Laparoscopic surgery for cancer: Are we ready?

R. Ceulemans, M. Henri, J. Leroy, J. Marescaux

IRCAD/EITS, European Institute of Telesurgery, University of Louis Pasteur, Strasbourg, France.

Abstract

Following feasibility studies more and more large prospective reports even randomised trials document the treatment of digestive cancer using a laparoscopic approach. While the spectre of port-site recurrences, once so alarming has faded, it has become a challenge for laparoscopic surgeons to provide long-term followup. There is good class II and III evidence that staging laparoscopy (SL) has a value for oesophageal, gastric, pancreatic and hepatobiliary cancer as well as for intra-abdominal lymphomas since it adds to primary staging and often alters the clinical stage of the disease and hence the management of the individual patient. For minimally invasive oesophagectomy and gastric cancer surgery several series have demonstrated shorter perioperative morbidity and hospital stay however at present most studies report smaller numbers of selected patients and long term follow up is rare. The laparoscopic resection of pancreatic malignancies is not reported to be feasible, safe or potentially beneficial for the patient while the curative resection of suspected early gallbladder cancer is a poor indication. Nevertheless laparoscopy is documented to be safe and applicable for small malignant liver lesions and the Lacy trial was significantly in favour of laparoscopy-assisted colectomy, predominantly for stage III disease. Bearing in mind that in many fields of digestive cancer surgery, laparoscopy should still be conducted as part of a trial, it is safe to say that "we are ready" for this revolution to arise. (Acta gastroenterol. belg., 2003, 66, 227-230).

Key words: laparoscopic surgery, cancer.

Introduction

Over the past 100 years surgery has evolved rapidly comprising the progress of many new techniques. The last decades we have seen a true explosion of evolution with the implementation of laparoscopy in our daily surgical practise. Although the laparoscopic management of surgical disease is presently well established, the role of laparoscopy in the treatment of cancer and certainly digestive cancer has been subject to debate and a hot topic for the past 5 years. Its general acceptance follows a much slower progress. The main reason for this delay is "the intention to cure" principle that has driven multidisciplinary teams to find the optimal treatment modality with the best evidence based chance to cure their patients. The two principles tools used to evaluate the efficiency of new surgical techniques in cancer treatment are 5 year survival and disease free interval whereas postoperative pain, hospital stay even morbidity have second place.

Therefore it has been a challenge for laparoscopic surgeons to provide long-term follow-up with significant numbers of procedures. Following feasibility studies more and more large prospective reports even randomised trials document the treatment of digestive cancer using a laparoscopic approach.

Port-site recurrences (PSR) have been the leading concern for the use of laparoscopy in cancer surgery. Although PSR certainly exists, large multicenter trials and collective data demonstrate that its incidence is no higher than wound metastasis in "open" surgery (1-2%) (1). Considering the routine use of widely published, reproducible measures to prevent PSR it is more and more accepted as evidence based practise to no further exploit PSR as a reason not to offer patients a laparoscopic approach in case of cancer. Furthermore the EAES consensus meeting concluded that proper surgical technique and practice reduces the likelihood of port site metastasis (2).

Staging laparoscopy

Staging laparoscopy is beneficial only if it can demonstrate advanced disease undetected by preoperative imaging studies, which would contraindicate a curative procedure. Although advances in imaging technologies have reduced its yield, recent studies seem to show a clear place for this more invasive diagnostic tool. SL enables the surgeon to appreciate more clearly the presence of T4 disease and carcinomatosis while laparoscopic ultrasound may provide additional information on liver metastasis and lymph node involvement. In many large centres optimal use of intensive care units and the issues of informed consent require precise preoperative staging to determine exactly what definitive treatment will be performed. In that perspective the procedure may be performed separately as a day-case surgery. Staging laparoscopy has the added potential of offering simultaneous palliative treatment for unresectable disease, in a minimally invasive way, with positive effect on quality of life.

Oesophageal cancer and gastric cancer

Laparoscopic peritoneal lavage was able to help select poor candidates for curative oesophago-gastric surgery by demonstrating free peritoneal tumour cells (FPTC's) in 11 out of 88 patients over a 2-year time period (3). Furthermore a prospective trial from the National Cancer Institute (4) demonstrated the feasibility of a

Correspondance to: Dr. R. Ceulemans, Departement of Digestive Surgery, Heilig Hart Ziekenhuis Mol, Gasthuisstraat 1, 2400 Mol, Belgium. E-mail: robrecht.ceulemans@pandora.be.

