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Relevance of using mpMRI for the diagnostic investigation of prostate cancer

mpMRI and prostate cancer diagnosis

English summary

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SUMMARY

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Introduction

Prostate cancer is the second most frequently diagnosed cancer in men in Québec after bronchial and lung cancer. Following an elevated prostate-specific antigen (PSA) result or the detection of a suspicious mass during digital rectal examination (DRE), prostate cancer is usually diagnosed by transrectal ultrasound (TRUS)-guided biopsy. While TRUS can locate the prostate, it cannot distinguish possible tumour lesions. Thus, TRUS-guided biopsies, referred to as systematic biopsies, are performed blindly. Depending on the lesions' characteristics and location, some that are clinically significant may not be diagnosed, while indolent lesions may be detected, which can lead to overdiagnosis and overtreatment. Furthermore, TRUS-guided biopsies are invasive procedures that can have adverse effects for patients and compromise their quality of life.

An alternative diagnostic approach involving the use of multiparametric magnetic resonance imaging (mpMRI) is being investigated to examine these issues and to promote optimal management of patients with suspected prostate cancer. The approach of coupling biopsies with mpMRI would decrease the number of patients requiring a biopsy as well increase the biopsy positivity rate by sampling only those abnormalities detected on mpMRI. Targeted biopsies would also permit sampling of the lesion with fewer specimens, which could reduce cost, risk of infection and patient discomfort.

Background to the request

The Programme québécois de cancérologie (PQC) (Quebec Oncology Program) asked INESSS for guidance on the relevance of using mpMRI for the diagnostic investigation of prostate cancer. This assessment was carried out in collaboration with the Unité d'évaluation des technologies et des modes d'intervention en santé (UETMIS) of the CHU de Québec, which was in turn asked by its urology department to determine whether this facility should include mpMRI in its offer of services.

The assessment questions addressed concern efficacy, safety, economic impact and organizational aspects of this diagnostic modality.

Methodology

A preliminary search of the scientific literature yielded a Cochrane systematic review containing meta-analyses on the use of mpMRI to diagnose prostate cancer [Drost *et al.*, 2019]. The objective of the review was to assess the diagnostic accuracy of mpMRI with or without targeted biopsy, and to assess the efficacy of targeted biopsy using this diagnostic

modality compared to systematic biopsy, for the detection and diagnosis of clinically significant prostate cancer. Given the concordance between the assessment objectives in the systematic review and some of the assessment questions in the present guidance, the Cochrane review was used as the starting point for selecting scientific studies. A literature update was conducted for a timeframe subsequent to the inclusion period used by the Cochrane systematic review to address all of the assessment questions. In addition, the present assessment is in line with the work of UETMIS at CHU de Québec - Université Laval on the use of mpMRI as a triage test.

A complementary literature search was performed in the MEDLINE (via the PubMed interface), Embase and EBM Reviews databases. A grey literature search was conducted to retrieve clinical practice guidelines and guidance documents on the use of mpMRI for prostate cancer diagnosis and for recommendations published by learned societies and scientific associations. Preference was given to systematic reviews with meta-analyses. Randomized clinical trials and matched diagnostic studies were retained as comparative studies.

Results

Diagnostic accuracy of mpMRI with or without targeted biopsy

The studies that have evaluated diagnostic accuracy during triage show that 9% of prostate cancers of grade 2 or higher would not be detected by imaging. In the real-world care setting, 28% of men with grade 2 or higher cancer would not be diagnosed when mpMRI (with or without biopsy) is used. In comparison, 37% of men with grade 2 or higher cancer would not be diagnosed following the standard continuum of care (TRUS-guided systematic biopsy).

Assuming a hypothetical prevalence of grade 2 or higher prostate cancer of 26%, 91% of men with a negative mpMRI result would not have grade 2 or higher prostate cancer (negative predictive value [NPV]). Compared to the standard continuum of care (TRUS-guided biopsy), with an estimated true prevalence of 34%, 84% of men with a negative result on TRUS-guided biopsy would not have grade 2 prostate cancer (NPV).

Efficacy of mpMRI-targeted biopsy

Biopsies that are targeted using mpMRI would increase detection rates of clinically significant lesions while decreasing detection rates of those that are clinically non-significant. Diagnosis would require less sampling, in addition to subjecting fewer patients (approximately 33%) to biopsy, when compared to systematic biopsy. Some cancers (approximately 30%) might not be detected by mpMRI but would still be diagnosed with systematic biopsy. However, the vast majority of the cancers detected in this way would be indolent. Approximately 3.4% would be clinically significant cancers.

Efficacy of mpMRI-targeted biopsy combined with systematic biopsy

The reported results are ambivalent as to the relevance of performing systematic biopsy in combination with mpMRI-targeted biopsy to maximize the detection and diagnosis of clinically significant prostate cancers.

Such a practice could increase detection rates of clinically significant cancers. However, performing systematic biopsy plus mpMRI-targeted biopsy would significantly increase the detection of clinically non-significant cancers compared to targeted biopsy alone.

