

CANCERS OF THE PERITONEUM – PSEUDOMYXOMA
PREFERRED MODEL OF CARE AND CRITERIA FOR REFERENCE CENTRES

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PREFERRED MODEL OF CARE AND CRITERIA FOR REFERENCE CENTRES

A. Type of cancer

Pseudomyxoma is one of the most occurring among the rare peritoneal tumours and by definition always discovered at a stage of peritoneal dissemination.

B. Short description of the cancer

Pseudomyxoma peritonei (PMP) refers to the accumulation of mucin and mucinous epithelial cell on the peritoneal surface. Peritoneal spread occurs most often in association with Low grade Appendiceal Mucinous Neoplasm (LAMN) and Mucinous Adenocarcinoma (MAA) (see the description of these lesions in the addendum). It is a clinically descriptive term and not a pathological diagnosis in itself. Most of the cases are due to the appendiceal tumour (LAMN or MAA). Exceptional cases of pseudomyxoma have been reported in association with mucinous carcinomas at other sites (colorectum, pancreas, urachus, stomach, and gallbladder). Rarely, an appendiceal-type mucinous tumour arises in an ovarian teratoma.

C. Model of care pathway suggested for adult patients with peritoneal pseudomyxoma

Model of care pathway	Preferred model
1. <u>Model 1: Reference Centres exclusively (from diagnosis to follow-up).</u> Once there is a suspicion of peritoneal pseudomyxoma or peritoneal pseudomyxoma has been diagnosed, the patient should be referred to a Reference Centre. A network with other Reference centres or with specific experts working in other centres is encouraged.	X
2. <u>Model 2: Shared care between Reference Centres and peripheral hospitals.</u> Part of the care pathway (e.g. diagnosis, MOC, surgical treatment, ..) is performed in the Reference Centre and for another part of the care pathway (e.g. chemotherapy, radiation therapy, follow-up, ..) the patient is referred (back) to the regional hospital.	

D. Phase(s) of the clinical pathway for which Reference Centres are required

	Phase of the Clinical Pathway	Reference Centre	Peripheral centre
1	MOC	X	
2	Diagnostic confirmation	X	
3	Comprehensive AP diagnosis	X	
4	Therapeutic modalities	X	
5	Follow-up	X	



Multidisciplinary Oncological Consult

Reference Centre. The team of the Reference Centre establishes the indication for surgery (complete cyto-reduction with HIPEC) or other treatment.

Diagnostic confirmation

- Complexity and new approaches
A consensus about Appendiceal Mucinous Tumour and Pseudomyxoma is necessary. Terminology and classification based on WHO 2010 are proposed (see addendum).
- Facilities and equipment required
 - Diagnostic tests may include CT scans, and the evaluation of tumour markers: Carcinoembryonic antigen (CEA), Cancer Antigen (CA-125 and CA-19.9). In most cases, colonoscopy is not a suitable diagnostic tool because cancer originating from the addendum spreads within the abdominal cavity and implants grow on the outside, not the inside of the colon (however, trans-serosal spread inside the colon is occasionally reported). PET scans are used for higher-grade cancers, but are not reliable for low-grade malignancy. New MRI procedures are being developed for disease monitoring, but standard MRIs are not typically used as a diagnostic tool. Diagnosis is confirmed through pathology.
 - Diagnosis of PMP often requires laparotomy or laparoscopy.
 - A pseudomyxoma peritonei centre should have access to a full range of general surgical and general medical back-up services on a 24 hour basis including an intensive therapy unit, specialist respiratory, renal, gastro-enterological and microbiological expertise.
- Professional expertise required both to perform the diagnostic procedure and to interpret the results
A team of experts: abdominal surgeon, medical or digestive oncologist, radiologist, pathologist and nuclear physician is necessary.

Comprehensive AP diagnosis: See addendum

Therapeutic modalities: Reference Centre

- Complexity, new therapeutic strategies: Need for trained team in surgical approach, i.e. cyto-reductive surgery and HIPEC.
- Facilities and equipment required:
 - Need for HIPEC
 - Intensive care-chemotherapy unit-surgical suites
- Expertise required to perform the treatment:
 - Surgeon with established training in cyto-reductive surgery and HIPEC, Anesthesiologist and ICU physicians with experience in intra-operative and peri-operative care of HIPEC patients
- Para-medical expertise required:
 - Stoma nurses
 - ICU nurses and operating room nurses with experience with HIPEC
 - Specialists in psycho-oncology



- o Social workers
- o Paramedic support (physiotherapist, nutritionist,...)
- o Staff for chemotherapy, pharmacy, radiology

Follow-up: Reference Centre

- Complexity:
 - o Need for standard follow-up methods and physician with an expertise in this type of cancer
- Facilities and equipment required:
 - o Standard follow-up modalities : CT-scan, lab, MRI, PET scan
- Medical expertise required:
 - o Experts in GI oncology or medical oncology
- Para-medical expertise required:
 - o Standard follow-up

E. General and specific criteria for Reference Centres

Human Resources and dedicated team

- Surgical team, anesthesiologist, ICU physician, pathologist, GI oncologist, radiologist
- Nutrition team
- Stoma nurses
- Support team
- HIPEC trained OR and ICU nurses, perfusionist

Multidisciplinary management (including, doctors, nurses, dieticians, physiotherapists, psychologists,...): Per guidance of the MOC

Required facilities and equipment

- Surgery
 - o CE approved chemoperfusion apparatus; adequate protocols and organization in place to allow intra-operative administration of chemotherapy
 - o The team should have access to a CE certified perfusion machine. Use of 'custom made' solutions (without formal certification) should probably be discouraged.
 - o The team should implement a formal safety procedure including written guidelines (handbook), training of staff, and communication with local workplace safety representatives regarding safe handling of cytotoxic drugs in the OR and in the postoperative phase. When using open abdomen perfusion, adequate care should be taken to protect the OR environment.