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combined thoracoscopic laparoscopic staging algorithm showing a high positive predictive value.

In gastric carcinomas, laparoscopy has the potential to avoid a laparotomy in asymptomatic patients with metastatic disease and to spare them the morbidity and hospital stay associated with it. A group from Memorial Sloan-Kettering (5) published their result 110 patients undergoing laparoscopy. All were judged to be free of intra-abdominal metastatic disease on preoperative computed tomography scan imaging. They found that laparoscopic exploration was successful in 110 of 111 patients and accurately staged 94% of the patients with respect to metastatic disease with a sensitivity of 84% and a specificity of 100%. Although their protocol required them to perform laparotomy to confirm their laparoscopic findings, 34% had metastatic disease and could have avoided a laparotomy. Others (6) have not found such an advantage, but have reported on a much smaller number of patients. The literature currently supports the use of staging laparoscopy for patients with gastric cancer and no evidence of metastatic disease on ultrasound or CT scan. Patients with gastric cancer and secondary obstruction or bleeding are better managed by laparotomy.

Pancreatic adenocarcinoma

Routine laparoscopic staging in patients with pancreas cancer can improve outcome if laparoscopic staging is able to identify patients with unresectable tumors. Diagnostic laparoscopy of peripancreatic malignancies has been reported to effectively assess tumor stage and reliably predict which patients will benefit from laparotomy (7). Laparoscopy enables the detection of small superficial metastases at the liver surface and the peritoneum that are easily missed with radiological staging techniques and often first encountered during laparotomy. Diagnostic laparoscopy can be combined with laparoscopic ultrasound (LUS), which is sensitive for detection of small intrahepatic metastases and for the evaluation of enlarged lymph nodes and tumor ingrowths in vascular structures. LUS is an accurate additional investigation for defining tumor resectability (8). Furthermore, surgical palliation can be offered to the patients, consisting of a hepaticojejunostomy, and a gastroenterostomy. The main limitation of SL for peripancreatic malignancies is that it may underestimate portal vein and regional lymph node involvement (8). A recent analysis (9) reported the results in 297 patients using systematic laparoscopic staging, laparoscopic ultrasonography and biopsy of suspicious lesions for patients with periampullary cancer. The overall benefits of staging laparoscopy for pancreatic cancer were concluded lower than expected.

Ampullary, duodenal and distal bile duct tumors were found to be understaged in one series when only using CT imaging since an additional 10% of patients (n = 144) were diagnosed with unresectable disease

using SL (10). Others recommend continued use of SL for pancreatic head and gallbladder cancer but not for ampullary tumors (11).

Hepatic tumours and extra-hepatic biliary tumors

Laparoscopy identified the majority of patients with occult unresectable disease, improved resectability and is recommended to be used routinely for potentially curative hepatic resection in a recent report of the Memorial Sloan-Kettering Cancer center (12). In case of hepatic colorectal metastases, only a small proportion of patients are candidates for resection for curative intent. Accurate staging is mandatory to avoid undue laparotomies. In a series of 50 patients with colorectal liver metastases (13), who were potential candidates for resection on the basis of preoperative studies, 38% (18 patients) were ruled out as candidates for resection by SL and LUS. A similar experience was reported in 256 patients with potentially resectable liver metastases from colorectal primaries (14). A total of 172 underwent successful laparoscopy. A laparotomy was avoided for 15% of these patients. The laparoscopic staging was found to be less accurate to detect perihepatic lymph nodes and additional hepatic disease. Furthermore laparoscopy identifies the majority of patients with unresectable hilar cholangiocarcinoma or gallbladder carcinoma reducing the incidence of unnecessary laparotomy (15). The authors recommend the use of SL in all potentially resectable primary gallbladder cancer and patients with T2/T3 hilar cholangiocarcinoma.

In summary, there is good class II and III evidence that SL has a value for oesophageal, gastric, pancreatic and hepatobiliary cancer as well as for intra-abdominal lymphomas since it adds to primary staging and often alters the clinical stage of the disease and hence the management of the individual patient (16).

