellington, n (%)	1–5*	0 (0.0%)	1–5*	1–5*	
Charlson index	Mean ± SD	0.16±0.50	0.46±0.86	0.26±0.92	0.30±0.84	0.4538
	Median (IQR)	0 (0–0)	0 (0–1)	0 (0–0)	0 (0–0)	0.2147
Charlson score	0, n (%)	14–18*	18–22*	46 (33.8%)	82 (29.2%)	0.2832
	1+, n (%)	1–5*	4–8*	7 (5.1%)	16 (5.7%)	
	None, n (%)	47 (71.2%)	53 (67.1%)	83 (61.0%)	183 (65.1%)	
PCa diagnosis after index date	PCa diagnosis	15 (22.7%)	69 (87.3%)	80 (58.8%)	164 (58.4%)	<0.0001
	No PCa diagnosis	51 (77.3%)	10 (12.7%)	56 (41.2%)	117 (41.6%)	

*Groups with small cells were censored for privacy purposes. IQR: interquartile range (25–75%); MRI: magnetic resonance imaging; PCa: prostate cancer; SD: standard deviation; TRUS: transrectal ultrasonography.

The clinical outcome of interest was hospital encounters within 14 days of the diagnostic procedure. The primary and secondary reasons for diagnosis were used to determine the reasons patients were seen at either an emergency department or if they were admitted to an inpatient ward.

An economic analysis was undertaken to understand the HCRU, costs associated with the diagnostic procedure, and subsequent costs until the end of followup. Overall total and mean cost per patient were reported in 2021 Canadian dollars, using a macro-based costing methodology called GETCOST, which is available from ICES.[8] As we took an all-systems approach to costing, all of the ICES databases mentioned above were used to capture the health resources used to which the GETCOST macro was able to apply a cost. For total

Table 2. Hospital encounters within 14 days of biopsy procedure

	Description	Source			TRUS n=136	MRI+ n=79
		Hospital	Hospital +ED*	ED		
Total	Gram-negative sepsis, unspecified Sepsis, unspecified organism Urinary tract infection, site not specified Acute prostatitis Inflammatory disease of prostate, unspecified Retention of urine Infection after a procedure Other surgical procedures as the cause of abnormal reaction of the patient, or of later complication Other medical procedures as the cause of abnormal reaction of the patient, or of later complication Gastrointestinal hemorrhage, unspecified Other and unspecified abdominal pain Complications of procedures, not elsewhere classified Hemorrhage of anus and rectum	12	0–10	0–10	21	<6

*Recorded as inpatient hospitalization and ED visit for the same individual. ED: emergency department; MRI: magnetic resonance imaging; TRUS: transrectal ultrasonography.

cost, the macro is programmed to determine the costs of short-term episodes (for example, hospital-based encounters) by multiplying the encounter resource intensity weight by an annual cost per weighted case. Long-term episode costs (for example, complex continuing care) are calculated by weighted days, and costs of visit-based encounters are determined at use (a bottom-up approach). As the GETCOST macro was able to run costs up until March 31, 2020, costing data in this report is up to that time. Costs for the cohorts included costing data up to death, end of OHIP eligibility, or end of followup. For costing analysis censoring happens at minimum of death or March 31, 2020, since complete data after this date was unavailable.

RESULTS

Table 1 presents the baseline characteristics of the 281 males that were included in our study. Almost half of the patients were in the TRUS biopsy group (48.4%), followed by the MRI+ (28.1%) and MRI- (23.5%) groups. The average age of all patients was 64.7±7.4 years, with the MRI+ group being slightly older and the MRI- group being slightly younger. A total of 164 patients were diagnosed with PCa (58.4%) after receiving their diagnostic procedure, including 80 patients (58.8%) from the TRUS biopsy group and 84 patients (57.9%) from the MRI group.

