CANCERS OF THE PERITONEUM – PERITONEAL MESOTHELIOMA

PREFERRED MODEL OF CARE AND CRITERIA FOR REFERENCE CENTRES

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- **The coordinators of the working groups and all the authors listed by chapter have worked autonomously under the supervision of the KCE team. The KCE experts are not co-authors of these proposals and did not necessarily validate their content.**
- **Hospitals with which coordinators and authors of these proposals are affiliated are not de facto considered Reference Centres. Similarly, Belgian hospitals that are not represented in these proposals are not de facto considered Peripheral Centres.**
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- **This addendum only exists in English. No French or Dutch translation was done.**
- **Finally, the report to which this addendum refers has been approved by common assent by the Executive Board.**

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A. Type of cancer

Malignant mesothelioma is a highly lethal malignancy of the serosal membranes of the pleura, peritoneum, and pericardium. The peritoneum is the second most frequent site of origin of mesothelioma, following the pleura. For example, Malignant Peritoneal Mesothelioma represents 26% of Rare Peritoneal Tumours in the French "RENAPE" Registry.

B. Short description of the cancer

Malignant Peritoneal Mesothelioma is a rare malignancy. In France the number of new cases of Malignant Mesothelioma (MM) is about 800-1 200 each year. Malignant Peritoneal Mesothelioma (MPeM) corresponds approximately to 10% of all Malignant Mesothelioma. MPeM is confined to the serosal surface of the peritoneal cavity with unequivocal stromal invasion. MPeM may be associated with more prolonged, heavy asbestos exposure than pleural MM. Other potential causes of MPeM include thorotrast[j], erionite[k], therapeutic radiation, familial Mediterranean fever, and other causes of chronic peritonitis. There is greater variability in the survival of patients with MPeM compared to those with pleural MM. Patients with MPeM are significantly younger than those with pleural MM.

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

Model of care pathway	Preferred model
1. Model 1: Reference Centres exclusively (from diagnosis to follow-up). Once there is a suspicion of peritoneal mesothelioma or peritoneal mesothelioma 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. Model 2: Shared care between Reference Centres and peripheral hospitals. 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. chemo therapy, radiation therapy, follow-up, ..) the patient is referred (back) to the regional hospital.	

j Thorotrast is a suspension containing particles of the radioactive compound thorium dioxide, ThO2, that was used as a radiocontrast agent in medical radiography in the 1930s and 1940s.

k Erionite is a natural fibrous mineral usually found in volcanic ash. Some properties of erionite are similar to the properties of asbestos.

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 (AP and/or medical imaging)	**X**	
3	Comprehensive AP diagnosis	**X**	
4	Therapeutic modalities	**X**	
5	Follow-up	**X**	

Multidisciplinary Oncological Consult

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

Diagnostic confirmation

- Complexity and new approaches
  - The first step in diagnosing peritoneal mesothelioma is a physical exam and patient history: work history and potential mesothelioma risk factors.
  - The second step is imaging of the abdomen: CT (or computed axial tomography) scan, or MRI may be performed.
  - The third step is biopsy to confirm the diagnosis. A consensus about terminology and classification is proposed in the addendum
- Facilities and equipment required
  - Abdominal computed tomography
  - Laparoscopic biopsy of the omentum and peritoneum is often needed to confirm the diagnosis of malignant peritoneal mesothelioma.
  - Panel of immunohistochemical staining is necessary for the diagnosis of mesothelioma peritonei (At least two positive mesothelial markers and Two negative stains to exclude other diagnosis)
  - A mesothelioma 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 in abdominal surgery, medical or digestive oncology, radiology, pathology and nuclear medicine is necessary.

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
  - Specialist in psycho-oncology
  - Social workers
  - Paramedic support
  - Staff for chemotherapy, pharmacy, radiology

Follow-up: Reference Centre

- Complexity:
  - Need for standard follow-up methods physician with a expertise in this type of cancer
- Facilities and equipment required:
  - Standard follow up modalities : CT-scan, lab, MRI, PET scan
- Medical expertise required:
  - Experts in GI oncology or medical oncology
- Para-medical expertise required:
  - 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
  - CE approved chemoperfusion apparatus; adequate protocols and organization in place to allow intra-operative administration of chemotherapy
  - The team should have access to a CE certified perfusion machine. Use of 'custom made' solutions (without formal certification) should probably be discouraged.
  - 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: CLASSIFICATION (WHO 2004)

Epithelioid mesothelioma (M-9052/3)

Sarcomatoid mesothelioma (M-9051/3)

Desmoplastic mesothelioma (M-9051/3)

Biphasic mesothelioma (M-9053/3)

NB: Borderline malignant potential: Well-differentiated papillary mesothelioma (M-9052/1)

Benign multicystic mesothelioma

- More common in the peritoneum than in the pleura
- More frequent in women
- Are not attributed to asbestos
- Rare cases of transformation to malignant mesothelioma (probably misdiagnosis)
- Indolent behavior but locally recurrent