Evaluation of diagnostics guidelines for hepatobiliary and pancreatic disease
Tilleman, E.H.B.M.
Summary and Conclusions
Summary

Since non-surgical palliation by means of endoprosthesis placement is generally accepted in patients with hepatobiliary or pancreatic malignancies, adequate tumor staging is important for the selection of patients who will benefit from a resection and those who will need palliation.

The use of guidelines may help to improve the accuracy of the diagnostic processes and therefore optimize patient selection. In this thesis, the accuracy of different radiological and surgical staging procedures as well as a complete diagnostic strategy are evaluated. Subsequently, the implementation of guidelines for diagnostic procedures and a diagnostic strategy as well as the implementation of a therapeutic guideline are evaluated.

Diagnostic laparoscopy might improve patient selection as it enables detection of small superficial liver metastases and peritoneal tumor deposits or local ingrowth which can be easily missed with radiological techniques. Laparoscopic ultrasound allows inspection of local tumor invasion, vascular and regional nodal involvement and distant metastatic spread to the liver. In Chapter 2 the accuracy of diagnostic laparoscopy for detection of unresectable disease and the prevention of unnecessary surgical exploration were studied in patients with a proximal bile duct tumor. Diagnostic laparoscopy avoided unnecessary laparotomy in 44 of the 110 patients (41%) with a malignant proximal bile duct obstruction that were resectable according to conventional imaging studies, whereas the additional value of laparoscopic ultrasonography was limited. Diagnostic laparoscopy should routinely be performed in the work-up of patients with a potentially resectable proximal bile duct tumor.

In the diagnostic work-up of patients with pancreatic carcinoma, CT is used to determine resectability of the tumor, and the accuracy is reported to be between 77% and 90%. However surgical resection itself is the most commonly used but not the best-defined and objective reference standard for the evaluation of the quality of CT scans. At laparotomy resectability partly depends on the opinion of the surgeon i.e. the decision whether a venous resection should be performed or whether a high risk for a tumor-positive resection margins should be accepted. A better reference test for detection of locally advanced disease would be the microscopic radicalness of the resection, but even this may partly depend on the attitude of the surgeon concerned. Clinically the more important reference could be survival of the patient. Therefore, in Chapter 3 the criteria of local extension of disease on preoperative CT scan are correlated with the survival in 72 patients who underwent an explorative laparotomy with the intention to perform a curative resection of a pancreatic head tumor. Prognostic factors for survival could be identified at the pre-operative CT scans.
Summary and conclusions

Tumor size more than 3 cm, tumor convexity grade DE, and the judgement of local unresectability at CT were slightly negatively correlated with survival and therefore may be accounted for in the selection of patients to undergo a resection.

The additional value of diagnostic laparoscopy also depends on the quality of the diagnostic procedures and might change over time, therefore in Chapter 4 potential changes in the additional value of diagnostic laparoscopy in the staging of periampullary carcinoma over the last decade are analyzed. Due to improved radiological staging, in particular of spiral CT scan the additional value of laparoscopy decreased from around 20% to 10%. Moreover, the outcome in patients who underwent surgical palliative treatment after laparoscopy was relatively good compared to non-surgical palliative treatment. As an unnecessary laparotomy can only be prevented in about 10% of the patients the routine use of this staging technique cannot be recommended.

The study described in Chapter 5 was conducted in order to facilitate the development of guidelines for the diagnostic work-up of patients in the district of the Comprehensive Cancer Center Amsterdam (IKA) to be able to develop a guideline for diagnostic work-up and treatment that will be applicable in all hospitals in the district. Two hundred fifty-three patients with a pancreatic carcinoma who presented in a general hospital were analyzed. The most important findings were that invasive diagnostic procedures are regularly performed before the non-invasive tests, that spiral CT was used minimally and that ERCP was frequently performed without subsequent biliary drainage. The mean period of diagnostic work-up is 4 weeks, a relatively long period of time for this group of patients with limited life expectancy. A guideline for diagnostic work-up and treatment adapted to local facilities might improve the efficacy of the diagnostic work-up in this group of patients.

Chapter 6 describes the reinterpretation of radiological examinations performed in referring hospitals. Patients with hepatobiliary or pancreatic cancer referred to a tertiary-care referral center are generally referred after radiological work-up elsewhere. The diagnostic facilities, accuracy and interpretation of these investigations differ between referring hospitals, according to the local circumstances concerning available equipment and local expertise. The clinical importance of reinterpretation of radiological investigations, as well as the value of additional investigations in a referral center was determined. Among 78 patients with a suspected pancreatic or hepatobiliary malignancy, reinterpretation of CT scans resulted in the discovery of 30% additional findings, and a change in treatment strategy in 10% of the patients. Additional ultrasound and CT scan in the referral center resulted in a change in treatment strategy in 31% and 32% of the patients respectively.
Therefore reinterpretation of previously performed radiological investigations by an experienced panel might be beneficial.