Laparoscopic digestive cancer treatment

Minimally invasive oesophagectomy for cancer can be performed through laparoscopic transhiatal approach or a combined laparoscopic thoracoscopic approach. Several series have demonstrated shorter perioperative morbidity and hospital stay (17,18) however at present most studies report smaller numbers of selected patients and long term follow up is rare.

Gastric cancer surgery using a laparoscopic approach has been described for formal gastrectomy for cancer with lymphadenectomy (19), treatment of gastric stromal neoplasms (20,21) and laparoscopic and/or endoscopic resection of mucosal and submucosal tumors (22, 23,24). Larger numbers and long term follow up are required to document its oncologic equivalency or superiority however the debate on the value of D1 versus D2 gastrectomy and total versus subtotal and local resection in Europe favours the future role of laparoscopy in gastric cancer. Further more laparoscopic gastrojejunostomy

may provide adequate palliation of gastric outlet obstruction in unresectable gastric cancer (25).

Pancreatic cancer treatment is considered to have surgery as its primary mainstay. Laparoscopy is at present recommended mainly for staging (26) and can be equally beneficial for palliation performing biliary bypass or gastro-jejunostomy surgery (27). Although laparoscopic pancreatic surgery is described for benign lesions (28,29) the laparoscopic resection of pancreatic malignancies is not reported to be feasible, safe or potentially beneficial for the patient. Moreover laparoscopic pancreaticoduodenectomy may be associated with increased morbidity (30) while new trends in pancreatic cancer as immuno- and gene therapy may change the role of extensive surgery (31).

Laparoscopic liver resection is increasingly being reported in the literature as feasible and safe for benign lesions (32). It is shown to be associated with a diminished stress response and better preservation of the immune function (33). Although this finding may be the basis of improved oncologic results, the role of laparoscopy for hepatocellular carcinoma (HCC) and liver metastasis remains controversial. The results of a large multicenter European study published last year (34) document the safety and applicability of laparoscopy for small malignant lesions (the mean size was 3.3 cm) located in the left lateral lobe and in the anterior segments of the right lobe. The use of laparoscopy for larger lesions and its long-term outcome for the treatment of malignant tumors need to be evaluated further in expert centres. Aside from laparoscopic resection laparoscopy is helpful in performing tumour ablation using radiofrequency or cryosurgery.

Extrahepatic biliary malignancies equally benefit from laparoscopy when it is used for staging (15). The curative resection of suspected early gallbladder cancer is nevertheless a poor indication for laparoscopy since there is a potential risk of bile spillage that may convert potentially curable early gallbladder cancer in incurable disease (35).

Colorectal cancer is undoubtfully the most extensively studied gastro-intestinal malignancy with regards to laparoscopic management. Laparoscopy is likely to have the largest impact on this patient population in the near future.

Laparoscopic colorectal surgery for cancer was initially restricted to palliative treatment or curative intent only in a prospective randomised setting. Port-site recurrences were the main cause of concern at the time (36). Different single and multicenter, retro- and prospective studies have now been published reporting the safety, feasibility and benefits of laparoscopic resection of colorectal malignancies (37-40). The spectre of port-site recurrences, once so alarming has faded (41). At present four large prospective randomised trials independently aim to evaluate laparoscopic colon surgery as the new standard of care in colon cancer using long-term data on survival and disease free interval.

The first data from the COST trial by the National Cancer Institute, published in the JAMA (42) early last year documented only minimal short-term quality of live benefits. However looking closely at the results laparoscopic assisted colectomy was associated with a significantly better Quality of Life Index (p < 0.05), fewer analgesic requirements (p < 0.001 and p < 0.03 for parenteral and oral) and shorter hospital stay (p < 0.01). Long-term survival data were still missing.

At last Lacy published his long awaited results of the Barcelona trial in the Lancet at the end of last year (43) showing results of a 5 year follow up of 219 randomised patients with non metastatic colon carcinoma. Their analysis was significantly in favour of laparoscopyassisted colectomy (LAC) for return of transit, oral intake and hospital stay but more importantly their data showed that the probability of cancer-related survival was significantly higher in the LAC group while LAC was independently associated with reduced risk of tumour relapse. The superiority of LAC was related mostly to outcome advantages of patients with stage III tumours. The COLOR trial (Dutch trial) included more than 1200 patient thus far and preliminary data are expected soon as for the CLASSIC trial.

