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Re: Critical Analysis of Early Recurrence after Laparoscopic Radical Cystectomy in a Large Cohort by the ESUT

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J Urol 2016; ***195****: 1710–1717.*

To the Editor: The authors critically analyze a large cohort by the European Association of Urology Section of Uro-Technology and assess early recurrences after laparoscopic radical cystectomy and evaluation of risk factors, including the impact of pneumoperitoneum. They focus their analysis on patients with favorable pathology (pT2 N0 R0 disease), finding that 27 of 311 patients (8.7%) experienced recurrences during the following 24 months. Surgical negligence was observed in only 1 patient, which was associated with the end bag rupturing during transvaginal extraction with subsequent vulvar and peritoneal tumor metastasis after 4 months. Among the 27 patients with recurrence a shorter recurrence-free survival was significantly predictive of cancer specific death (HR 0.86, 95% CI 0.78–0.94, $p = 0.001$) as well as carcinoma in situ on pathological examination (HR 3.68, 95% CI 1.07–12.7, $p = 0.039$). While analyzing causes of early recurrence, the authors suggest that the continuous insufflation-desufflation and leakage of gas around the ports—with consequent aspiration of tumor cells via a chimney effect—may promote tumor seeding (TS).[1]

The hypothesis correlating a cause and effect relationship of their findings with CO2 pneumoperitoneum conditions is coherently founded and extensively studied by implementation of animal models, in vitro experiments, case reports and a prospective study.[2,3] A model of desufflation during laparoscopic surgery was designed by means of in vitro cell culture tools. The impact of desufflation on survival and invasion capacities of cancer cells was tested compared to continuous CO2 insufflation by means of an in vitro pneumoperitoneum gas box model.[4] Survival and invasion capacities of cancer cells were superior in the desufflation model and were associated with oxidative stress. In that study desufflation during CO2 pneumperitoneum was highlighted as the triggering factor of postoperative cancer cell survival and invasion.

However, the impact of CO2 pneumoperitoneum desufflation cannot be considered the only triggering factor associated with port site metastasis (PSM) and TS. Indeed, in an Italian survey on laparoscopic cystectomy an interesting aspect was the absence of tumor seeding in 83 cases despite the longer operative time compared to open surgery (520 vs 330 minutes).[5] This finding suggests that respect of surgical oncologic principles is important to prevent TS.

Another important factor associated with TS and PSM is the origin of the tumor and its malignant and metastatic potential. Transitional cell carcinoma is one of the most malignant urinary tract tumors with a high grade of dissemination. Most of the published data on TS and PSM in the urological literature are related to transitional cell carcinoma.[5] Albisinni et al suggest that tumor stage is an important prognostic factor for TS but we believe that tumor grade is another important predictor of worse prognosis. Tumor grade usually follows tumor stage, and patients with high grade carcinoma have higher stage disease.[6] In a recent survey Micali et al showed that in all patients with TS the histological features demonstrated a high grade status.[7]

PSM is suggested as a rare complication of robotic and laparoscopic minimally invasive surgery.[8,9] We believe that superior laparoscopic surgical skills and broad oncologic expertise should be well consolidated to perform challenging procedures such as cystectomy. In this era of

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worldwide expanded laparoscopic technologies and use of laparoscopic approaches in patients with advanced cancer TS and PSM should be considered when planning such treatment, and desufflation should be avoided during laparoscopic procedures.

Respectfully,

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Reply by Authors: We agree with the points highlighted by Mynbaev et al. We wish to emphasize that most of the recurrences observed were due to hematogeneous spread, thus advancing the hypothesis that the cancerous cells spread through the venous system rather than in the peritoneal cavity as a consequence of bladder pedicle squeezing in the Batson plexus. We want to stress the need for further studies exploring the effect of pneumoperitoneum on urothelial cancer dissemination, challenging the adequacy of minimally invasive surgery in the management of such a lethal disease.

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