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Press review

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■ Article 1

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Rullier E, Vendrely V, Asselineau J, et al. Organ preservation with chemoradiotherapy plus local excision for rectal cancer: 5-year results of the GRECCAR 2 randomised trial. *Lancet Gastroenterol Hepatol* 2020;5(5):465–74. [Epub 2020 Feb 7. PMID: 32043980]
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Background

GRECCAR 2 was the first multicentre, randomised trial to compare local excision with total mesorectal excision in downstaged low rectal cancer. Encouraging oncological results were noted at 3 years' follow-up but needed to be corroborated with longer follow-up. In this study, we aimed to report the 5-year oncological outcomes, including local recurrence, metastatic disease, and survival.

Methods

Patients age 18 years and older with T2T3 low rectal cancer, of maximum size 4 cm, who were clinically good responders after chemoradiotherapy (residual tumour ≤ 2 cm) were randomly assigned before surgery to either local excision or total mesorectal excision. Randomisation was centralised and not stratified and used permuted blocks of size eight. In the local excision group, a completion total mesorectal excision was performed if pathological tumour stage was ypT2-3. The primary objective of this study was to assess the 5-year oncological outcomes of local recurrence, metastatic disease, disease-free survival, overall survival, and cancer-specific mortality, which were the secondary endpoints of GRECCAR 2. We used Kaplan-Meier estimates and Cox modelling to estimate and compare recurrence and survival in modified intention-to-treat and as-treated populations. This trial was registered with ClinicalTrials.gov, number NCT00427375.

Findings

Between March 1, 2007, and Sept 24, 2012, 148 patients who were good clinical responders were randomly assigned to treatment, three patients were excluded after randomisation (because they had metastatic disease, tumour > 8 cm from anal verge, or withdrew consent), leaving 145 for analysis: 74 in the local excision group and 71 in the total mesorectal excision group. Median follow-up was 60 months (IQR: 58–60) in the local excision group and 60 months (57–60) in the total mesorectal excision group. Twenty-three patients died and five were lost to follow-up. In the local excision group, 26 had a completion total mesorectal excision for ypT2-3 tumour. In the modified intention-to-treat analysis, there was no difference between the local excision and total mesorectal excision groups in 5-year local recurrence (7% [95% CI: 3–16] vs 7% [3–16]; adjusted hazard ratio [HR] 0.71 [95% CI: 0.19–2.58]; $P=0.60$), metastatic disease (18% [CI: 11–30] vs 19% [11–31]; 0.86 [0.36–2.06]; $P=0.73$), overall survival (84% [73–91] vs 82% [71–90]; 0.92 [0.38–2.22]; $P=0.85$), disease-free survival (70% [58–79] vs 72% [60–82]; 0.87 [0.44–1.72]; $P=0.68$), or cancer-specific mortality (7% [3–17] vs 10% [5–20]; 0.65 [0.17–2.49]; $P=0.53$).

Interpretation

The 5-year results of this multicentre randomised trial corroborate the 3-year results, providing no evidence of difference in oncological outcomes between local excision and total mesorectal excision. Local excision can be proposed in selected patients having a small T2T3 low rectal cancer with a good clinical response after chemoradiotherapy.

Funding

National Cancer Institute of France.

Comments

1. These results, together with those from the first GRECCAR2 publication, establish the most robust data with regard to rectal preservation in the management of small locally advanced rectal cancer. This approach is safe from an oncologic viewpoint and therefore can now be proposed outside therapeutic trials, in accordance with the

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indications proposed in this trial, and now is included in the French recommendations [1].

2. Currently, there are no data that show that this approach is superior, even if avoiding a major intervention represents an enormous advantage for the patient. Of note, the GRECCAR2 trial, a superiority trial, was negative, and therefore did not show that rectal preservation was superior to the classical approach.
3. The absence of superiority in this trial is due, at least partly, to the poor results observed in patients who required a secondary proctectomy, and in particular, in terms of postoperative morbidity and long-term sequelae [2]. The fear was that this could also lead to poorer oncologic results. This long-term analysis showed that this was not the case, which is reassuring.
4. It will be interesting to know the long-term functional results, the gastrointestinal and urinary tract sequelae and quality of life of the different groups to determine whether this new approach is of any benefit.

References

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 [2] Lancet 2017;390(10093):469–79.

■ Article 2

Ahmed O, Lefevre JH, Collard MK, et al. Is ileostomy mandatory for ileal-pouch-anal anastomosis? A propensity matched analysis of 388 procedures. *Surgery* 2020 [S0039-6060(20)30113-6. Online ahead of print. PMID: 32299627] <https://doi.org/10.1016/j.surg.2020.03.001>

Background

Restorative proctocolectomy with ileal-pouch-anal anastomosis is the standard treatment for patients with ulcerative colitis or familial adenomatous polyposis. This procedure has undergone many changes and varies in 1, 2, or 3 stages. A diverting ileostomy can be created with the aim of reducing the consequence of an anastomotic leakage; however, its use is still unknown.

Method

The value of defunctioning ileostomy was studied in a population of 388 patients undergoing restorative proctocolectomy with ileal-pouch-anal anastomosis between 2005 and 2017. Leakage rate and postoperative morbidity were assessed. Patients were matched on a propensity score using the following criteria: American Society of Anesthesiologists score, body mass index, diagnosis, surgical approach, and year.