Conclusion

Laparoscopy for cancer has been hot topic for many years. While finally it is now gaining worldwide acceptance in an increasing number of surgical fields, laparoscopic surgery for digestive cancer is expected to be the center of discussion for the years to come. An evidence based multidisciplinary approach to cancer may preclude laparoscopic surgeons correctly from performing a laparoscopic approach routinely for all cancer cases in the near future. Still the laparoscopic management of malignant tumors, either diagnostic or therapeutic has found a more than valuable place in a digestive surgical practise. It may proof to be the standard of care for the future when further trials document significant survival and disease free benefits over "open" surgery. Bearing in mind that in many fields of digestive cancer surgery, laparoscopy should still be conducted as part of a trial, it is safe to say that "we are ready " for this revolution to arise.

References

- HUBENS G. Port site metastases: where are we at the beginning of the 21st century? Acta Chir. Belg., 2002 Aug, 102: 230-7.
- 2. VELDKAMP R., GHOLGHESAEI M., BUUNEN M., MEIJER D.W., H. JAAP BONJER E. LEZOCHE, HIMPENS J., JACOBI C.A., WHELAN R.L., LACY A.M., MORINO M., HAGLIND E., JAKIMOWICZ J.J., CUESTA M.A., NEUGEBAUER E., ANDERBERG B., GUILLOU P.J., MONSON J.W., JEEKEL J., FINGERHUT A., Sir CUSCHIERI A., KOECKERLING F., FLESHMAN J.W., WEXNER S.D. Laparoscopic Resection of Colonic Carcinoma EAES consensus conference Lisbon, June 2, 2002. Online publication http://www.eaes-eur.org/ rescolframe.html.

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 BRYAN R.T., CRUICKSHANK N.R., NEEDHAM S.J., MOFFITT D.D., YOUNG J.A., HALLISSEY M.T., FIELDING J.W. Laparoscopic peritoneal lavage in staging gastric and oesophageal cancer. Eur. J. Surg. Oncol., 2001 Apr, 27: 291-7.

