Journal of Visceral Surgery (2015) 152, 385—392

Available online at ScienceDirect www.sciencedirect.com

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Press review

C. Mariette[a,*], S. Benoist[b]

[a] Service de chirurgie digestive et générale, hôpital C.-Huriez, CHRU, place de Verdun, 59037 Lille cedex, France
[b] Service de chirurgie digestive, hôpital du Kremlin-Bicêtre, 78, rue du Général-Leclerc, 94275 Le Kremlin-Bicêtre, France

Available online 30 October 2015

■ Kumar S, Huang J, Abbassi-Ghadi N, et al. Mass spectrometric analysis of exhaled breath for the identification of volatile organic compound biomarkers in esophageal and gastric adenocarcinoma. Ann Surg 2015. doi:10.1097/SLA.0000000000001101

Objective

The present study assessed whether exhaled breath analysis using Selected Ion Flow Tube Mass Spectrometry could distinguish esophageal and gastric adenocarcinoma from non-cancer controls.

Background

The majority of patients with upper gastrointestinal cancer present with advanced disease, resulting in poor long-term survival rates. Novel methods are needed to diagnose potentially curable upper gastrointestinal malignancies.

Methods

A Profile-3 Selected Ion Flow Tube Mass Spectrometry instrument was used for analysis of volatile organic compounds (VOCs) within exhaled breath samples. All study participants had undergone upper gastrointestinal endoscopy on the day of breath sampling. Receiver operating characteristic analysis and a diagnostic risk prediction model were used to assess the discriminatory accuracy of the identified VOCs.

Results

Exhaled breath samples were analyzed from 81 patients with esophageal ($n=48$) or gastric adenocarcinoma ($n=33$) and 129 controls including Barrett's metaplasia ($n=16$), benign upper gastrointestinal diseases ($n=62$), or a normal upper gastrointestinal tract ($n=51$). Twelve VOCs — pentanoic acid, hexanoic acid, phenol, methyl phenol, ethyl phenol, butanal, pentanal, hexanal, heptanal, octanal, nonanal, and decanal — were present at significantly higher concentrations ($P<0.05$) in the cancer groups than in the non-cancer controls. The area under the ROC curve using these significant VOCs to discriminate esophageal and gastric adenocarcinoma from those with normal upper gastrointestinal tracts was 0.97 and 0.98, respectively. The area under the ROC curve for the model and validation subsets of the diagnostic prediction model was 0.92 ± 0.01 and 0.87 ± 0.03, respectively.

Conclusions

Distinct exhaled breath VOC profiles can distinguish patients with esophageal and gastric adenocarcinoma from non-cancer controls.

Comments

1. As is the case for many other cancers, esophageal and gastric carcinoma are often diagnosed late because the specific alarm-sounding symptoms appear tardily. Any new screening process is therefore of interest.
2. Exhaled breath analysis, even though rather complex, with more than 250 volatile organic components identified, and standardized logistics, is a promising screening technique. A canine scent detection analysis of exhaled breath samples and stools has been used with success to detect colorectal cancer in humans [1].
3. Remarkably, the control group included patients with non-specific digestive symptoms for which fibroendoscopy was performed. This underlines the good specificity of the test to detect cancer. Of note, also, there were no patients with cancers other than esophageal or gastric carcinoma in the control group.
4. The advantages of this technique are the rapid data acquisition (15 min) and its non-invasive character, easily accepted by patients.
5. Aside from the value in initial diagnosis, it would have been pertinent to also evaluate the usefulness of this investigation for early diagnosis of recurrence.

* Corresponding author.
E-mail address: christophe.mariette@chru-lille.fr (C. Mariette).

1878-7886/$ — see front matter
http://dx.doi.org/10.1016/j.jviscsurg.2015.10.002

Reference
[1] Gut 2011;60:814—9.

■ Robb WB, Dahan L, Mornex F, et al. Impact of neoadjuvant chemoradiation on lymph node status in esophageal cancer: post-hoc analysis of a randomized controlled trial. Ann Surg 2015;261:902—8. doi:10.1097/SLA.0000000000000991

Objective

The study objectives were to analyze the impact of the number of lymph nodes (LNs) reported as resected (NLNr) and the number of LNs invaded (NLNi) on the prognosis of esophageal cancer (EC) after neoadjuvant chemoradiotherapy.

Background

Pathological LN status is a major disease prognostic factor and marker of surgical quality. The impact of neoadjuvant chemoradiation (nCRT) on LN status remains poorly studied in EC.

Methods

Post-hoc analysis from a phase III randomized controlled trial comparing nCRT and surgery (group nCRT) to surgery alone (group S) in stage I and II EC (NCT00047112). Only patients who underwent surgical resection were considered ($n = 170$).