Results

Two hundred and three ileal-pouch-anal anastomosis for ulcerative colitis and 185 for familial adenomatous polyposis were performed representing 165 1-stage (61.6%), 79 classic 2-stage, 74 modified 2-stage, and 70 3-stage procedures. Regardless of the surgical strategy adopted, there were no significant differences in postoperative morbidity (P .416), leakage rate (P .369), and reoperation (P .237), whether a diverting ileostomy was performed or not. After propensity score matching, there was no significant difference in postoperative morbidity (P .363), leakage rate (P .247), or reoperation (P .243). The rate of persistent ileostomy at 1 year was higher in cases of classic 2-stage or 3-stage procedures (P .036).

Conclusion

After propensity score matching, defunctioning ileostomy for ileal-pouch-anal anastomosis does not reduce leakage rate or postoperative morbidity, independent of the surgical

strategy. Systematic ileostomy for ileal-pouch-anal anastomosis is probably not justified, and its place should be redefined in a randomized trial.

Comments

1. The results of this propensity score analysis showed that a diverting ileostomy did not reduce the risk of anastomotic leakage after ileoanal anastomosis. Although not a controlled study, the methodological quality of this work is acceptable.
2. The potential value of an ileostomy is not only to reduce the fistula rate but also to limit the consequences when a fistula occurs. The results of this study seem to indicate that the absence of routine ileostomy does not endanger the anastomosis itself nor the possibility of ulterior restoration of intestinal continuity. In reality, it seems that, to the contrary, the proportion of patients with an ileostomy at one year was greater when the patient did not have an ileostomy performed at the first operation. Nonetheless, this result should be analyzed with caution because it might just be due to a selection bias in this retrospective series.
3. The absence of routine ileostomy does not seem to be deleterious and could even be associated with less morbidity and better functional outcome. Morbidity related to stoma closure and the functional result of the anastomosis were not analyzed in this study. Hopefully, the answers to these open questions will be found in the French "IDEAL" controlled trial, currently underway under the auspices of Groupe d'Étude Thérapeutique des Affections Inflammatoires du tube Digestif (GETAID) (Study group for the treatment of inflammatory bowel disease).

■ Article 3

Boudjema K, Locher C, Sabbagh C, et al. Simultaneous versus delayed resection for initially resectable synchronous colorectal cancer liver metastases: a prospective, open-label, randomized, controlled trial. *Ann Surg* 2020. [Online ahead of print. PMID: 32209911] <https://doi.org/10.1097/SLA.0000000000003848>

Objective

To answer whether synchronous colorectal cancer liver metastases (SLM) should be resected simultaneously with primary cancer or should be delayed.

Summary background data

Numerous studies have compared both strategies. All were retrospective and conclusions were contradictory.

Methods

Adults with colorectal cancer and resectable SLM were randomly assigned to either simultaneous or delayed resection of the metastases. The primary outcome was the rate of major complications within 60 days following surgery. Secondary outcomes included overall and disease-free survival.

Results

A total of 105 patients were recruited. Eighty-five patients (39 and 46 in the simultaneous- and delayed-resection groups, respectively) were analyzed. The percentage of major perioperative complications did not differ between groups (49% and 46% in the simultaneous- and delayed-resection groups, respectively, adjusted OR: 0.84, 95% CI: 0.35–2.01; P 0.70, logistic regression). Complications rates were 28% and 13% (P 0.08, $\times 2$ test) at colorectal site and 15% and 17% (P 0.80, $\times 2$ test) at liver site, in simultaneous- and delayed-resection groups,

respectively. In the delayed-resection group, 8 patients did not reach the liver resection stage, and this was due to disease progression in 6 cases. After 2 years, overall and disease-free survival tended to be improved in simultaneous as compared with delayed-resection groups (P 0.05), a tendency which persisted for OS after a median follow-up of 47 months.

Conclusions

Complication rates did not appear to differ when colorectal cancer and synchronous liver metastases are resected simultaneously. Delayed resection tended to impair overall survival.

Comments

1. This is a difficult area for clinical research because patients with colorectal cancer and synchronous liver metastases (LM) represent a heterogeneous population, varying according to the site of the primitive tumor, the existence of complications related to the primary tumor, the number of LM... The investigators are to be commended for having set up a controlled trial on this topic. Unfortunately, patients were included in this study over a long period of time during which strategies have evolved greatly (preoperative chemotherapy, reversed strategy ('liver first'), place of laparoscopy...), patient accrual was not complete and the analysis lacked statistical power.
2. Certainly, simultaneous resection did not increase the proportion of patients with severe complications but this strategy did not decrease it either, even though there was only a single operation. Although the difference was not statistically significant, the risk of complications of the primary tumor site was higher in patients undergoing simultaneous treatment compared to patients who had the sequential procedure (28% vs. 13%, $P=0.08$). Consequently, patients must be selected carefully and in the case of primary rectal cancer, where we know morbidity is higher, this approach is not recommended [1,2].
3. Simultaneous resection could have an advantage from the oncologic standpoint. This tendency was observed for overall survival but not for recurrence-free survival, which is unusual. Moreover, although the sample was not large enough to answer this question, this tendency, not statistically significant *stricto sensu*, must be taken with caution.
4. Most likely, neither strategy should be abandoned on the basis of the results of this study, but a multi-disciplinary discussion to define the best approach is probably the most important element to stay on the correct track.

