

Canadian Association of General Surgeons and American College of Surgeons Evidence Based Reviews in Surgery. 22.

The use of PET/CT scanning on the management of resectable pancreatic cancer

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CAGS Evidence Based Reviews in Surgery

The term “evidence-based medicine” was first coined by Sackett and colleagues as “the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients.”¹ The key to practising evidence-based medicine is applying the best current knowledge to decisions in individual patients. Medical knowledge is continually and rapidly expanding, and it is impossible for an individual clinician to read all the medical literature. For clinicians to practise evidence-based medicine, they must have the skills to read and interpret the medical literature so that they can determine the validity, reliability, credibility and utility of individual articles. These skills are known as critical appraisal skills. Generally, critical appraisal requires that the clinician have some knowledge of biostatistics, clinical epidemiology, decision analysis and economics, as well as clinical knowledge.

The Canadian Association of General Surgeons and the American College of Surgeons jointly sponsored a program entitled “Evidence Based Reviews in Surgery (EBRS),” which is supported by an educational grant from ETHICON and ETHICON ENDO SURGERY, both units of Johnson & Johnson Medical Products, a division of Johnson & Johnson, and ETHICON INC. and ETHICON ENDO-SURGERY, INC. divisions of Johnson & Johnson Inc. The primary objective of this initiative is to help practising surgeons improve their critical appraisal skills. During the academic year, 8 clinical articles are chosen for review and discussion. They are selected not only for their clinical relevance to general surgeons but also because they cover a spectrum of issues important to surgeons; for example, causation or risk factors for disease, natural history or prognosis of disease, how to quantify disease (measurement issues), diagnostic tests and the early diagnosis of disease, and the effectiveness of treatment. A methodological article is supplied that guides the reader in critical appraisal of the clinical article. Both methodological and clinical reviews of the article are performed by experts in the relevant areas and posted on the EBRS Web site. As well, a listserv discussion is held where participants can discuss the monthly article. Members of the Canadian Association of General Surgeons and the American College of Surgeons can access Evidence Based Reviews in Surgery through the Canadian Association of General Surgeons Web site (www.cags-accg.ca) or the American College of Surgeons Web site (www.facs.org). All journal articles and reviews are available electronically through the EBRS Web site. We also have a library of past articles and reviews that can be accessed at any time. Surgeons who participate in the monthly packages can obtain Royal College of Physicians and Surgeons of Canada Maintenance of Certification credits and/or continuing medical education credits for the current article only by reading the monthly articles, participating in the listserv discussion, completing the monthly online evaluation and answering the online multiple choice questionnaire. For further information about EBRS, the reader is directed to the CAGS or ACS Web site or should email the administrator, Marg McKenzie, at mmckenzie@mtsina.on.ca.

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In addition to making the reviews available through the CAGS and ACS Web sites, 4 of the reviews are published in condensed versions in the *Canadian Journal of Surgery* and 4 in the *Journal of the American College of Surgeons* each year. We hope readers will find EBRS useful in improving their critical appraisal skills and also in keeping abreast of new developments in general surgery. Comments regarding EBRS may also be directed to mmckenzie@mtsina.on.ca.

Reference

1. Evidence-Based Medicine Working Group. Evidence-based medicine. *JAMA* 1992;268:2420-5.

Selected article

Heinrich S, Goerres GW, Schäfer M, et al. Positron emission tomography/computed tomography influences on the management of resectable pancreatic cancer and its cost effectiveness. *Ann Surg* 2005;242(2):235-43.

Abstract

Question: What is the impact of positron emission tomography (PET) and computed tomography (CT) on the management of presumed resectable pancreatic cancer?

Design: Prospective cohort study.

Setting: One university centre in Switzerland. **Patients:** Fifty-nine patients with a focal lesion in the pancreas or with a clinical suspicion of pancreatic cancer were eligible for the study.

Description of test and diagnostic standard: All patients had an abdominal CT scan, chest x-ray and CA19-9 measurement in addition to a fluorodeoxyglucose PET/CT. Findings were compared with the histological diagnosis in 52 patients. In 7 patients, a definitive diagnosis was not available, so patients were observed with further imaging for 6 to 18 months. **Main outcomes:** Ability of PET/CT to differentiate benign from malignant lesions. **Main results:** Compared with the gold standard, PET/CT had 89% (41/46) sensitivity; 69% (9/13) sensitivity; 91% (41/45) positive predictive value (PPV); and 64% (9/14) negative predictive value (NPV) for differentiating benign and malignant lesions. The likelihood ratio (LR) for a positive test was 2.9 and for a nega-

tive test was 0.16. The CT sensitivity was 93% and for specificity was 21%. PET/CT findings impacted on the oncological management of patients in 32% (15/46) of patients, whereas standard staging impacted on management in 20% (9/46) of patients. **Conclusion:** PET/CT is useful for staging procedure before pancreatic resection for cancer.