- Radiotherapy
- Chemotherapy
HIPEC perfusion machine, pharmacy accredited for chemotherapy preparation
- Interventional imaging
Both diagnostic and therapeutic interventional radiology
- Collaboration with a reference laboratory for pathology
To facilitate the collaboration between the different laboratories and to improve the delay of answers, the Working Group recommends using Telepathology
- Intensive Care Unit

Patient centred care

- *Waiting and throughout times:* Review of referred patient within two weeks (including review of imagery, pathology and MOC). Operating waiting list under 6 weeks.
- *Continuity of care:* At least one surgeon experienced with peri-operative complications and care of HIPEC patients on call at all time
- *Support services for the patient:* HIPEC care coordinator, structured patient information (website, brochures, etc....)
- *National and international networking with other Reference Centres:* Dedicated referral pattern and protocol for external (national and international) patients.

Minimal volume of patients

- Number of patients admitted/diagnosed, surgically/medically treated:
 - 2 per year.
 - at least 50 HIPEC in the last 5 years for all indications.
- Number of second opinions (annual volume of referrals and second opinions): 5 per year

Quality Assurance

- Compulsory prospective registration of quality indicators (indications treatment, incidents and complications, re-interventions, 30-day mortality, 1-, 3- and 5-year survival, permanent stoma rate)
- Compulsory registration with the Cancer Registry
- Compliance with existing guidelines and documentation of deviations from guidelines: Implementation of KCE guidelines on HIPEC
- Involvement in quality initiatives (e.g. benchmarking)
- Annual activity report ensuring transparency: Compulsory



- All teams should keep a prospective database of all procedures including indications, complications (Dindo Clavien system) and outcome. Ideally, this should be a shared web based database. For Belgian patients, reimbursement should probably be conditional on delivery of a minimal clinical dataset, or on providing data to a central, government organized database.

Research and other scientific activities: Referral centre should be able to demonstrate participation in international research protocols

- Involvement in clinical studies (RCTs, cohort studies, translational studies), participation rate in clinical trials. Expert or Reference Centres should demonstrate involvement in clinical and/or translational research in the field of carcinomatosis or HIPEC.
- Publications in peer-reviewed journals: At least one peer reviewed, PubMed cited publication in the field of carcinomatosis and/or HIPEC
- Compulsory Link with a tumour bank
- Compulsory Development of clinical practice guidelines for diagnosis and care

Educational activities: Teaching and dissemination

Established active participation in scientific and educational efforts in the HIPEC field

ADDENDUM

A consensus about Appendiceal Mucinous Tumour and Pseudomyxoma is necessary. Terminology and classification based on WHO 2010 are proposed

Appendiceal tumours

1. LOW GRADE APPENDICEAL MUCINOUS NEOPLASM (M-8480/1)
 - o low grade cytologic atypia – villous or flat mucinous epithelium proliferation
 - o undulating epithelium (small papillary excrescences)
 - o penetrate into or through appendiceal wall
 - o lesions in which breach of the appendiceal wall cannot be evaluated
 - o included the “old term” of mucinous tumours of uncertain malignant potential (any mucin outside the appendice or extruding on to the serosal surface, pools of acellular mucin in the wall)
 - o the majority of the lesion consist of extracellular mucin
 - o can spread to the peritoneal cavity and correspond to well differentiated mucinous adenocarcinoma (G1) in PP
 - NB: term adenomucinosis should be avoided
 - adenoma is a “benign” (intra-mucosal) lesion: tubular - villous adenoma or sessile serrated adenoma
 - o the muscularis mucosae is clearly intact
 - o do not infiltrate the appendiceal wall
 - o not present on the serosa or in extra appendiceal mucin



- o if there any doubt, use low grade appendiceal mucinous neoplasm
 - Cystadenoma: purely descriptive term – do not imply a specific lesion
 - Mucocele: distended organ (retention cyst) resulting from inflammation or post inflammation; gross description – not a pathological diagnosis.
- 2. HIGH GRADE MUCINOUS OR INVASIVE ADENOCARCINOMA (M-8480/3)
 - o high grade cytologic atypia (G2-G3) – nuclear stratification, vesicular nuclei, prominent nucleoli, mitotic activity
 - o destructive invasion in the wall

NB: term mucinous cystadenocarcinoma should be avoided

Pseudomyxoma peritoneal

- clinically descriptive term
- pathological diagnosis should indicate the histological type and grade of the neoplasm and its origin if possible

1. MUCINOUS LOW GRADE ADENOCARCINOMA:

- o low cellularity (epithelium less than 10% of the surface)
- o epithelium non stratified, focally proliferative, cuboidal, few mitoses
- o well differentiated mucinous adenocarcinoma
 - NB: If mucin is acellular, tissue sampling must be wide
 - Term disseminated peritoneal adenomucinosis should be avoided

2. HIGH GRADE MUCINOUS ADENOCARCINOMA

- o high cellularity
- o poorly or moderately differentiated
- o numerous mitosis
- o cribriform structures , signet ring cells ...

RECOMMENDATIONS

When **pseudomyxoma peritonei**: Appendice must be submitted entirely for microscopic evaluation

- Origin should be known : use IHC (CK 20, CDX2, MUC 2, CK7)
- Extravasations of acellular mucin rarely result in recurrence. however extra appendiceal mucin must be completely examined microscopically to confirm absence of cells