References

- [1] Colorectal Dis 2017;19(2):115–22.
- [2] J Visc Surg 2011;148(3):e171–82.

■ Article 4

COVIDSurg Collaborative. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study [published online ahead of print, 2020 May 29]. *Lancet* 2020 [S0140-6736(20)31182-X]
[https://doi.org/10.1016/S0140-6736\(20\)31182-X](https://doi.org/10.1016/S0140-6736(20)31182-X)

Background

The impact of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on postoperative recovery needs to be understood to inform clinical decision making during and after the COVID-19 pandemic. This study reports 30-day

mortality and pulmonary complication rates in patients with perioperative SARS-CoV-2 infection.

Methods

This international, multicentre, cohort study at 235 hospitals in 24 countries included all patients undergoing surgery who had SARS-CoV-2 infection confirmed within 7 days before or 30 days after surgery. The primary outcome measure was 30-day postoperative mortality and was assessed in all enrolled patients. The main secondary outcome measure was pulmonary complications, defined as pneumonia, acute respiratory distress syndrome, or unexpected postoperative ventilation.

Findings

This analysis includes 1128 patients who had surgery between Jan 1 and March 31, 2020, of whom 835 (74.0%) had emergency surgery and 280 (24.8%) had elective surgery. SARS-CoV-2 infection was confirmed preoperatively in 294 (26.1%) patients. Thirty-day mortality was 23.8% (268 of 1128). Pulmonary complications occurred in 577 (51.2%) of 1128 patients; 30-day mortality in these patients was 38.0% (219 of 577), accounting for 82.6% (219 of 265) of all deaths. In adjusted analyses, 30-day mortality was associated with male sex (odds ratio: 1.75 [95% CI: 1.28–2.40], $P<0.0001$), age 70 years or older versus younger than 70 years (2.30 [1.65–3.22], $P<0.0001$), American Society of Anesthesiologists grades 3–5 versus grades 1–2 (2.35 [1.57–3.53], $P<0.0001$), malignant versus benign or obstetric diagnosis (1.55 [1.01–2.39], $P=0.046$), emergency versus elective surgery (1.67 [1.06–2.63], $P=0.026$), and major versus minor surgery (1.52 [1.01–2.31], $P=0.047$).

Interpretation

Postoperative pulmonary complications occur in half of patients with perioperative SARS-CoV-2 infection and are associated with high mortality. Thresholds for surgery during the COVID-19 pandemic should be higher than during normal practice, particularly in men aged 70 years and older. Consideration should be given for postponing non-urgent procedures and promoting non-operative treatment to delay or avoid the need for surgery.

Comments

1. This study is certainly far from perfect from a methodologic viewpoint. Operative mortality may have been over-estimated as patients with mild or asymptomatic COVID disease underwent surgery. Nonetheless, the data warrant our attention: pulmonary complications occurred in more than half of patients, operative mortality in nearly one fourth of patients.
2. French and International learned societies did not wait for this study to propose recommendations [1]. During the epidemic, all non-urgent surgery was postponed in France and other countries. This attitude was largely justified if we base the decision on the results of this study.
3. As soon as the pressure related to the epidemic decreases, surgical activity must be re-organized, but because of the severity of disease in the perioperative period, routine screening for all patients should be the rule before surgery. Many if not most structures in France have adopted this measure.
4. In COVID-positive patients who must undergo an emergency procedure, there is not, at the present time, any effective measure to prevent progression to a more severe form of disease. This study shows that the main risk factors for death – male sex, age, co-morbidity – are the same as those observed in the overall population and are not modifiable.

Reference

[1] J Visc Surg 2020 [S1878-7886(20)30070-9].

■ Article 5

Romain B, Renard Y, Binquet C, et al. Recurrence after elective incisional hernia repair is more frequent than you think: an international prospective cohort from the French Society of Surgery. *Surgery* 2020 [S0039-6060(20)30101-X. Online ahead of print. PMID: 32305229]
<https://doi.org/10.1016/j.surg.2020.02.016>

Background

The French Society of Surgery has endorsed a cohort aiming to prospectively assess the frequency of recurrence after incisional hernia repair and to identify the risk factors.

Methods

Consecutive patients undergoing incisional hernia repair in the participating centers were included in the prospective French Society of Surgery cohort over a 6-month period. Patients were followed up with a computed tomography scan at 1 y and a clinical assessment by the surgeon at 2 years.

Results

A total of 1075 patients undergoing incisional hernia repair were included in 61 participating centers. The median follow-up was 24.0 months (interquartile range: 14.0–25.3). The follow-up rates were 83.0% and 68.5% at 1 and 2 years, respectively. The recurrence rates were 18.1% at 1 year and 27.7% at 2 years. Recurrence risk factors at 2 years were a history of hernia (odds ratio = 1.57, 95% confidence interval = 1.05–2.35, $P = .028$), a lateral hernia (odds ratio = 1.84, 95% confidence interval = 1.19–2.86, $P = .007$), a concomitant digestive operation (odds ratio = 1.97, 95% confidence interval = 1.20–3.22, $P = .007$), and the occurrence of early surgical site complications (odds ratio = 1.90, 95% confidence interval = 1.06–3.38, $P = .030$). The use of surgical mesh was strongly associated with a lower risk of recurrence at 2 years ($P < .001$).