The second part of the thesis describes the implementation processes of guidelines. Diagnostic laparoscopy had been performed routinely in patients with a periampullary malignancy at the Academic Medical Center since 1992. As shown in Chapter 4, the benefit of this staging procedure did decrease significantly due to improved radiological staging. Therefore, laparoscopy has been abandoned as a routine procedure since 1998. In Chapter 7 the implementation of a new guideline, i.e. not to perform diagnostic laparoscopy in periampullary malignancy, is evaluated. The new guideline was used in 177 of the 186 patients (95%) undergoing an explorative laparotomy. Resection could not be performed in 64 patients (34%), in 29 of them (16%) due to metastatic disease. Metastatic disease was found more frequently at laparotomy in patients with a pancreatic head and distal CBD carcinoma (19% and 18%, respectively) than in patients with a papillary and duodenum carcinoma (6% and 0%, respectively). Since the sensitivity of laparoscopy for the detection of metastatic disease is around 60%, overall laparoscopy might have prevented an unnecessary laparotomy in 10% of the patients. The outcome after bypass surgery in terms of survival seemed to improve; however statistical significance was not reached. It was concluded that the limited number of metastases detected at laparotomy together with the outcome after bypass surgery in terms of survival confirm that the potential benefit of staging laparoscopy is too limited to justify its use as a routine staging procedure.

As mentioned earlier, a new "IKA/IKST guideline for diagnostic work-up and treatment of pancreatic carcinoma" was developed. Chapter 8 describes the implementation of this guideline. After an implementation period of six months following the introduction of this new guideline in the IKA/IKST district, a random sample of 110 patients in 9 hospitals was analyzed in order to evaluate whether the guideline had changed and improved the diagnostic work-up process described in chapter 5. The use of investigations not focused on pancreas pathology remained about 35%. The use of CT scan increased to 76%. The most important finding was that in 88% (compared to 51%) of the patients undergoing ERCP subsequently biliary drainage was performed. The introduction of the guideline did not lead to reduction in invasive diagnostic procedures or to an increase in pathological proof of the tumor. It is concluded that, despite an active development scheme and a multilevel implementation process of the ‘IKA/IKST guideline for diagnostic work-up and treatment of pancreatic carcinoma’ improvement of the diagnostic staging process was limited.

Controversy remains about whether or not implementation of a guideline for a diagnostic procedure or even a diagnostic strategy is more complicated than
implementation of a straight forward treatment protocol. Therefore, in Chapter 9 the implementation of the guideline to perform laparoscopic cholecystectomy in day-care compared to a clinical admittance was evaluated 3 years after its introduction. Furthermore, it was evaluated whether a shift to day-care treatment had appeared at a countrywide level in The Netherlands. The study shows that in the Academic Medical Center 93% of the patients with uncomplicated gallstone disease suitable for day-care treatment was planned to undergo a laparoscopic cholecystectomy in day-care and that an average of 90% of these patients had really been treated in day-care. So, the implementation of the new treatment strategy succeeded in the center where the guideline was developed. However, the recommendations are not followed in The Netherlands in general as only 1.7% of the patients undergo a laparoscopic cholecystectomy in day-care.

Conclusion

The efficacy of diagnostic tests, for example diagnostic laparoscopy is depends on the type of tumor. Diagnostic laparoscopy has been shown to be an effective staging tool in proximal bile duct tumors but not in pancreatic cancer. The reduction in benefit in pancreatic cancer might be due to a better selection of patients eligible for laparoscopy due to increased quality of CT scan for staging the disease. Therefore, the efficacy of a diagnostic test should be reevaluated on a regular basis as the accuracy might be depending on tests performed earlier in the staging process. It is difficult to extrapolate the efficacy of a single diagnostic test to a diagnostic strategy in particular if this strategy should be evaluated in other hospitals. Furthermore, if patients are referred with different radiological investigations previously performed in the referring hospital, reinterpretation of these investigations by an experienced panel might improve staging.

Implementation of the guideline not to perform a diagnostic laparoscopy as a routine staging procedure in pancreatic carcinoma in the hospital where the guideline was developed did succeed. Implementation of the ‘IKA/IKST guideline for diagnostic staging and treatment of pancreatic carcinoma’ in the district of the Comprehensive Cancer Center Amsterdam and Stedendriehoek Twente was disappointing, although it had been developed in a multidisciplinary setting implemented according to a thorough strategy. Comparable results were found for a therapeutical guideline to perform laparoscopic cholecystectomy in day-care. Implementation in the center where it was developed was successful, in contradiction to the use of the guideline in other hospitals in The Netherlands.
So, implementation of a simple diagnostic or therapeutic guideline did succeed in the hospital where it was developed. However application of these guidelines or even a diagnostic strategy in other hospitals has limitations.