Table 2 presents the distribution of inpatient hospitalizations and emergency department (ED) visits within 14 days after patients received either TRUS or targeted biopsy (MRI+). There were 21 patients from the TRUS biopsy group who were seen at a hospital due to reasons such as sepsis, infections, and inflamed prostate, compared to <6 patients from the MRI+ group (in the database, for rare events, frequency was recorded as <6 rather than as discrete numbers).

Table 3. Mean per person per year costs

Group	n	Mean PPPY cost	Standard deviation	Median	Interquartile range
TRUS biopsy	136	$7828	$12 394	$17 015	$8108–25 276
All MRI	145	$8525	$15 841	$18 106	$6276–28 506
MRI-	66	$5216	$6767	$9706	$4331–20 023
MRI+	79	$11 289	$20 201	$21 572	$10 558–34 024

MRI: magnetic resonance imaging; PPPY: per person per year; TRUS: transrectal ultrasonography.

Table 3 provides the mean per person per year (PPPY) costs for the TRUS and all MRI groups (MRI- and MRI+). The costs in these two groups are similar. Patients in the MRI- group had the lowest cost, with $5216±6767, followed by the TRUS biopsy group with $7828±12 394, and finally the MRI+ group, with $11 289±$20 201. The all MRI group (MRI+ and MRI-) did not incur significantly higher costs than the TRUS biopsy group. It should be noted that when costs were further stratified by patients with and without PCa, the mean PPPY costs were significantly higher for the patients who were diagnosed with PCa.

DISCUSSION

This study included 281 men, of which 136 (48.4%) were in the TRUS biopsy group and 145 were in the MRI group. In the MRI group, 79 (28.1%) were MRI+ and 66 (23.5%) MRI-. Approximately, 15% of patients who received a TRUS biopsy had a hospital encounter within 14 days compared to 6% or less in the MRI+ group. Since the MRI+ group had targeted biopsies only (less biopsy cores), this could suggest that the number of cores taken during the biopsy is correlated with the risk of hospitalization. These hospitalizations can be grouped as procedure-related, prostate/urinary-related, and/or infection-related; however, there is no guarantee that these hospitalizations were as a direct result of the biopsy procedure. The costing results suggest that MRI imaging prior to biopsy does not lead to a significant increase in costs.

The findings in our study align with other studies that also suggest the diagnostic approach to imaging men with a suspicion of PCa prior to biopsy may be more cost-effective in the long run. Callender et al showed that not only was MRI prior to biopsy more cost-effective, it also led to few biopsies, less overdiagnoses, and fewer deaths.[9] Similarly, de Rooij et al found that although costs for MRI-biopsy and TRUS biopsy were similar, the MRI strategy led to an improvement in quality of life.[10] Findings from Hao et al suggest that TRUS biopsy is more costly and less effective than MRI-first strategies.[11] Finally, the Cheng et al study also showed that MRI targeted biopsy is more cost-effective than TRUS biopsy.[12] All these studies suggest that MRI prior to a biopsy can be more cost-effective because it allows patients to be categorized as higher-risk (require biopsy) or lower-risk (do not require biopsy), whereas the TRUS biopsy method requires that all patients be biopsied regardless of risk, resulting in more unnecessary biopsies.

Strengths and limitations

A major strength of this study was the ability to link clinical trial data study patients with administrative data to collect followup information, such as hospital encounters and costing information. Although the PRECISE trial did collect adverse event information at every six-month visit, the hospitalization data collected within the study was based on only patient report. Patients were asked to fill out an adverse events form; however, using the ICES databases, we were more accurately able to capture all hospital visits in the two weeks after biopsy. A limitation of this study was the modest sample size of 281 patients, which limits the generalizability of the findings. Another limitation of this study is that the PRECISE trial will follow patients for eight years and capture a lot of information, such as future biopsies and diagnoses; however, the trial data used for this study does not incorporate that followup data as that has yet to be collected.

COMPETING INTERESTS: The authors do not report any competing personal or financial interests related to this work.

This paper has been peer-reviewed.

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