Conclusion

After incisional hernia repair, the 2-year recurrence rate is as high as 27.7%. History of hernia, lateral hernia, concomitant digestive operation, the onset of surgical site complications, and the absence of mesh are strong risk factors for recurrence.

Comments

1. This recurrence rate might seem enormous, but it reflects reality. The risk of recurrence after incisional hernia is high and can involve more than 25% of patients two years after surgery.
2. Among the potential risk factors, few are modifiable aside from concomitant gastrointestinal surgery, often unpredictable because the procedure becomes necessary “accidentally”.
3. There is some evidence that suggests that laparoscopic repair or intraperitoneal mesh are risk factors for recurrence. In this un-controlled series where neither laparoscopic repair nor insertion of an intraperitoneal mesh seem to influence the risk of recurrence consequently, caution is warranted in the interpretation.
4. This is a large, multicenter study but certain factors related to the technique that could have influenced the outcome (size of the mesh in relation to the defect, fixation modalities, facial closure...) were not studied. Considering the results of this study, there is certainly a wide unexplored area of research.

■ Article 6

Pan L, Mu M, Yang P, et al. Clinical characteristics of COVID-19 patients with digestive symptoms in Hubei, China: a descriptive, cross-sectional, multicenter study. *Am J Gastroenterol* 2020;115(5):766–73
<https://doi.org/10.14309/ajg.0000000000000620>

Objective

Since the outbreak of Coronavirus Disease 2019 (COVID-19) in December 2019, various digestive symptoms have been frequently reported in patients infected with the virus. In this study, we aimed to further investigate the prevalence and outcomes of COVID-19 patients with digestive symptoms.

Methods

In this descriptive, cross-sectional, multicenter study, we enrolled confirmed patients with COVID-19 who presented to 3 hospitals from January 18, 2020, to February 28, 2020. All patients were confirmed by real-time polymerase chain reaction and were analyzed for clinical characteristics, laboratory data, and treatment. Data were followed up until March 18, 2020.

Results

In the present study, 204 patients with COVID-19 and full laboratory, imaging, and historical data were analyzed. The average age was 52.9 years ($SD \pm 16$), including 107 men and 97 women. Although most patients presented to the hospital with fever or respiratory symptoms, we found that 103 patients (50.5%) reported a digestive symptom, including lack of appetite (81 [78.6%] cases), diarrhea (35 [34%] cases), vomiting (4 [3.9%] cases), and abdominal pain (2 [1.9%] cases). If lack of appetite is excluded from the analysis (because it is less specific for the gastrointestinal tract), there were 38 total cases (18.6%) where patients presented with a gastrointestinal-specific symptom, including diarrhea, vomiting, or abdominal pain. Patients with digestive symptoms had a significantly longer time from onset to admission than patients without digestive symptoms (9.0 days vs 7.3 days). In 6 cases, there were digestive symptoms, but no respiratory symptoms. As the severity of the disease increased, digestive symptoms became more pronounced. Patients with digestive symptoms had higher mean liver enzyme levels, lower monocyte count, longer prothrombin time, and received more antimicrobial treatment than those without digestive symptoms.

Discussion

We found that digestive symptoms are common in patients with COVID-19. Moreover, these patients have a longer time from onset to admission, evidence of longer coagulation, and higher liver enzyme levels. Clinicians should recognize that digestive symptoms, such as diarrhea, are commonly among the presenting features of COVID-19 and that the index of suspicion may need to be raised earlier in at-risk patients presenting with digestive symptoms. However, further large sample studies are needed to confirm these findings.

Comments

1. This study confirms that the symptomatology of COVID-19 infection can be polymorphous and that a large proportion of patients can present with gastrointestinal symptoms. Anorexia is probably not very specific, but aside from this symptom, nearly 20% of patients have diarrhea, vomiting or abdominal pain.
2. Although rare in this study, certain patients can present with gastrointestinal symptoms only. These results

underscore once again the importance of testing patients admitted for emergencies in the current COVID era.

3. This study does not allow to determine if the observed symptomatology is related to gastrointestinal involvement by the virus. Viral RNA has been found by RT-PCR in the stools of infected patients [1], but we do not know whether the virus is viable in stools or whether it can induce lesions in the gastrointestinal tract [2].
4. A large proportion of patients with gastrointestinal symptoms received anti-infective treatments (hydroxychloroquine, azithromycin). This study does not allow to determine whether these medications could have been responsible for the symptoms observed, since diarrhea and nausea can often be attributed to drug toxicity.

References

- [1] Emerg Infect Dis 2020;26. [Epub ahead of print March 09, 2020].
 [2] Gastroenterology 2020;158(6):1831–1833.e3.

■ Article 7

Karoui M, Rullier A, Piessen G, et al. Perioperative FOLFOX 4 versus FOLFOX 4 plus cetuximab versus immediate surgery for high-risk stage II and III colon cancers: a phase II multicenter randomized controlled trial (PRODIGE 22). *Ann Surg* 2020;271(4):637–45
<https://doi.org/10.1097/SLA.0000000000003454>

Background

Perioperative chemotherapy has proven valuable in several tumors, but not in colon cancer (CC).