- KRASNA M.J., REED C.E., NEDZWIECKI D., HOLLIS D.R., LUKETICH J.D., DECAMP M.M., MAYER R.J., SUGARBAKER D.J., CALGB THORACIC SURGEONS. CALGB 9380: a prospective trial of the feasibility of thoracoscopy/laparoscopy in staging esophageal cancer. *Ann. Thorac. Surg.*, 2001 Apr, 71: 1073-9.
- BURKE E.C., KARPEH JR. M.S., CONLON K.C., BRENNAN M.F. Laparoscopy in the management of gastric adenocarcinoma. *Ann. Surg.*, 1997, 225: 262-7.
- LEHNERT T., RUDEK B., KIENLE P., BUHL K., HERFARTH C. Impact of diagnostic laparoscopu on the management of gastric cancer: prospective study of 120 consecutive patients with primary gastric adenocarcinoma. *Br. J. Surg.*, 2002, 89: 471-5.
- MENACK M.J., SPITZ J.D., ARREGUI M.E. Staging of pancreatic and ampullary cancers for resectability using laparoscopy with laparoscopic ultrasound. Surg. Endosc., 2001 Oct, 15: 1129-34.
- TAYLOR A.M., ROBERTS S.A., MANSON J.M. Experience with laparoscopic ultrasonography for defining tumour resectability in carcinoma of the pancreatic head and periampullary region. *Br. J. Surg.*, 2001 Aug, 88: 1077-83
- VAN DIJKUM, ROMJIN, TERWEE et al. Laparoscopic staging and subsequent palliation in patients with peripancreatic carcinoma. Ann. Surg., 2003, 237: 66-73.
- BROOKS A.D., MALLIS M.J., BRENNAN M.F., CONLON K.C. The value of laparoscopy in the management of ampullary, duodenal, and distal bile duct tumors. *J. Gastrointest. Surg.*, 2002 Mar-Apr, 6: 139-45, discussion 145-6.
- VOLLMER C.M., DREBIN J.A., MIDDLETON W.D., TEEFEY S.A., LINEHAN D.C., SOPER N.J., EAGON C.J., STRASBERG S.M. Utility of staging laparoscopy in subsets of peripancreatic and biliary malignancies. *Ann. Surg.*, 2002 Jan, 235: 1-7.
- D'ANGELICA M., JARNAGIN W., DEMATTEO R., CONLON K., BLUMGART L.H., FONG Y. Staging laparoscopy for potentially resectable noncolorectal, nonneuroendocrine liver metastases. *Ann. Surg. Oncol.*, 2002 Mar. 9: 204-9.
- RAHUSEN F.D., CUESTA M.A., BORGSTEIN P.J. et al. Selection of patients for resection of colorectal metastases to the liver using diagnostic laparoscopy and laparoscopic ultrasonography. Ann. Surg., 1999, 230: 31-37
- 14. GROBMYER R.S., D'ANGELICA M., DEMATTEO P.R., FONG Y., BLUMGART H.L., JARNAGIN R.W. Utility of Diagnostic Laparoscopy Prior to Planned Hepatic Resection in Patients with Hepatic Metastasis from Colorectal Cancer: Experience in Over 250 Cases. J. Gastrointest. Surg., 2003. 7: 277.
- WEBER S.M., DEMATTEO R.P., FONG Y., BLUMGART L.H., JARNAGIN W.R. Staging laparoscopy in patients with extrahepatic biliary carcinoma. Analysis of 100 patients. Ann. Surg., 2002 Mar, 235: 392-9.
- CUSCHIERI A. Role of video-laparoscopy in the staging of intra-abdominal lymphomas and gastrointestinal cancer. Semin. Surg. Oncol., 2001, 20: 167-72.
- NGUYEN N.T., FOLLETTE D.M., WOLFE B.M., SCHNEIDER P.D., ROBERTS P., GOODNIGHT J.E. Jr. Comparison of minimally invasive esophagectomy with transthoracic and transhiatal esophagectomy. *Arch. Surg.*, 2000 Aug, 135: 920-5.
- WAJED S.A., PETERS J.H. Laparoscopic and endoscopic surgery in esophageal malignancy. Surg. Oncol. Clin. N. Am., 2001 Jul., 10: 493-510, vii.
- BALLESTA LOPEZ C., RUGGIERO R., POVES I., BETTONICA C., PROCACCINI E. The contribution of laparoscopy to the treatment of gastric cancer. Surg. Endosc., 2002 Apr., 16: 616-9.
- YAHCHOUCHY-CHOUILLARD E., ETIENNE J.C., FAGNIEZ P.L., ADAM R., FINGERHUT A. A new "no-touch" technique for the laparoscopic treatment of gastric stromal tumors. Surg. Endosc., 2002 Jun, 16: 962-4.
- MATTHEWS B.D., WALSH R.M., KERCHER K.W., SING R.F., PRATT B.L., ANSWINI G.A., HENIFORD B.T. Laparoscopic vs open resection of gastric stromal tumors. *Surg. Endosc.*, 2002 May, 16: 803-7.
- SHIMIZU S., NOSHIRO H., NAGAI E., UCHIYAMA A., MIZUMOTO K., TANAKA M. Laparoscopic wedge resection of gastric submucosal tumors. *Dig. Surg.*, 2002, 19: 169-73.

23. LUDWIG K., WILHELM L., SCHARLAU U., AMTSBERG G., BERN-HARDT J. Laparoscopic-endoscopic rendezvous resection of gastric tumors. Surg. Endosc., 2002 Nov, 16: 1561-5.

