European Journal of Surgical Oncology 45 (2019) 1511–1512

Contents lists available at ScienceDirect

European Journal of Surgical Oncology

journal homepage: www.ejso.com

Does lymphovascular invasion really associate with decreased overall survival for patients with resected cholangiocarcinoma?

Keywords:
Lymphovascular invasion
Cholangiocarcinoma
Prognosis

To the editor,

We read with interest the recent publication by Lurje et al. [1] which presents a retrospective, single-institutional series of 162 patients with cholangiocellular carcinoma (CCA) conducted from 2011 to 2016. They concluded that lymphovascular invasion (LVI) is associated with adverse overall survival (OS) and disease-free survival (DFS), supporting the assessment of LVI may be useful in identifying high-risk CCA patients for adjuvant treatments. Their study is indeed an interesting series on the field, and we congratulate the authors for their clinically relevant contribution, but several issues need further consideration and discussion.

First, Lurje et al. reported that the median OS and DFS of patients who suffered LVI were significantly worse than those not in patients with perihilar cholangiocarcinoma (pCCA) (median OS: 8 vs 41 months, median DFS: 19 vs 65 months, respectively, all < 0.05). However, similar result was found only in the OS (median OS: 4 vs 40 months, $P < 0.05$) but not DFS (median DFS: 13 vs 45 months, $P = 0.244$) for patients with intrahepatic cholangiocarcinoma (iCCA). LVI and lymph node metastasis were both independently associated with OS and DFS. The presence of LVI has been reported correlated with the presence of lymph node metastasis, which correlates with the observed difference in survival. We are curious whether the relevance of LVI and lymph node metastasis has been verified by Lurje et al.

Second, the prognostic value of LVI in patients with CCA is still controversial. In addition to Lurje et al.'s report, Kim et al. reported that LVI has no impact on survival in dCCA [1]. Fisher et al. found that LVI might have an adverse effect on survival in patients with iCCA [1]. We recently published a study found that LVI has no impact on survival in patients with pCCA [2]. Why is there such a difference? We found a common feature in the above three researches is that the sample sizes were small. Only 162 patients (32 with LVI, 130 not) in Lurje et al.'s study, 91 patients (23 with LVI, 168 not) in Kim et al.'s, and 58 patients (23 with LVI, 35 not) in Fisher et al.'s study. However, there were 290 patients (43 with LVI, 247 not) in our study. Therefore, we hypothesize that the controversiality of the prognostic value of LVI on CCA may be attributed to the relative small sample sizes. However, the systematic lymphadenectomy and adjuvant treatments is necessary because lymph node metastasis has been proved one of the most important factors affecting prognosis of CCA.

Third, Lurje et al. found that resection margin status was not associated with impaired outcome in neither the pCCA- nor the iCCA-cohort. An R0 resection has been demonstrated to be a critical factor associated with improved survival after resection of HCCA and is the only factor that can be modified by operative technique [3]. Because the proximal longitudinal invasion of HCCA tumors ranges from 0.6 to 18.8 mm in the submucosal layer, It has been suggested achieving a proximal, tumor-free resection margin of at least >5 mm to maximize survival and an R0 resection. We also found that the survival of patients after R0 resection with a narrow margin ($\leq$5 mm) did not differ from that of patients who received R1 resection [4]. Therefore, we thought the findings from Lurje et al. may be attributed to the use of an R0 resection being defined as the absence of tumor at the resection margin, which itself may be too narrow of a resection margin for an "R0" resection.

Because the relative small sample size offered by Lurje et al., we are curious that if the prognostic role of LVI and resection margin status could be further investigated by expanding their sample size. Besides this, we wonder if the authors could re-evaluate the resection margins using the criteria of at least a 5 mm or greater tumor-free margin to define an R0 resection.

Author contributions

Wen-jie Ma performed the majority of manuscript; **Nan-Sheng Cheng**, and **Fu-yu Li** revised the manuscript critically and gave the final approval of the version to be published.

Foundation item

Sichuan Science and Technology Program (2018JY0019) and Innovation Spark Project of Sichuan University (2019SCUH).

Competing interests

There is no competing interests.

Acknowledgements

DOI of original article: https://doi.org/10.1016/j.ejso.2019.04.019.

https://doi.org/10.1016/j.ejso.2019.05.025

We acknowledge the Sichuan Science and Technology Program (2018JY0019), the Fundamental Research Funds for the Central Universities (2019SCUH), and Wu Jieping Medical Foundation for Clinical Research (320.2710.1825).

References

[1] Lurje G, et al. The prognostic role of lymphovascular invasion and lymph node metastasis in perihilar and intrahepatic cholangiocarcinoma. Eur J Surg Oncol 2019;45(8):1468–78. https://doi.org/10.1016/j.ejso.2019.04.019.
[2] Ma WJ, et al. Extended lymphadenectomy versus regional lymphadenectomy in resectable hilar cholangiocarcinoma. J Gastrointest Surg 2019. https://doi.org/10.1007/s11605-019-04244-7. In Press.
[3] Tang Z, et al. The clinicopathological factors associated with prognosis of patients with resectable perihilar cholangiocarcinoma: a systematic review and meta-analysis. Medicine (Baltim) 2018;97:e11999.
[4] Ma W-J, et al. Effectiveness of additional resection of the invasive cancer-positive proximal bile duct margin in cases of hilar cholangiocarcinoma. Hepatobiliary Surg Nutr 2018;7:251–69.

Wen-Jie Ma, Fu-Yu Li**, Nan-Sheng Cheng*
Department of Biliary Surgery, West China Hospital, Sichuan University, Chengdu, 610041, China

* Corresponding author. Department of Biliary Surgery, West China Hospital of Medicine, Sichuan University, No. 37 Guo Xue Xiang, Chengdu, Sichuan, 610041, PR China.

** Corresponding author.
E-mail addresses: lfy_74@hotmail.com (F.-Y. Li), nanshengcheng2014@hotmail.com (N.-S. Cheng).

11 May 2019
Available online 31 May 2019