Objective

The aim of this study was to evaluate the efficacy and safety of perioperative chemotherapy in patients with locally advanced non-metastatic CC.

Methods

This is a French multicenter randomized phase II trial in patients with resectable high-risk T3, T4, and/or N2 CC on baseline computed tomography (CT) scan. Patients were randomized to receive either 6 months of adjuvant FOLFOX after colectomy (control) or perioperative FOLFOX for 4 cycles before surgery and 8 cycles after (FOLFOX peri-op). In RAS wild-type patients, a third arm testing perioperative FOLFOX-cetuximab was added. Tumor Regression Grade (TRG1) of Ryan et al. was the primary endpoint. Secondary endpoints were toxicity, perioperative morbidity, and quality of surgery.

Results

A total of 120 patients were enrolled. At interim analysis, the FOLFOX-cetuximab arm was stopped (lack of efficacy). The remaining 104 patients (control, $n = 52$; FOLFOX preop $n = 52$) represented our intention-to-treat population. In the FOLFOX perioperative group, 96% received the scheduled 4 cycles before surgery. R0 resection and complete mesocolic excision rate were 94% and 93%, respectively. Overall, mortality and morbidity rates were similar in both groups. Perioperative FOLFOX chemotherapy did not improve major pathological response rate (TRG1 = 8%) but was associated with a significant pathological regression (TRG1-2 = 44% vs 8%, $P < 0.001$) and a trend to tumor downstaging as compared to the control group. CT scan criteria were associated with a 33% rate of overstaging in control group.

Conclusions

Perioperative FOLFOX for locally advanced resectable CC is feasible with an acceptable tolerability but is not associated with an increased major pathological response rate as expected. However, perioperative FOLFOX induces

pathological regression and downstaging. Better preoperative staging tools are needed to decrease the risk of overtreating patients.

Trial registration

ClinicalTrials.gov NCT01675999.

Comments

1. The results of this phase 2 study are negative with regard to the principal endpoint; however, tumor downstaging was observed in patients treated preoperatively. Results of the primary tumor response in patients treated for metastatic colonic cancer (CC) have already been published [1]. However, the benefit of this preoperative tumor response in terms of prognosis for non-metastatic disease has not been shown.
2. Of interest, one major finding from this study was that CT scan overstaged the disease in one third of cases, essentially because of over-estimation of lymph node involvement. There is a need for more reliable preoperative selection criteria for chemotherapy.
3. These results are in favor of preoperative chemotherapy to obtain downstaging and enable R0 resection in patients with locally advanced CC (T4) where resection might otherwise not be complete. This point was highlighted in the FOxTROT where the R0 resection rate was 95% in the group treated preoperatively, versus 80% in the group managed by initial surgery ($P = 0.002$) [2].
4. Additionally, the tolerance of chemotherapy was acceptable while postoperative morbidity and mortality were not increased in patients treated preoperatively in this study.

References

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 [2] *Lancet Oncol* 2012;13:1152–60.

■ Article 8

Bachellier P, Addeo P, Faitot F, Nappo G, Dufour P. Pancreatectomy with arterial resection for pancreatic adenocarcinoma: how can it be done safely and with which outcomes? A single institution's experience with 118 patients. *Ann Surg* 2020;271(5):932–40
<https://doi.org/10.1097/SLA.0000000000003010>

This study assesses the safety and outcomes of the largest cohort of pancreatectomy with arterial resection (P-AR).

Background

A high postoperative mortality rate and uncertain oncologic benefits have limited the use of P-AR for locally advanced pancreatic adenocarcinoma.

Methods

We retrospectively reviewed a prospectively maintained database of patients who underwent P-AR between January 1990 and November 2017. Univariate and multivariate Cox analyses were used to assess prognostic factors for survival.

Results

There were 118 consecutive resections (51 pancreaticoduodenectomies, 18 total pancreatectomies, and 49 distal splenopancreatectomies). Resected arterial segments included the coeliac trunk (50), hepatic artery (29), superior mesenteric artery (35), and other segments (4). The overall mortality and morbidity were 5.1% and 41.5%, respectively. There were 84 (75.4%) patients who received neoadjuvant chemotherapy, 105 (89%) simultaneous venous resections, and 101 (85.5%) arterial reconstructions. The rates of R0 resection and pathologic invasion of venous and arterial walls were 52.4%, 74.2%, and 58%, respectively. The

overall survival was 59%, 13%, and 11.8% at 1, 3, and 5 years, respectively. The median overall survival after resection was 13.70 months (95% CI: 11–18.5 mo). In multivariate analysis, R0 resection (HR: 0.60; 95% CI: 0.38–0.96; $P=0.01$) and venous invasion (HR: 1.67; 95% CI: 1.01–2.63; $P=0.04$) were independent prognostic factors.

Conclusion

In a specialized setting, P-AR for locally advanced pancreatic adenocarcinoma can be performed safely with limited mortality and morbidity. Negative resection margin and the absence of associated venous invasion might predict favorable long-term outcomes.

