

Diagnostic Performance of Imaging Techniques Used for the Preoperative Locoregional Staging of Rectal Cancer: A Systematic Review Summary

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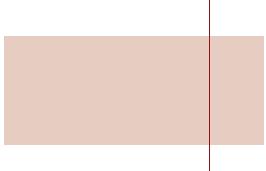
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Summary

Report prepared for AETMIS by
Cathy Gosselin

July 2007

*Agence d'évaluation
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FOREWORD



Colorectal cancer is one of the most common types of cancer in Québec, where it ranks third in incidence. It is estimated that, in 2007, 5400 new cases of colorectal cancer will be diagnosed and 2400 deaths from this disease will occur in Québec.

In September 2005, at a forum on colon and rectal cancer organized by the *Direction de la lutte contre le cancer*, about 50 specialists from Québec and Ontario in the fields of surgery, radiation oncology, gastroenterology, hematologic oncology and epidemiology, among others, gathered to discuss colorectal cancer statistics and treatments. Given these specialists' observation that Québec lags behind the rest of Canada with regard to colon and rectal cancer mortality, several strategies for improving patient management were discussed.

One of the many solutions proposed was to improve access to medical imaging for better rectal cancer staging and better candidate selection for preoperative treatments in particular. During the course of the forum the specialists had, in fact, also discussed problems with access to endorectal ultrasonography and magnetic resonance imaging in Québec.

As part of the measures taken following the forum's recommendations, the *Direction de la lutte contre le cancer*, on the recommendation of the *Comité de l'évolution des pratiques en oncologie* (CEPO), asked AETMIS to examine the currently available evidence on the diagnostic performance of the imaging techniques used for the preoperative locoregional staging of rectal cancer.

This report is a systematic review of the literature on this topic. Because of its limited scope, in that it does not examine related organizational and economic issues, no recommendations can be made. However, its conclusions are intended to support decision-making aimed at improving imaging services, and to provide the CEPO with a basis for the development of clinical practice guidelines.

Juan Roberto Iglesias, M.D., MSc, President and Chief Executive Officer

EXECUTIVE SUMMARY

Preoperative locoregional staging of rectal cancer is crucial for guiding clinicians in choosing the best treatment for patients with this disease. A number of imaging techniques are available for this purpose, such as endoscopic ultrasonography (EUS), magnetic resonance imaging (MRI), computed tomography (CT) and positron-emission tomography/computed tomography (PET/CT).

This report evaluates these different techniques with regard to each of the different elements that define the stage of rectal cancer: the degree of rectal wall invasion (T stage) and regional lymph node involvement (N stage), and involvement of the circumferential resection margin (CRM). Since distant metastases (M stage) are not included in the locoregional evaluation of cancer, they are not covered in this report. Lastly, only studies involving patients who had not received any neoadjuvant therapy were considered.

The search and examination of the relevant literature show both its paucity and significant methodological weaknesses. Furthermore, comparative studies of the techniques in the same patients are rare. The methodological weaknesses of the studies call for caution when interpreting the results of this report. In addition, it is unlikely that new, well-designed studies exclusively involving patients who have not received any preoperative therapy will be carried out, as this treatment modality has become the practice standard.

Based on the available evidence, AETMIS concludes that:

- EUS and MRI are two valid techniques, but provide complementary information for staging the disease;
- If used as the only diagnostic test, MRI provides more useful information for the choice of treatment than EUS alone, especially in cases requiring total mesorectal excision;
- In the rarer cases where T-stage assessment is important for the choice of treatment, consideration should be given to performing EUS in addition to MRI;
- MRI is the only modality that offers a certain degree of certainty for evaluating regional lymph nodes and the circumferential resection margin, the two factors most likely to influence patient management, regardless of the T stage;
- CT alone is not a good tool for staging rectal tumours. Multidetector technology may improve performance, but evidence of this is still insufficient;
- The role of PET/CT in staging rectal cancer will need to be monitored in the future. Its contribution to diagnosing lymph node involvement still needs to be confirmed, but there appear to be great hopes for this new technology.

These conclusions, which stem from an evaluation of the diagnostic performance of imaging techniques, are intended to contribute to the development of clinical practice guidelines. This particular activity and subsequent actions will also have to be based on an examination of the associated organizational and economic issues, which is not within the scope of this assessment.

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CONFLICT OF INTEREST

None declared.

SUMMARY

Introduction and context

Colorectal cancer is one of the most common types of cancer in Québec, and its associated mortality rates are higher in this province than in the rest of Canada. Specialists at a Québec forum held in 2005 called attention to this difference, as well as to problems with access to endorectal ultrasonography and magnetic resonance imaging in Québec. These imaging techniques are used to establish a preoperative diagnosis (locoregional staging) and treatment plans for patients with rectal cancer. To bring about the appropriate corrective measures, the *Direction de la lutte contre le cancer*, on the recommendation of the *Comité de l'évolution des pratiques en oncologie* (CEPO), asked AETMIS to carry out a comparative evaluation of the technologies used for staging rectal cancer. The results of this assessment are intended to assist CEPO in the development of clinical practice guidelines.

Preoperative locoregional staging of rectal cancer involves determining the depth of invasion of the primary tumour (T stage) and regional lymph node involvement (N stage). The T stage refers to the successive invasion of the lamina propria (Tis), submucosa (T1), muscularis propria (T2), perirectal tissue (T3) and adjacent organs (T4). The N stage amounts to the presence (N1/N2 or N+) or absence (N0 or N-) of regional lymph node metastases. Finally, locoregional staging also includes determining the involvement of the circumferential resection margin (CRM) or mesorectal fascia invasion.

