ECRONICON OPEN ACCESS

EC GASTROENTEROLOGY AND DIGESTIVE SYSTEM

Editorial

Management of Pancreatic Cysts (PC) – Based on Cumulative Knowledge

Hauge T[1,3]*, Ånonsen KV[1,3] and Buanes T[2,3]

[1]*Department of Gastroenterology, Oslo University Hospital, Oslo, Norway*

[2]*Department of Hepato-Pancreato-Biliary Surgery, Oslo University Hospital, Oslo, Norway*

[3]*Institute of Clinical Medicine, University of Oslo, Oslo, Norway*

***Corresponding Author**: Hauge T, Department of Gastroenterology, Oslo University Hospital and Institute of Clinical Medicine, University of Oslo, Oslo, Norway.

Received: April 19, 2017; **Published:** April 21, 2017

The different risk of malignancy in various cystic pancreatic neoplasms has been well known for more than two decades, and therapeutic management has been improved accordingly. Numerous guidelines have directed the progress, based on the technological development in health care within imaging, endoscopy and surgery. Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) and minimally invasive/laparoscopic techniques are relevant examples.

The carcinogenesis in PC results in pancreatic adenocarcinoma, associated with high mortality, and the early removal of a premalignant cystic lesion in advance of infiltrative tumor growth is an important clinical improvement. On the other hand, numerous unnecessary pancreatic resections have resulted from the limited diagnostic accuracy of PC with malignant potential. However, combined clinical and translational research generates accelerating progress.

The clinical management of a patient with recently diagnosed PC is different in primary health care and a tertiary referral centers with specialized hepatopancreaticobiliary (HPB) surgeons and endoscopists. The American Gastroenterological Association (AGA) published guidelines for PC management [1], also focusing the concern every general practitioner (GP) should face, considering referral of a PC patient: The result might be lifelong follow-up with imaging/EUS-FNA or pancreatic surgery with a potential for severe complications, even if the lesion does not bear any risk of malignancy. On the other hand, numerous clinical studies have focused on the potential diagnostic delay of curative surgery when the cystic lesion is an infiltrating carcinoma or has malignant potential. This issue of the EC Gastroenterology and Digestive System presents a cohort study with 190 patients [2], referred with PC, 15 tumors (8%) were unresectable pancreatic adenocarcinomas. In 65 patients undergoing pancreatic resection, 46 tumors (71%) were carcinomas or had malignant potential. For the remaining 110 patients (60%) the MDT conclusion was conservative follow-up. The treatment algorithm was based on cross-sectional imaging and EUS-FNA, particularly on cyst fluid analysis, focusing CEA concentration, enabling discrimination between benign and premalignant/malignant PC in most cases. Area under the curve (AUC) in the ROC analysis was 0.71. The frequency of unnecessary pancreatic resections was significantly reduced by the introduction of EUS-FNA, compared with an earlier report from the same center, when 61% of resected tumors had no malignancy potential [3]. Present guidelines [1,4] recommend surgical resection of main duct (MD) and mixed type IPMN-lesions whereas surveillance strategies are advised for small branch duct (BD) IPMN without worrisome features (WF), e.g. intramural nodules. A recent report [5] conveys an incremental value of EUS-FNA over cross-sectional imaging, identifying malignant BD-IPMNs with WF. The discriminant value of cyst fluid CEA concentration, presently documented by Ånonsen., *et al.* [2], with the increased sensitivity for identifying intramural nodules with EUS, implies that EUS-FNA should be the surveillance modality of choice for PC [6].

However, progression to malignancy does not take place in every IPMN lesion of any subgroup, variance from 38 - 68% has been reported in MD-IPMNs, 12 - 47% in BD-IPMNs [7]. Accordingly, numerous PCs undergo surgical resection even though the patient is never going to develop invasive pancreatic cancer. Additional follow-up data should be encouraged, and may disclose more knowledge of malignant progression.