Comments

1. This retrospective monocenter study analyzed the short- and long-term outcomes of pancreatectomies associated with arterial resection for patients with either borderline (27%) or locally advanced (73%) pancreatic adenocarcinoma.
2. The short-term results, particularly the low mortality (5.1%), are rather exceptional for pancreatectomy associated with arterial resection. Mortality was 18.4% in the Heidelberg series of arterial resections, leading these authors to abandon pancreatectomy combined with arterial resection [1].
3. This study included patients operated between 1990 and 2017, but, as underlined by the authors, the management protocol was modified in 2008, with the introduction of systematic preoperative chemotherapy. It probably would have been better to have analyzed only those patients treated after 2008 ($n=92$), which would have been in conformity with the current recommendations.
4. In this study, 17 (15%) patients had liver (15) or peritoneal (1) metastases that were resected during the same operation. The presence of metastases remains a contraindication to resection; these patients should have been excluded to ensure the homogeneity of the study population.
5. After a median follow-up of 15.7 months, the median overall survival was 13.7 months. In patients who had received preoperative chemotherapy, median overall survival, calculated starting from the beginning of chemotherapy, was 22.85 months. In the LAP 07 study, that compared continuation of chemotherapy vs. radiochemotherapy in patients with locally advanced adenocarcinoma stabilized by chemotherapy, median survival was 16.5 months after a median follow-up of 34 months [2]. Moreover, in the meta-analysis by Suker et al., median overall survival for patients with locally advanced adenocarcinoma treated with FOLFIRINOX, with or without radiochemotherapy, was 24.4 months [3].
6. Taking into account these results, and in spite of excellent short-term results in this series, it is difficult to conclude in favor of the long-term value of pancreatectomy associated with arterial resection in patients with pancreatic adenocarcinoma with arterial involvement.

References

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- [2] JAMA 2016;315(17).
- [3] Lancet Oncol 2016;17(6):801–10.

■ Article 9

Chen QY, Xie JW, Zhong Q, et al. Safety and efficacy of indocyanine green tracer-guided lymph node dissection during laparoscopic radical gastrectomy in patients with gastric

cancer: a randomized clinical trial. JAMA Surg 2020. [Epub ahead of print]

<https://doi.org/10.1001/jamasurg.2019.6033>

Importance

The application of indocyanine green (ICG) imaging in laparoscopic radical gastrectomy is in the preliminary stages of clinical practice, and its safety and efficacy remain controversial.

Objective

To investigate the safety and efficacy of ICG near-infrared tracer-guided imaging during laparoscopic D2 lymphadenectomy in patients with gastric cancer.

Design, setting, and participants

Patients with potentially resectable gastric adenocarcinoma (clinical tumor stage cT1-cT4a, N0/+, M0) were enrolled in a prospective randomized clinical trial at a tertiary referral teaching hospital between November 2018 and July 2019. Patients were randomly assigned to the ICG group or the non-ICG group. The number of retrieved lymph nodes, rate of lymph node noncompliance, and postoperative recovery data were compared between the groups in a modified intention-to-treat analysis. Statistical analysis was performed from August to September 2019.

Interventions

The ICG group underwent laparoscopic gastrectomy using near-infrared imaging after receiving an endoscopic peritumoral injection of ICG to the submucosa 1 day before surgery.

Main outcomes and measures

Total number of retrieved lymph nodes.

Results

Of 266 participants randomized, 133 underwent ICG tracer-guided laparoscopic gastrectomy, and 133 underwent conventional laparoscopic gastrectomy. After post-surgical exclusions, 258 patients were included in the modified intention-to-treat analysis, which comprised 129 patients (86 men and 43 women; mean [SD] age, 57.8 [10.7] years) in the ICG group and 129 patients (87 men and 42 women; mean [SD] age, 60.1 [9.1] years) in the non-ICG group. The mean number of lymph nodes retrieved in the ICG group was significantly more than the mean number retrieved in the non-ICG group (mean [SD], 50.5 [15.9] lymph nodes vs 42.0 [10.3] lymph nodes, respectively; $P<.001$). Significantly, more perigastric and extraperigastric lymph nodes were retrieved in the ICG group than in the non-ICG group. In addition, the mean total number of lymph nodes retrieved in the ICG group within the scope of D2 lymphadenectomy was also significantly greater than the mean number retrieved in the non-ICG group (mean [SD], 49.6 [15.0] lymph nodes vs 41.7 [10.2] lymph nodes, respectively; $P<.001$). The lymph node noncompliance rate of the ICG group (41 of 129 patients [31.8%]) was lower than that of the non-ICG group (74 of 129 patients [57.4%]; $P<.001$). The postoperative recovery process was comparable, and no significant difference was found between the ICG and non-ICG groups in the incidence (20 of 129 patients [15.5%] vs 21 of 129 [16.3%], respectively; $P=.86$) or severity of complications within 30 days after surgery.

Conclusions and relevance

Indocyanine green can noticeably improve the number of lymph node dissections and reduce lymph node noncompliance without increased complications in patients undergoing D2 lymphadenectomy. Indocyanine green fluorescence imaging can be performed for routine lymphatic mapping during laparoscopic gastrectomy, especially total gastrectomy.

Trial registration

ClinicalTrials.gov Identifier: NCT03050879.