Commentary

Adenocarcinoma of the pancreas is regarded as one of the most lethal visceral neoplasms. Cancers in the head of the pancreas tend to be aggressive, with a tendency to local lymphatic and perineural invasion. Because of the anatomic relation, local vascular invasion is common, resulting in difficulty achieving local regional control. Further, the Whipple procedure continues to have high rates of morbidity and mortality even in high-volume centres. Thus, surgery should be limited to patients who do not have metastatic disease and in whom resection of all local disease is possible. Even with modern imaging, it is often difficult to confirm that a patient has a malignant lesion and, if so, that it is localized and resectable. Thus, this study, which assesses the value of the PET/CT scan, is of interest.

The study was performed on a small group of patients who were entered into a phase II trial of neoadjuvant chemotherapy. They were highly selected, in that 55% (25 of 46) underwent surgery for histologically proven pancreatic cancer. Patients underwent a standardized work-up with various modalities, in-

cluding abdominal CT scan. In addition, a PET/CT scan was performed. It is unclear how the PET/CT scan impacted on the decision to operate. It seems that all the tests were used to make this decision. Further, histology was the gold standard against which the tests were compared. Histology was not available in 7 (12%) patients, whose long-term outcome (up to 18 months) was determined by follow-up and further imaging.

This article presents the results as sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). PET/CT scan seems to be very useful in diagnosing a malignant lesion, with a PPV of 91%. This is similar to that of an abdominal CT scan. The authors report that PET/CT scan has a higher specificity (67%), compared with CT scan (21%), but both are poor tests for excluding malignancy (64% NPV). That is, cancer could not be excluded in one-third of the patients.

Likelihood ratios are more useful measures of test characteristics because they tell how much the chance of a specific diagnosis increases or decreases after the test, compared with the pretest probability. A likelihood ratio of 1 means that there is no change in the likelihood of the patient having a disease or disorder. Likelihood ratios of 10 or greater, or less than 0.1, are considered to be very significant. In this study, the positive likelihood ratio was 2.9; thus, after the PET/CT scan was performed, the chance of the patient having a malignancy was about 3 times more likely. If the PET/CT scan was negative, then the chance of malignancy was

about 0.19 times as likely as before the test. These are considered to be relatively small changes.

There are limitations: a small number of selected patients were included in the study (limiting the interpretation of the results) and there was no gold standard for comparison. Further, it is difficult to compare the value of PET/CT scanning to other types of imaging (e.g., abdominal CT scan) because there is uncertainty regarding whether the tests were reviewed independently without knowledge of other tests. What can we learn from this study? Likely, there is a limited role for CT/PET scanning in this setting. The algorithm for managing indeterminate pancreatic lesions includes several important clinical factors: existing symptoms, tumour size, cystic versus solid nature of the tumour and patient age. There is increasing evidence that the overall incidence of invasive malignancy is low, especially in cystic lesions, and that observation is an appropriate and safe option for smaller

lesions. The ability of PET/CT to differentiate invasion versus a pre-malignant state in mucinous lesions has yet to be determined.

In this study, no data are presented regarding the ability of PET/CT to delineate the extent of the direct local spread of the lesion and thus to determine its resectability. PET/CT may have an important role in the detection of distant metastases. In this series, 5 of 16 patients with distant metastases were identified only by PET/CT. Interestingly, PET/CT was particularly useful in identifying metastatic disease in locations other than the liver. As well, 2 rectal cancers were detected. The authors state that the oncological management was affected in 33% of patients after the PET/CT scan, compared with only 20% with standard staging. Unfortunately, as stated previously, it is difficult to ascertain whether the tests were performed and treatment decisions made with knowledge of the results of each test independently or when all of the test results were considered.

The authors of this study have demonstrated that PET/CT scan is another test that can be used in the diagnosis and staging of pancreatic neoplasms. It has a high predictive value in diagnosing malignant lesions; however, the authors have not shown that it is of value in determining whether the pancreatic lesion is resectable. It may be of value in identifying metastatic lesions that would otherwise be missed by other imaging techniques. Based on the results of this study, however, it is hard to recommend that it should be part of the standard work-up of pancreatic cancers. The most important potential role is in differentiating benign from malignant lesions. A negative PET/CT scan is of little use in ruling out cancer. The cost effectiveness analysis, which was not commented on in this review, was incomplete and confusing and therefore does not address this question adequately.

Competing interests: None declared.

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