Results

nCRT resulted in tumoral downstaging (pT0, 40.7% vs. 1.1%, $P < 0.001$), LN downstaging (pN0, 69.1% vs. 47.2%, $P = 0.016$), and reduction in the median NLNr [16.0 (range, 0—47.0) vs. 22.0 (range, 3.0—58.0), $P = 0.001$] and NLNi [0 (range, 0—25) vs. 1.0 (range, 0—25), $P = 0.001$]. A good histological response (TRG1/2) in the resected esophageal specimen correlated with reduced median NLNi [0 (range, 0—10) vs. 1.0 (range, 0—4), $P = 0.007$]. After adjustment by treatment, NLNi [hazards ratio (HR) (1—3 vs. 0) 3.5, 95% confidence interval (CI): 2.3—5.5, and HR (> 3 vs. 0) 3.5, 95% CI: 2.0—6.2, $P < 0.001$] correlated with prognosis, whereas NLNr [HR (< 15 vs. $\geq$ 15) 0.95, 95% CI: 0.6—1.4, $P = 0.807$ and HR (< 23 vs. $\geq$ 23) 1.4, 95% CI: 0.9—2.0, $P = 0.131$] did not. In Poisson regression analysis, nCRT was an independent predictive variable for reduced NLNr [exp(coefficient) 0.80, 95% CI: 0.66—0.96, $P = 0.018$].

Conclusions

nCRT is not only responsible for disease downstaging but also predicts fewer LNs being identified after surgical resection for EC. This has implications for the current quality criteria for surgical resection.

Comments

1. In esophageal cancer, as in other cancers, more and more studies suggest that when more lymph nodes are resected, not only is staging improved, but there is a survival benefit. The number of invaded lymph nodes as well as the number of lymph nodes resected are prognostic factors [1,2].
2. The threshold of 23 lymph nodes to be removed in esophageal cancer stems from studies where patients underwent surgery initially, and was used as an indicator of surgical quality. The results reported herein suggest that neoadjuvant chemoradiotherapy (nCRT) decreases the number of lymph nodes available for analysis by 27%, thereby challenging the continuing use of this criterion as a quality marker of surgery that follows nCRT.
3. Interestingly, while the number of invaded lymph nodes remains a prognostic factor after nCRT, the prognostic value of the number of lymph nodes removed disappears after nCRT. This suggests that less extensive lymphadenectomy can be performed after nCRT. Nonetheless, this policy can obviously not be recommended in the absence of solid proof, and, in any case, lymphadenectomy for esophageal cancer is rarely responsible for severe morbidity.
4. Comparable results have been found in rectal cancer, the number of lymph nodes removed as well as the number of lymph nodes invaded is less after nCRT; this is usually thought to attest to a good tumor response to nCRT and is considered a favorable prognostic factor [3,4].

References
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[2] Ann Surg 2008;248:549—56.
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[4] Dis Colon Rectum 2008;51:277—83.

■ Cauchy F, Fuks D, Nomi T, et al. Risk factors and consequences of conversion in laparoscopic major liver resection. Br J Surg 2015;102:785—95. doi:10.1002/bjs.9806

Background

Although recent reports have suggested potential benefits of the laparoscopic approach in patients requiring major hepatectomy, it remains unclear whether conversion to open surgery could offset these advantages. This study aimed to determine the risk factors for and postoperative consequences of conversion in patients undergoing laparoscopic major hepatectomy (LMH).

Methods

Data for all patients undergoing LMH between 2000 and 2013 at two tertiary referral centres were reviewed retrospectively. Risk factors for conversion were determined using multivariable analysis. After propensity score matching, the outcomes of patients who underwent conversion were compared with those of matched patients undergoing laparoscopic hepatectomy who did not have conversion, operated on at the same centres, and also with matched patients operated on at another tertiary centre during the same period by an open laparotomy approach.

Results

Conversion was needed in 30 (13.5%) of the 223 patients undergoing LMH. The most frequent reasons for conversion were bleeding and failure to progress, in 14 (47%) and nine (30%) patients respectively. On multivariable analysis, risk factors for conversion were patient's age above 75 years [hazard ratio (HR) 7.72, 95% CI 1.67 to 35.70; $P = 0.009$], diabetes (HR 4.51, 1.16 to 17.57; $P = 0.030$), body mass index (BMI) above 28 kg/m^2 (HR 6.41, 1.56 to 26.37; $P = 0.010$), tumour diameter greater than 10 cm (HR 8.91, 1.57 to 50.79; $P = 0.014$) and biliary reconstruction (HR 13.99, 1.82 to 238.13; $P = 0.048$). After propensity score matching, the complication rate in patients who had conversion was higher than in patients who did not (75 versus 47.3% respectively; $P = 0.038$), but was not significantly different from the rate in patients treated by planned laparotomy (79 versus 67.9% respectively; $P = 0.438$).

Conclusion

Conversion during LMH should be anticipated in patients with raised BMI, large lesions and biliary reconstruction.