Comments

1. The positive points of this study are that it was randomized and that surgical technique, ICG imaging and lymph node area analysis were standardized.
2. ICG was injected the evening before surgery, under endoscopic control (rather than intra-operative sub-serosal injection) because this technique seemed easier and did not prolong the operative procedure. However, this constitutes a supplementary invasive procedure.
3. ICG imaging allowed to increase the number of lymph nodes analyzed, without modification of the TN stage. Moreover, as survival outcome was not available, the carcinologic impact remains unknown.
4. Of note, the diagnostic sensitivity and specificity of ICG were low.
5. All in all, these results do not allow any conclusion as to the generalizability of this technique.

■ Article 10

Sakamoto T, Fujiogi M, Lefor AK, Matsui H, Fushimi K, Yasunaga H. Stent as a bridge to surgery or immediate colectomy for malignant right colonic obstruction: propensity-scored, national database study. *Br J Surg* 2020. [Epub ahead of print]
<https://doi.org/10.1002/bjs.11561>

The aim of this study was to compare perioperative outcomes of urgent colectomy and placement of a self-expanding metallic stent followed by colectomy for patients with malignant right colonic obstruction. Right-sided malignant obstruction is less common than left-sided. Stenting for malignant left colonic obstruction has been reported to reduce postoperative complications. However, the impact of stenting for malignant right colonic obstruction remains undefined.

Methods

The study included patients with right-sided malignant obstruction or stenosis undergoing colectomy between April 2012 and March 2017 identified from a nationwide database. Propensity score matching analysis was used to compare mortality and morbidity rates, proportion receiving a stoma and postoperative stay between urgent colectomy and stent groups.

Results

From 9572 patients, 1500 pairs were generated by propensity score matching. There was no significant difference in in-hospital mortality between the urgent colectomy and stent groups (1.6 versus 0.9 percent respectively; $P=0.069$). Complications were more common after urgent colectomy than stenting (22.1 versus 19.1 percent; $P=0.042$). Surgical site infection was more likely with urgent colectomy (7.1 versus 4.4 percent; $P=0.001$). There was no significant difference between the two groups in anastomotic leakage (3.8 versus 2.6 percent; $P=0.062$). The proportion of patients needing a stoma was higher with urgent colectomy than primary treatment with stents (5.1 versus 1.7 percent; $P<0.001$). Postoperative stay was longer after urgent colectomy (15 versus 13 days; $P<0.001$).

Conclusion

Stenting followed by colectomy in patients with malignant right colonic obstruction may provide more favorable perioperative outcomes than urgent colectomy.

Comments

1. One of the drawbacks of this analysis is its retrospective character, which does not allow an intention-to-treat analysis, and consequently, there is no information concerning the success rate of stent insertion, the rate of complications after stent insertion, the number of patients operated after stent insertion, as well as the type of surgery (type of stoma, extension of the colectomy...).
2. The complication rate was higher in the initial colectomy group, but essentially because of operative site infection, which might be related to the higher number of laparotomies in the initial surgery group. Although one of the purported advantages of stents would be to decrease the fistula rate and the number of stomas, no statistically significant difference was found in the postoperative fistula rates (although the rate of fistula was lower in the stent group). Of note, the authors did not report the rate of definitive stomas or that of stents still in place at one year.
3. Taking into consideration the potential difficulties of stent insertion on the right side and the need for an experienced team, one alternative might be to create an emergency lateral ileostomy laparoscopically to relieve the obstruction, then perform right colectomy with anastomosis later, but during the same hospitalization.
4. There was a major selection bias in this study as patients receiving a stent were managed in centers where the yearly number of colonic stents was higher than that in centers where stents were not inserted in the surgery group (8.2/year vs. 3.6/year).
5. Last, one of the main questions in this management scheme is the long-term outcome and the potential impact of stent insertion on oncologic prognosis, information that is not available in this study.

■ Article 11

Seidel D, Diedrich S, Herrle F, et al. Negative pressure wound therapy vs conventional wound treatment in subcutaneous abdominal wound healing impairment: the SAWHI randomized clinical trial. *JAMA Surg* 2020. [Epub ahead of print]
<https://doi.org/10.1001/jamasurg.2020.0414>

Importance

Negative pressure wound therapy (NPWT) is an established treatment option, but there is no evidence of benefit for subcutaneous abdominal wound healing impairment (SAWHI).

Objective

To evaluate the effectiveness and safety of NPWT for SAWHI after surgery in clinical practice.

Design, setting, and participants

The multicenter, multinational, observer-blinded, randomized clinical SAWHI study enrolled patients between August 2, 2011, and January 31, 2018. The last follow-up date was June 11, 2018. The trial included 34 abdominal surgical departments of hospitals in Germany, Belgium, and the Netherlands, and 539 consecutive, compliant adult patients with SAWHI after surgery without fascia dehiscence were randomly assigned to the treatment arms in a 1:1 ratio stratified by study site and wound size using a centralized web-based tool. A total of 507 study participants (NPWT,

256; CWT, 251) were assessed for the primary end point in the modified intention-to-treat (ITT) population.

Interventions

Negative pressure wound therapy and conventional wound treatment (CWT).

Main outcomes and measures

The primary outcome was time until wound closure (delayed primary closure or by secondary intention) within 42 days. Safety analysis comprised the adverse events (AEs). Secondary outcomes included wound closure rate, quality of life (SF-36), pain, and patient satisfaction.