The imaging technologies used for this staging include endoscopic ultrasonography (EUS), magnetic resonance imaging (MRI) and computed tomography (CT). Positron-emission tomography/computed tomography (PET/CT) is a new tool whose contribution to the initial staging process is currently being investigated. Conventional EUS combines an endoscope and a probe that emits sound waves. This technique is used to examine the rectal wall and to look for suspicious lymph nodes in real time. MRI uses an electromagnetic field to produce images of tissues and organs. The use of a phased-array coil allows a complete examination of the perirectal tissue, mesorectal fascia and regional lymph nodes. CT uses radiation to produce images—in the form of slices—of organs, tissues and bones. It is used to diagnose tumour invasion of perirectal tissue and adjacent organs. PET/CT constructs images by combining metabolic and anatomical information provided by PET and CT, respectively. Staging results obtained through imaging have repercussions on patient management, both in terms of the choice of surgery (local or radical) and as to whether neoadjuvant radiotherapy or chemoradiotherapy is indicated.

Methodology

This report is a systematic review of the literature on the performance of EUS, phased-array coil MRI, CT and PET/CT in the preoperative locoregional staging of rectal cancer. Its primary objective is to evaluate the diagnostic performance of these techniques in determining invasion (at a minimum) of the muscularis propria, perirectal tissue, adjacent organs, regional lymph nodes or the CRM in patients who have not received neoadjuvant therapy. The studies selected used the histopathologic findings in an excision specimen as gold standard. The present assessment includes an analysis

of studies published between January 1996 and September 2006 for EUS and CT, and between January 2000 and September 2006 for MRI and PET/CT.

Results

An examination of the latest clinical practice recommendations, mainly from North American organizations, reveals that these are generally vague with regard to the choice of technology: they suggest EUS or MRI and/or CT.

As for the studies included in the present report, they are of poor quality in general, and most involve small samples of patients. Study designs and methodological details are not always presented clearly. The studies examine the techniques one at a time, permitting only an indirect comparison.

EUS and MRI are very sensitive for detecting tumours that have invaded the muscularis propria (stage $\geq T2$), but the specificity of MRI is difficult to determine. The performance of staging modalities in diagnosing tumour invasion of perirectal tissue (stage $\geq T3$) varies. Although EUS seems to be more sensitive than MRI, it is difficult to clearly establish its superiority, and one must keep in mind both the rapid evolution of MRI technology and the limitations of EUS in cases of stenosis. Because of the variability in the results, it is not possible to compare the specificity of the three techniques (EUS, MRI, CT) for diagnosing perirectal tissue invasion. We do, however, note that a considerable proportion of T2 tumours are overstaged by EUS and especially by MRI. EUS, MRI and CT have excellent specificity for diagnosing invasion of adjacent organs (T4). However, many T4 tumours are not identified by these three techniques.

None of the three modalities offers good performance for detection of regional lymph node involvement (stage N+). Nonetheless, MRI seems to be far superior than EUS and CT in this regard. The use of PET/CT as an adjunct to the conventional methods for confirming or ruling out regional lymph node involvement is sparking interest among clinicians. However, there is still too little evidence available on its performance.

The studies examined provide little information on the sensitivity of MRI in diagnosing an involved circumferential resection margin, but its specificity and negative predictive value are very high. EUS is of no use for visualizing the mesorectal fascia, and the published data on CT are insufficient.

Because of the importance of the N stage and the CRM for therapeutic decision-making, MRI used as a first-line diagnostic test is less likely to require complementary EUS than vice versa. In all cases presumed to be stage N+ or CRM+, and in the majority of cases of tumours presumed to be T3 and T4, an MRI examination would suffice. On the other hand, when a tumour presumed to be T3 on the basis of MRI is located in the middle rectum, and in cases assumed to be T1-T2, N0 and CRM-, the additional T-stage information provided by EUS could make the difference for the choice of treatment.

Conclusions

This report assesses the diagnostic performance of imaging techniques for staging rectal cancer. The literature is sparse and presents important methodological weaknesses. The near-complete absence of comparative studies involving the same patients who have not received neoadjuvant therapy limits our ability to reach firm conclusions about the diagnostic superiority of one technique over another. Caution should therefore be exercised when interpreting the results presented.

However, the currently published studies tend to show that:

- EUS and MRI are two valid techniques but provide complementary information for staging the disease;
- If used as the only diagnostic test, MRI provides more useful information for the choice of treatment than EUS alone, especially in cases requiring total mesorectal excision;
- In the rarer cases where T-stage assessment is important for the choice of treatment, consideration should be given to performing EUS in addition to an MRI;
- MRI is the only modality that offers a certain degree of certainty for evaluating regional lymph nodes and the circumferential resection margin, the two factors most likely to influence patient management, regardless of the T stage;
- CT alone is not a good tool for staging rectal tumours. Multidetector technology may improve performance, but evidence of this is still insufficient;
- The role of PET/CT in staging rectal cancer will need to be monitored in the future. Its contribution to diagnosing lymph node involvement still needs to be confirmed, but there appear to be great hopes for this new technology.

We do not expect to see better studies published in the future involving a direct comparison of the diagnostic performance of these techniques in patients who have not received any neoadjuvant treatment, since such therapy is accepted as the practice standard.

This report is intended to assist with the development of a clinical practice guide. It should be noted that the economic and organizational issues involved in choosing and implementing one or other of the technologies examined are not covered in this assessment. The costs associated with these technologies and their maintenance, waiting lists, the availability of clinicians, training needs and the maintenance of clinical competence were not examined, but should be taken into consideration. Finally, given the limited strength of the conclusions presented, due mainly to the poor methodological quality of the available studies, it will be all the more important to take these different issues into account when developing a clinical practice guide, and during the course of other activities undertaken following the publication of the present report.



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