- TAGAYA N., MIKAMI H., KOGURE H., KUBOTA K., HOSOYA Y., NAGAI H. Laparoscopic intragastric stapled resection of gastric submucosal tumors located near the esophagogastric junction. *Surg. Endosc.*, 2002 Jan, 16: 177-9.
- CHOI Y.B. Laparoscopic gatrojejunostomy for palliation of gastric outlet obstruction in unresectable gastric cancer. Surg Endosc, 2002 Nov, 16: 1620-6.
- SPANKNEBEL K., CONLON K.C. Advances in the surgical management of pancreatic cancer. Cancer J., 2001 Jul-Aug, 7: 312-23.
- BURDILES P., ROSSI R.L. Laparoscopy in pancreatic and hepatobiliary cancer. Surg. Oncol. Clin. N. Am., 2001 Jul, 10: 531-55.
- FERNANDEZ-CRUZ L., SAENZ A., ASTUDILLO E., MARTINEZ I., HOYOS S., PANTOJA J.P., NAVARRO S. Outcome of laparoscopic pancreatic surgery: endocrine and nonendocrine tumors. World J. Surg., 2002 Aug, 26: 1057-65.
- PARK A.E., HENIFORD B.T. Therapeutic laparoscopy of the pancreas. Ann. Surg., 2002 Aug, 236: 149-58.
- GENTILESCHI P., GAGNER M. Laparoscopic pancreatic resection. Chir. Ital., 2001 May-Jun, 53: 279-89.
- MATSUNO S., EGAWA S., ARAI K. Trends in treatment for pancreatic cancer. J. Hepatobiliary Pancreat. Surg., 2001, 8: 544-8.
- MALA T., EDWIN B., GLADHAUG I., FOSSE E., SOREIDE O., BERGAN A., MATHISEN O. A comparative study of the short-term outcome following open and laparoscopic liver resection of colorectal metastases. Surg. Endosc., 2002 Jul, 16: 1059-63.
- BURPEE S.E., KURIAN M., MURAKAME Y., BENEVIDES S., GAGNER M. The metabolic and immune response to laparoscopic versus open liver resection. Surg. Endosc., 2002 Jun, 16: 899-904.
- 34. GIGOT J.F., GLINEUR D., SANTIAGO AZAGRA J., GOERGEN M., CEUTERICK M., MORINO M., ETIENNE J., MARESCAUX J., MUTTER D., VAN KRUNCKELSVEN L., DESCOTTES B., VALLEIX D., LACHACHI F., BERTRAND C., MANSVELT B., HUBENS G., SAEY J.P., SCHOCKMEL R. Hepatobiliary and Pancreatic Section of the Royal Belgian Society of Surgery and the Belgian Group for Endoscopic Surgery. Laparoscopic liver resection for malignant liver tumors: preliminary results of a multicenter European study. Ann. Surg., 2002 Jul, 236: 90-7.
- WEILAND S.T., MAHVI D.M., NIEDERHUBER J.E., HEISEY D.M., CHICKS D.S., RIKKERS L.F. Should suspected early gallbladder cancer be treated laparoscopically? *J. Gastrointest. Surg.*, 2002 Jan-Feb, 6: 50-6, discussion 56-7.
- WEXNER S.D., COHEN S.M. Port site metastases after laparoscopic colorectal surgery for cure of malignancy. Br. J. Surg., 1995 Mar, 82: 295-8
- 37. POULIN E.C., MAMAZZA J., SCHLACHTA C.M., GREGOIRE R., ROY N. Laparoscopic resection does not adversely affect early survival curves in patients undergoing surgery for colorectal adenocarcinoma. *Ann. Surg.*, 1999 Apr, 229: 487-92.
- READ T.E., MUTCH M.G., CHANG B.W., MC NEVIN M.S., FLESH-MAN J.W., BIRNBAUM E.H., FRY R.D., CAUSHAJ P.F., KODNER I.J. Locoregional recurrence and survival after curative resection of adenocarcinoma of the colon. *J. Am. Coll. Surg.*, 2002 Jul, 195: 33-40.
- HASEGAWA H., KABESHIMA Y., WATANABE M., YAMAMOTO S., KITAJIMA M. Randomized controlled trial of laparoscopic versus open colectomy for advanced colorectal cancer. Surg. Endosc., 2003 Feb 10, [epub ahead of print].
- FRANKLIN M.E., KAZANTSEV G.B., ABREGO D., DIAZ-E J.A., BALLI J., GLASS J.L. Laparoscopic surgery for stage III colon cancer: long-term follow-up. Surg. Endosc., 2000 Jul, 14: 612-6.
- HARTLEY J.E., MONSON J.R. The role of laparoscopy in the multimodality treatment of colorectal cancer. Surg. Clin. North Am., 2002 Oct, 82: 1019-33.
- WEEKS J.C., NELSON H., GELBER S., SARGENT D., SCHROEDER G. Clinical Outcomes of Surgical Therapy (COST) Study Group. Short-term quality-of-life outcomes following laparoscopic-assisted colectomy vs open colectomy for colon cancer: a randomized trial. *JAMA*, 2002 Jan 16, 287: 321-8.
- 43. LACY A.M., GARCIA-VALDECASAS J.C., DELGADO S., CASTELLS A., TAURA P., PIQUE J.M., VISA J. Laparoscopy-assisted colectomy versus open colectomy for treatment of non-metastatic colon cancer: a randomised trial. *Lancet*, 2002 Jun 29, 359: 2224-9.