Adverse effects of mpMRI with or without targeted biopsy

Comparative studies have shown that, in general, the proportion of patients who reported complications or adverse effects was lower for those who had had targeted biopsy with mpMRI than for those who had had systematic biopsy.

Efficiency analysis and budget impact

Although marked by significant uncertainty, the economic analysis performed suggests that the use of mpMRI as a triage test followed by targeted biopsy, in the situation where the result of the first test is positive for prostate cancer diagnosis could constitute an efficient diagnostic approach. Based on the currently available data and the assumptions made, in men with suspected prostate cancer who have never had a diagnostic biopsy, the mean incremental cost-utility ratio (ICUR) is estimated at $11,544 CAD / quality-adjusted life year (QALY) gained, with an 87% probability of efficiency at the $50,000 CAD per QALY threshold. In men who have had a diagnostic biopsy with a negative result but there is a high suspicion of prostate cancer, the mean incremental cost-utility ratio is estimated at $8,443 CAD / QALY gained, with a 96% probability of efficiency at the $50,000 CAD per QALY threshold. This echoes the conclusions of studies found in the scientific literature.

Public coverage of mpMRI as a diagnostic modality for prostate cancer could increase costs by approximately $6,5 million CAD over 3 years. However, this analysis, which is subject to a certain degree of uncertainty, does not take the potential need for additional imaging platforms and equipment into account.

Professional and organizational issues and impact on resources

There was broad consensus among the experts consulted regarding the relevance of using mpMRI for the diagnostic investigation of prostate cancer. However, they stressed the need to follow the minimum technical recommendations published in the PI-RADS (Prostate Imaging - Reporting and Data System) guide to ensure safe and standardized MRI use. They believe that image fusion guiding is recommended to ensure the technique’s accuracy.

As for the organizational issues, the experts emphasized that the experience of hospitals and clinicians is an important factor that influences the interpretation and reliability of mpMRI for prostate cancer diagnosis. Thus, training the key professionals was considered essential. A major concern was expressed by all the experts consulted regarding the ability of Québec’s health care system to handle the increased demand for MRI if this practice is implemented.

The organization of services must take this increase in volume into account to ensure timely management of patients undergoing diagnostic investigation for prostate cancer, without compromising the management of other patient groups. In addition, regional accessibility issues were raised by the experts and stakeholders consulted. Access to magnetic resonance imaging for this population could require travel to major centres.

To limit the use of this diagnostic modality to the most relevant situations, the experts are of the opinion that only urologists should order mpMRI following an elevated PSA result or if the digital rectal examination result is abnormal.

Recommendation

The totality of the analysis performed showed that mpMRI is an effective and safe diagnostic modality that increases diagnostic accuracy for clinically significant cancer and reduces the number of specimens required during biopsy. Although it is associated with significant uncertainty, the economic analysis also suggests that mpMRI could potentially constitute an efficient diagnostic approach. However, certain issues were raised regarding the organization of and access to this service.

In light of these findings, the Institut national d'excellence en santé et en services sociaux (INESSS) recognizes the relevance of using multiparametric magnetic resonance imaging for the diagnostic investigation of prostate cancer and recommends that it be included in the continuum of care and services, if the following conditions are met:

