Department of Medicine
Military University Hospital Prague

Detection of Sporadic Pancreatic Cancer (SPC) – Time for Change

P. Frič[1], J. Škrha[2], A. Šedo[3], P. Bušek[3],
M. Laclav[1], P. Škrha[5], B. Seifert[4], M. Zavoral[1]

[1]Department of Medicine, Military University Hospital, [2]3rd Department of Medicine, [3]Institute of Biochemistry and Experimental Oncology, [4]Institute of General Medicine, General University Hospital, 1st Faculty of Medicine, [5]2nd Department of Medicine, 3rd Faculty of Medicine, Charles University, Prague, Czech Republic

Survey

Surface proteases and SPC

Risk groups of early SPC

Steps of early SPC detection

Diagnostic strategy of SPC

Surface proteases in SPC – Our Contribution (1)

Follow-up of the surface proteases, dipeptidyl-peptidase-4 (DPP-4) and fibroblast activation protein alpha (FAPalpha) in the course of pancreatic carcinogenesis

- DPP-4 Function: Splitting of peptides with proline or alanine at the N2-position of the primary structure
- Substrates: some glucoregulative hormones, cytokines, and other biopeptides

Surface proteases in SPC – Our Contribution (2)

- Location:
  - DPP-4 is attached at the membrane surface of various cell types (epithelia, endothelia, fibroblasts, lymphocytes – membrane form) as well as in body fluids (soluble form).
  - FAPalpha is a structural homologue of DPP-4 selectively expressed in different cancers. It may be considered the **„driver of pancreatic carcinogenesis“**.
- Our findings: In SPC **DPP-4 activity is ↑** and expressed similarly to FAPalpha by SPC-cells and activated myofibroblasts. ↑DPP-4 activity occurs particularly in patients with the early symptoms (new-onset diabetes, loss of weght).

Risk Groups of SPC Subjects (aged >50 years) (1)

1. (a) Subjects with the early symptoms: new-onset prediabetes or diabetes (≤2years) and the loss of body weight (>2kg),

   (b) Subjects with new-onset unstable diabetes (within 30 days) requiring insulin therapy and with anorexia as the only clinical symptom.

2. Patients with atypical reaction to or failure of the introductory antidiabetic therapy: no improvement or normalization of the glucose homeostasis, stagnancy or ongoing decrease of the body weight.

Risk Groups of SPC Subjects (aged >50 years) (2)

3. If the patient does not fullfil during the initial 3 months of antidiabetic therapy the criterion of decreased body weight (>2kg): The therapy is supported by addition of a second antidiabetic drug for the next 3 months. In the case of ongoing disturbance of glucoregulation and decrease of body weight to >2kg after this step, the program of an early SPC detection should be also recommended.

Risk Groups of SPC Subjects (aged >50 years) (3)

4. The patients with long-term diabetes and/or obesity with recent failure of antidiabetic treatment (during the last 6 months) and newly manifested weight loss.

The key-players of the 1st round of early SPC detection are the GPs and out-patients diabetologists.

The next steps of early SPC detection in subjects of the risk groups should be started without delay before local and systemic symptoms appear.

Early SPC Detection – Individual Steps (1)

1. The GP or diabetologist informs the gastroenterologist (preferentially at the tertiary medical center) about a subject with suspected early SPC. The subject is registered by the gastroenterologist.
2. The test of the pancreatic polypeptide (PP) secretion after nutritional (stimulation: Ensure Abbvie 237ml or Booster Nestlé 300ml). Controls, DM2 patients: Increased PP secretion after stimulation. Pancreatogenic diabetes (T3cDM with the ↑risk of SPC): no increase of PP secretion after stimulation.
3. If the test is unavailable or negative, the following steps are also recommended.

Early SPC Detection – Individual Steps (2)

3. The first round of the high resolution imaging methods (HRIMs): CT, MRCP or EUS.

4. In case of a positive finding during the first round of HRIMs (eg. a mass, cyst, alterations of the duct system) the patient is followed at the tertiary center up to the confirmation or exclusion of a PC-precursor or PC.

Early SPC Detection – Individual Steps (3)

5. If the first round of HRIMs is negative, the subject is simultaneously followed at the primary center (GP or diabetologist) by the determination of fasting blood glucose and body weight values (at a 3-month interval) and at the tertiary center by repeated HRIMs rounds at fixed intervals: EUS – 6 months, MRCP and CT-12 months („**the hybrid screening**“). During the intervals the biomarkers (oncomarkers, miRNAs) are evaluated.

6. In subjects of the preceding group the endoscopic methods may be supplemented by a short-term endoscopic nasopancreatic drainage (ENPD – for one day) with repeated aspiration of secretin-stimulated pancreatic secretion and its cytology.

Early SPC – Diagnostic Strategy

The remote character of the **risk factors** (long-term DM, obesity) and **early symptoms** (new-onset DM, loss of weight) of SPC cause a **diagnostic delay** that should be restricted or removed. The task may initiate only **the gastroenterologists by a close co-operation with the general practitioners and diabetologists**.

The education of these partners about the risk factors, early symptoms of SPC, ultrasonographic findings, and the significance of the repeated HRIMs-indication is unavoidable in this program.

The common aim: the creation of an active and cooperative team including GPs, diabetologists, gastroenterologists, and other specialists.