Journal of Visceral Surgery (2018) xxx, xxx—xxx

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Press review

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Article 1: Ovarian cancer: hyper-thermic intra-peritoneal chemotherapy after cytoreductive surgery increases survival: results of a controlled randomized trial

van Driel WJ, Koole SN, Sikorska K, Schagen van Leeuwen JH, Schreuder HWR, Hermans RHM, et al. Hyperthermic intraperitoneal chemotherapy in ovarian cancer. N Engl J Med 2018;378(3):230—240.
https://doi.org/10.1056/NEJMoa1708618

Comments

1. This article is a lesson for all! The methodology is faultless and the manuscript is marvelously well written!
2. The is the first randomized trial evaluating the potential benefit of hyperthermic intra-peritoneal chemotherapy (HIPEC) in women with stage III ovarian cancer, as well as the first trial comparing cytoreductive surgery + HIPEC to cytoreductive surgery alone in any sort of peritoneal malignancy, underscoring its major importance.
3. The results of a similarly designed French trial (PRODIGE 7), evaluating outcomes for patients with peritoneal malignancy of colorectal origin, should be available this coming year.
4. The absence of a statistically significant difference in morbidity between grades 3 and 4 is surprising (25% vs. 27%, $P = 0.76$). Effectively, it is of note that a French trial [1] that aimed to evaluate the morbidity of oxaliplatin-based HIPEC as consolidation treatment (after cytoreductive surgery and 6 cycles of systemic chemotherapy) for stage III ovarian cancer was stopped prematurely because of the high complication rate, particularly hemoperitoneum related to oxaliplatin toxicity (this concerned nine of 13 patients with HIPEC).

Reference

[1] Eur J Surg Oncol 2010;36:589—93.

Article 2: Laparoscopy versus open resection of colorectal liver metastases: results of the OSLO-COMET randomized controlled trial

Fretland ÅA, Dagenborg VJ, Bjørnelv GMW, Kazaryan AM, Kristiansen R, Fagerland MW, et al. Laparoscopic versus open resection for colorectal liver metastases: the OSLO-COMET randomized controlled trial. Ann Surg 2018;267(2):199—207.
https://doi.org/10.1097/SLA.0000000000002353

Comments

1. This is a methodologically sound controlled monocenter superiority trial.
2. The characteristics of patients and colorectal liver metastases (CRLM) were similar, except for a higher rate of antecedent hepatectomy in the ''laparoscopic'' arm.
3. These results are in agreement with the literature concerning the feasibility and safety of laparoscopic hepatic surgery for CRLM [1,2]. However, it is surprising that the rate of blood loss and transfusions were the same in the two groups, since they are most often reported to be less with laparoscopic surgery. The reason might be that the resections were limited or minor.
4. Effectively, 60% of surgical procedures were in the low level of difficulty according to the Iwate criteria [3].
5. The complication rate was clearly lower in the « laparoscopic » arm, essentially because of the lower grades 2 and 4, respectively 10/129 vs. 24/133 and 1/129 vs. 8/133. With regard to grade 2 complications (identical to Dindo-Clavien grade 2), the difference concerned essentially the number of parietal complications that occurred more frequently in the ''open'' arm (7 vs. 1). As for grade 4 complications (corresponding to Dindo-Clavien grades IIIb and IVa), the re-operation rate was higher in the ''open'' arm (5 vs. 1).

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https://doi.org/10.1016/j.jviscsurg.2018.02.007
1878-7886/

6. It is surprising that the authors did not use the Dindo-Clavien classification, although the two classifications were quite similar.
7. There was no statistically significant difference found in costs for the two procedures; the duration of hospital stay was shorter and the quality of life at 1 and 4 months was better for laparoscopy, perhaps compensating for the higher costs related to the laparoscopic approach.

References

[1] Ann Surg 2015;262:794—802.
[2] Ann Surg 2009;250:849—55.
[3] Ann Surg 2015;261:619—29.

■ Article 3: Prognostic impact of involved resection margins after pancreatoduodenectomy for pancreatic adenocarcinoma: results of a French prospective study

Delpero JR, Jeune F, Bachellier P, Regenet N, Le Treut YP, Paye F, Carrere N, Sauvanet A, Adham M, Autret A, Poizat F, Turrini O, Boher JM. Prognostic value of resection margin involvement after pancreaticoduodenectomy for ductal adenocarcinoma: updates from a French prospective multicenter study. Ann Surg 2017;266:787—96.