With regard to use of mpMRI for triage purposes

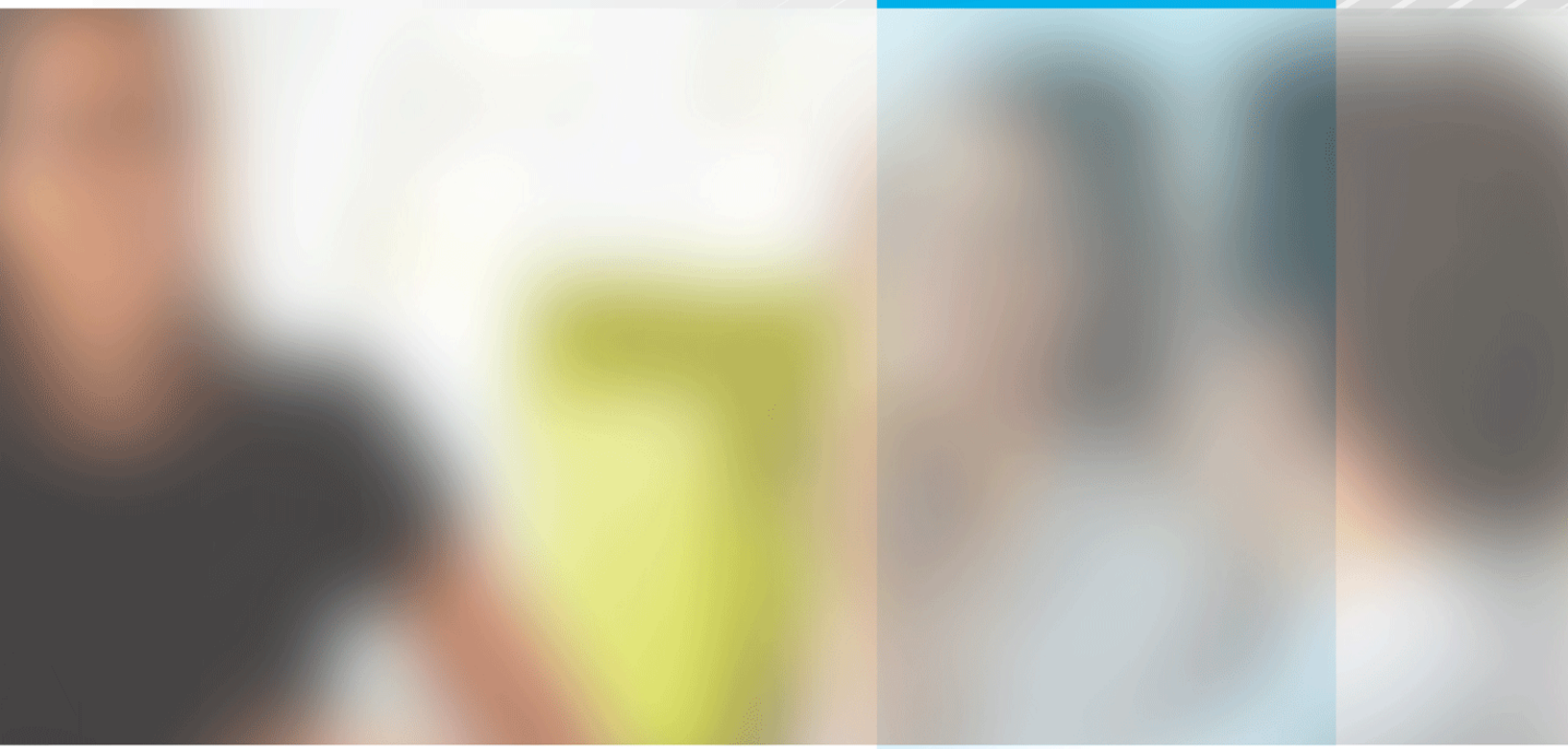
- Multiparametric magnetic resonance imaging should be used as a triage test to select patients for whom a biopsy is required, namely men with:
  - high suspicion of prostate cancer (high PSA result or abnormal DRE) who have never had a diagnostic systematic biopsy;
  - high suspicion of prostate cancer (high PSA result or abnormal DRE), but who have had negative results on diagnostic systematic biopsy.
- Consideration should be given to using mpMRI after discussing, with the patient, the advantages and disadvantages of using this diagnostic modality compared to TRUS-guided systematic biopsy.
- The use of mpMRI should be limited to patients for whom the test result is likely to influence their management. Thus, the use of mpMRI should not be considered for:
  - Men whose clinical signs show no ambiguity regarding the diagnosis of clinically significant prostate cancer. For these patients, TRUS-guided systematic biopsy should be considered;
  - Men for whom the suspicion of prostate cancer following PSA and DRE screening does not warrant a diagnostic investigation (based on the clinical parameters and the clinician's judgment). Rather, routine follow-up is preferable.

With regard to management based on mpMRI results during triage

- For patients with a negative mpMRI result (PI-RADS ≤ 2), routine follow-up is recommended (PSA and DRE). Such a decision has to be made only after discussion with the patient.
- For patients with an intermediate mpMRI result (PI-RADS = 3), targeted biopsy could be considered, based on the clinician's judgment. Additional risk factors (e.g., PSA level, PSA-related tests, age, comorbidities and family history) must be considered when making a decision.
- For patients with a positive mpMRI result (PI-RADS ≥ 4), mpMRI-targeted biopsy is recommended to maximize the detection of clinically significant prostate cancer.

With regard to optimization of practice and organization of care and services

- The acquisition of equipment for performing mpMRI and the interpretation of results should be based on the guidelines and recommendations published in PI-RADS v2.1.
- Specific training should be provided to key professionals to ensure optimal mpMRI use in the diagnostic investigation of prostate cancer.
- Image fusion guiding is recommended for mpMRI-targeted biopsy. Although this type of guiding must be favoured, cognitive guiding could be used when the image fusion approach is not available. However, the cognitive practice requires clinician experience to correctly target the biopsy and should be used only as a last resort.
- mpMRI for the diagnostic investigation of prostate cancer should be ordered by a urologist when following up on an elevated PSA result or an abnormal DRE or if prostate cancer is strongly suspected.
- An assessment of the availability of technical platforms (equipment and personnel) and potential impact on delays associated with the management of patients waiting for an investigation for prostate cancer, and for other patients using the same technical platforms, should be carried out in order to mitigate the potential negative effects on clients for whom this imaging modality is needed.



Siège social

2535, boulevard Laurier, 5e étage
Québec (Québec) G1V 4M3
418 643-1339

Bureau de Montréal

2021, avenue Union, 12e étage, bureau 1200
Montréal (Québec) H3A 2S9
514 873-2563
inesss.qc.ca

Institut national d'excellence en santé et en services sociaux
Québec