Diagnosis, differentiation and prevention in pancreatic diseases

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SECTION V

CLOSING REMARKS

John William Waterhouse - Destiny (1900)

CHAPTER 9 - SUMMARY

SECTION II IMAGING AND ARTIFICIAL INTELLIGENCE

Pancreatic cancer is a deadly disease for which efforts are underway to improve early detection. **Chapter 2** presents a retrospective, single-center matched case-control study evaluating pre-diagnostic CT and MRI scans of patients with pancreatic cancer vs. controls without pancreatic disease. In the blinded retrospective evaluation conducted by two radiologists, a mass was suspected on ~50% of pre-diagnostic CTs, and on 55-70% of MRIs. For controls, this was ~1% on CT and 0-3% on MRI. Secondary findings, including pancreatic duct (PD) dilatation or interruption, focal atrophy, perivascular soft tissue and features of acute pancreatitis were significantly more common in cases. Missed or misinterpreted findings, occurring in the majority of pre-diagnostic scans, were most frequently attributed to underreading, satisfaction of search, and faulty reasoning. These results provide a substrate for developing AI algorithms that could function as a second reader in pancreatic cancer detection, aiming to mitigate human error in image interpretation.

Chapter 3 provides a scoping review of AI applications in gastroenterology. Regarding pancreatic diseases, AI algorithms have been developed for outcome prediction in acute pancreatitis, differentiation between benign and malignant pancreatic conditions (on EUS and CT), multimodal classification of pancreatic cystic neoplasms, and early detection or risk stratification of pancreatic ductal adenocarcinoma (PDAC) using imaging and electronic health records. Deep learning models, particularly convolutional neural networks (CNNs), performed exceptionally well across these applications.

Chapter 4 contains the initial steps in AI development for the pancreas on MRI. A single-center dataset of 53 MRIs from individuals at high-risk of pancreatic cancer, including both those with and without cancer, was split into multiple iterations to train a U-Net CNN pancreas segmentation model. A preliminary model provided a concept segmentation for the annotator to correct after each training iteration, resulting in a 16-fold reduction in segmentation time vs traditional manual segmentation. The final model achieved a Dice-Sørensen coefficient of 83% on the hold-out test set, comparable to current benchmarks.

SECTION III BIOMARKERS

Non-invasive biospecimen collection is complementary to imaging in pancreatic cancer detection; with blood and pancreatic juice as appealing sources. In **Chapter 5**, a previously developed panel of three methylated-DNA-markers in pancreatic juice (PJ-MDMs) was validated in a multi-center prospective cohort, including PDAC cases, normal pancreases and diseased controls. When the PJ-MDM panel was combined with plasma-based CA19.9, the AUROC was significantly higher at

0.95 than the 3-MDM PJ panel or plasma CA 19-9 alone (0.87 and 0.91, respectively). Sensitivity for pancreatic cancer detection was 89% for all cancer stages and 83% for early stage detection (stage I/II) at a specificity of 88%.

Chapter 6 similarly delves into combining multiple approaches for disease detection. Patients undergoing an ERCP have a 10% risk of adverse events; post-ERCP pancreatitis occurs most frequently. A urinary trypsinogen-2 (UT-2) dipstick was combined with a risk-factor based discharge tool to determine who could be safely discharged after ERCP. In a multi-center prospective cohort, the combination of methods performed better than the individual strategies with a sensitivity of 67% and NPV of 95% for all adverse events.

SECTION IV RISK PREDICTION & PREVENTION

By focusing on risk recognition and prophylaxis use by endoscopists for the prevention of post-ERCP pancreatitis, **Chapter 7** reports the results of two nationwide surveys amongst advanced endoscopists. In 2020, universal uptake of rectal NSAIDs was found, followed by pancreatic duct stenting (78%) and intravenous hyperhydration (33%); the use of all strategies had increased in the latter of the two surveys. Ampullectomy, and PD contrast injection or cannulation were seen as risk factors that warranted the combined use of rectal NSAIDs and PD stenting.

Avoiding an ERCP in its totality is another strategy for an absolute reduction in post-ERCP adverse events. The ESGE guideline for choledocholithiasis, the most common ERCP indication, attempts this by stratifying patients into low, intermediate and high likelihood groups. Overall guideline adherence in the multi-center retrospective cohort of **Chapter 8** regarding the use of EUS or MRCP was 60% and highest in the intermediate likelihood-group (84%). In all who underwent additional imaging, 28% ERCPs could be avoided. For future consideration, performing an EUS in the high-likelihood group could prevent futile ERCPs and associated adverse events.