The ongoing translational research search for tools enabling safe diagnostic distinction is important. Proteomic mucin profiling in cyst fluid has been shown to be robustly differentiating premalignant from benign PC [8], and numerous translational achievements in the field of pancreatic cancer [9] have resulted in new biomarkers; miRNA-combinations [10], exosomes [11] and others. The combination of three proteins in urine and plasma Ca 19-9 [12] may enable identification of early invasive pancreatic carcinoma. For clinical application of molecular markers, we have to wait for the results from validation studies.

At present, surveillance of numerous patients with PC based on imaging and EUS-FNA is mandatory, and increasing patient volumes generate raising health care costs. Short-protocol MRI has recently been reported to provide information equivalent to more comprehensive and costly protocols [13], illustrating a beneficial clinical evaluation at the current level of comprehension in this field. But the future perspective of accurate and safe diagnostic identification of patients with premalignant PC underline the importance of intensified translational research [14].

Numerous critical questions remain unanswered, first, what should selection criteria be for not referring patients with small, non-symptomatic PC from a GP? Second, the diagnostic uncertainty, remaining after imaging and EUS-FNA is still generating delay of potentially curative treatment or – on the other hand - unnecessary surgery. Finally, surveillance strategy prerequisites are not evidence-based, and lifelong serial imaging for an increasing number of patients – until unfit for surgery – should be carefully considered and evaluated.

Bibliography

1. Vege SS., *et al*. "American gastroenterological association institute guideline on the diagnosis and management of asymptomatic neoplastic pancreatic cysts". *Gastroenterology* 148.4 (2015): 819-822.

2. Ånonsen K., *et al*. "Cyst Fluid CEA Concentration Discriminates Between Benign and Premalignant/Malignant Pancreatic Cystic Lesions. A Prospective Cohort Study". *EC Gastroenterology and Digestive System* 2.3 (2017): 373-383.

3. Ånonsen KV., *et al*. "Outcome of laparoscopic surgery in patients with cystic lesions in the distal pancreas". *Journal of the Pancreas* 16.3 (2015): 266-270.

4. Mukewar S., *et al*. "Fukuoka criteria accurately predict risk for adverse outcomes during follow-up of pancreatic cysts presumed to be intraductal papillary mucinous neoplasms". *Gut* (2016).

5. Ridtitid W., *et al*. "Management of branch-duct intraductal papillary mucinous neoplasms: a large single-center study to assess predictors of malignancy and long-term outcomes". *Gastrointestinal Endoscopy* 84.3 (2016): 436-445.

6. Basar O and Brugge WR. "Which guidelines should be used for branch-duct intraductal papillary mucinous neoplasms?" *Gastrointestinal Endoscopy* 84.3 (2016): 446-449.

7. Basar O and Brugge WR. "Do molecular tests really differentiate malignant IPMNS from benign?" *Endoscopy International Open* 4.12 (2016): E1236-E1237.

8. Jabbar KS., *et al*. "Proteomic mucin profiling for the identification of cystic precursors of pancreatic cancer". *Journal of the National Cancer Institute* 106.2 (2014): djt439.

9. Buanes TA. "Updated therapeutic outcome for patients with periampullary and pancreatic cancer related to recent translational research". *World Journal of Gastroenterology* 22.48 (2016): 10502-10511.

10. Sandhu V., *et al*. "Differential expression of miRNAs in pancreatobiliary type of periampullary adenocarcinoma and its associated stroma". *Molecular Oncology* 10.2 (2016): 303-316.

11. Costa-Silva B., *et al*. "Pancreatic cancer exosomes initiate pre-metastatic niche formation in the liver". *Nature Cell Biology* 17.6 (2015): 816-826.

12. Radon TP., *et al*. "Identification of a Three-Biomarker Panel in Urine for Early Detection of Pancreatic Adenocarcinoma". *Clinical Cancer Research* 21.15 (2015): 3512-3521.

13. Pozzi-Mucelli RM., *et al*. "Pancreatic MRI for the surveillance of cystic neoplasms: comparison of a short with a comprehensive imaging protocol". *European Radiology* 27.1 (2017): 41-50.

14. Del Chiaro M and Verbeke C. "Cystic tumors of the pancreas: Opportunities and risks". *World Journal of Gastrointestinal Pathophysiology* 6.2 (2015): 29-32.

Volume 2 Issue 5 April 2017