Comments

1. This study underlines the value of a standardized pathological examination and the necessity for interaction between surgeon and pathologist in carcinological surgery.
2. The standardization of the definitions of R0 and R1 resections is also indispensable to analyze the results of different series and setting up clinical trials. The authors underscore the weakness of R0/R1 status, which corresponds to complete resection of the tumor but not the tumor margin. The latter seems more appropriate to evaluate prognosis. Consequently, the authors recommend that the minimal resection margin, instead of the R0/R1 status, be mentioned in the pathology report, as is the case for rectal cancer.
3. However, the prognostic character of R1 resection remains debated because of the weight of other prognostic factors such as lymph node involvement (ratio of positive lymph nodes/number of examined lymph nodes), and the presence of occult metastases that can explain early metastatic recurrence.
4. This study also underscores the potential role of pre-operative radiochemotherapy that could decrease the rate of R1 resections [1,2] and lead to better local control. This strategy was evaluated for borderline [3] or locally advanced adenocarcinoma and not for cancers that were initially resectable. In France, a trial evaluating the benefit of pre-operative chemotherapy (based on Folfirinox) for resectable pancreatic adenocarcinoma is currently underway (PANACHE01-PRODIGE48).

References

[1] HPB 2011;13:64—9.
[2] Am J Surg Pathol 2015;39:1395—403.
[3] JAMA Surg 2016;151:e161137

■ Article 4: Association of primary tumor location with mortality risk in patients with metastatic colorectal cancer receiving bevacizumab or cetuximab

Aljehani MA, Morgan JW, Guthrie LA, Jabo B, Ramadan M, Bahjri K, et al. Association of primary tumor site with mortality in patients receiving bevacizumab and cetuximab for metastatic colorectal cancer. JAMA Surg 2018;153:60—7. https://doi.org/10.1001/jamasurg2017.3466

Comments

1. From a methodological viewpoint this was a retrospective analysis of registry data, for which there are problems concerning the quality of data and the comparability of treatment groups. Effectively, the two groups of patients (right and left colonic cancer) were not comparable with regard to the known prognostic factors (mucinous histology, signet ring cells...). Moreover, several of the prognostic, possibly confounding, factors were missing, hampering any robust survival analysis.
2. Nonetheless, this study confirms the negative prognostic impact of right-sided colonic cancer, that may be explained by molecular [1,2] histological and bacterial [3] differences between right and left-sided colonic cancer. Anti-EGFR drugs have been reported to be less effective in right-sided metastatic colonic cancer [4,5].
3. The small number of patients receiving cetuximab (8.4%) is characteristic of American practice.
4. This study suggests that right-sided colonic cancer, even those that are RAS-wild, does not respond to cetuximab. This is in agreement with the latest American recommendations that advocate first line cetuximab in patients who are CCRm, RAS-wild, in left-sided colonic cancer only (NCCN 2017), whereas in Europe, the recommendations of the ESMO are a less clear.
5. The prognostic impact of right/left colonic colon is the consequence of tumoral and biological heterogeneity within the overall group of colonic cancer and certainly, prognostic analysis according to the CMS molecular classification CMS [6] would be more appropriate in future clinical trials.

References

[1] Br J Cancer 2015;112:1921—8.
[2] Br J Cancer 2016;115:25—33
[3] Clin Transl Gastroenterol 2007;11:e200.
[4] J Clin Oncol 2016;34(15):3504.
[5] Ann Oncol 2017. doi:10.1093/annonc/mdx175.
[6] Nat Med 2015;21:1350—6.

■ Article 5: Post-operative ERAS program characteristics have the greatest impact on optimal recovery patterns

Aarts MA, Rotstein OD, Pearsall EA, Victor JC, Okrainec A, McKenzie M, et al.; iERAS group. Post-operative ERAS interventions have the greatest impact on optimal recovery: experience with implementation of ERAS across multiple hospitals. Ann Surg 2018 [Epub ahead of print] https://doi.org/10.1097/SLA.0000000000002632

Comments

1. This is an original multi-center prospective study with sound methodology. However, there was no comparative analysis of compliance between the centers involved.
2. The pre-, intra- and post-operative components [1] corresponded to the usual recommendations (pre-operative information, solid food allowed until midnight, carbohydreate loading (sweet drinks) up to 2 h before surgery, analgesia and non-steroidal anti-inflammatory medication in the operating room, no naso-gastric tube, early