Results

Of the 507 study participants included in the modified ITT population, 287 were men (56.6%) (NPWT: 155 [60.5%] and CWT: 132 [52.6%]) and 220 were women (43.4%) (NPWT: 101 [39.5%] and CWT: 119 [47.4%]). The median (IQR) age of the participants was 66 (18) years in the NPWT arm and 66 (20) years in the CWT arm. Mean time to wound closure was significantly shorter in the NPWT arm (36.1 days) than in the CWT arm (39.1 days) (difference: 3.0 days; 95% CI: 1.6–4.4; $P < .001$). Wound closure rate within 42 days was significantly higher with NPWT (35.9%) than with CWT (21.5%) (difference: 14.4%; 95% CI: 6.6%–22.2%; $P < .001$). In the therapy-compliant population, excluding study participants with unauthorized treatment changes (NPWT: 22; CWT: 50), the risk for wound-related AEs was higher in the NPWT arm (risk ratio: 1.51; 95% CI: 0.99–2.35).

Conclusions and relevance

Negative pressure wound therapy is an effective treatment option for SAWHI after surgery; however, it causes more wound-related AEs.

Trial registration

ClinicalTrials.gov Identifier: NCT01528033.

Comments

1. The quality of the methodology of this randomized trial is good, although the cross-over rate was high (50 of 251 patients in the CWT group underwent NPWT). Moreover, the conventional management plan was not standardized, probably because it was a multicenter trial and reflecting different practices between centers.
2. This study confirms that time to closure is better with NPWT with respect to local care; however, the delay to closure of post-surgical wounds was long, even with NPWT, as 71.2% of the wounds had not healed after 42 days (NPWT, 64.1%; CWT, 78.5%). Consequently, a longer follow-up would have been more appropriate.

■ Article 12

de Savornin Lohman EAJ, van der Geest LG, de Bitter TJJ, et al. Re-resection in incidental gallbladder cancer: survival and the incidence of residual disease. *Ann Surg Oncol* 2020;27(4):1132–42. [Epub 2019 Nov 18]
<https://doi.org/10.1245/s10434-019-08074-4>

Re-resection for incidental gallbladder cancer (iGBC) is associated with improved survival but little is known about residual disease (RD) and prognostic factors. In this study, survival after re-resection, RD, and prognostic factors are analyzed.

Methods

Patients with iGBC were identified from the Netherlands Cancer Registry, and pathology reports of re-resected

patients were reviewed. Survival and prognostic factors were analyzed.

Results

Overall, 463 patients were included; 24% ($n = 110$) underwent re-resection after a median interval of 66 days. RD was present in 35% of patients and was most frequently found in the lymph nodes (23%). R0 resection was achieved in 93 patients (92%). Median overall survival (OS) of patients without re-resection was 13.7 (95% confidence interval [CI]: 11.6–15.6), compared with 52.6 months (95% CI: 36.3–68.8) in re-resected patients ($P < 0.001$). After re-resection, median OS was superior in patients without RD versus patients with RD (not reached vs. 23.1 months; $P < 0.001$). In patients who underwent re-resection, RD in the liver (hazard ratio [HR] 5.54; $P < 0.001$) and lymph nodes (HR: 2.35; $P = 0.005$) were the only significant prognostic factors in multivariable analysis. Predictive factors for the presence of RD were pT3 stage (HR: 25.3; $P = 0.003$) and pN1 stage (HR: 23.0; $P = 0.022$).

Conclusion

Re-resection for iGBC is associated with improved survival but remains infrequently used and is often performed after the optimal timing interval. RD is the only significant prognostic factor for survival after re-resection and can be predicted by pT and pN stages

Comments

1. This retrospective study found that re-resection improved survival in patients with T2 and T3 gallbladder cancer diagnosed incidentally on gallbladder specimen pathology. Improved survival could be explained by better staging (but patients did not receive pre- or postoperative treatment based on staging...), but above all, by more R0 resections when re-resection was performed. Effectively, one of the principal prognostic factors was the presence of residual disease that was more frequently observed in patients with advanced T stages.
2. The French Thesaurus National de Cancérologie Digestive recommends liver resection associated with lymph node dissection for T1b and T2 gallbladder tumors [1], which increases 5-year survival [1]. Otherwise, IVb-V bisegmental liver resection with lymph node dissection and eventual resection of the bile duct is recommended. Resection of the gallbladder bed represents an alternative to bi-segmentectomy, particularly when the cancer is small and located on the free edge of the gallbladder. Bile duct resection is recommended only when the cystic duct lymph nodes are involved.
3. Nonetheless, the benefit of re-resection in patients with stage Ib disease discovered incidentally remains a topic of debate.
4. This analysis did not take into account the location of the cancer [peritoneal border (T2a) versus liver border (T2b)]. Of note, T2b tumors are associated with worse prognosis (high recurrence rate in the liver (23% vs. 3%) and lymph nodes (16% vs. 3%) in spite of complementary surgery with curative intent) [2].
5. This retrospective study contains several biases (decision to re-operate or not, type of resection...) warranting caution in sub-group analysis with small patient samples.

References

- [1] *Ann Surg* 2008;247(1):104–8.
- [2] *Ann Surg* 2015;261(4):733–9.