

The burden of peritoneal metastases

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Impact

This thesis focused on epidemiological and clinical aspects of peritoneal metastases. Although peritoneal metastases are traditionally considered a less common mode of cancer spread, its impact on a significant number of patients each year appears to be substantial across various types of primary tumors. The results described in this thesis underscore the frequent occurrence of peritoneal metastases in gastric cancer and colorectal cancer (CRC). Additionally, it shed light on less-known origins of peritoneal metastases, being liver cancer, biliary tract cancer, lung cancer or cancer of unknown primary.

While brain, liver, bone and lung metastases have received considerable attention in terms of treatment strategies, peritoneal metastases have historically been less explored. Studies have shown that peritoneal metastases are not as rare as previously believed. In fact, the occurrence of peritoneal metastases may be equal or even surpass the proportion of metastases to the brain, liver, bone, or lung in certain cancer types. Ever since the developments in surgical techniques, a more proactive attitude has been adopted towards peritoneal metastases. These developments entail cytoreductive surgery (surgical procedure in which all visible tumor is removed; CRS) and hyperthermic intraperitoneal chemotherapy (deliver localized, heated chemotherapy in the abdomen; HIPEC), as well as intraperitoneal chemotherapy. Furthermore, modern systemic therapy has shown promising results in patients with peritoneal metastases from a selected group of primary tumors.

Relevance

In concomitance with the renewed interest in peritoneal metastases, more reliable, up-to-date epidemiological information was warranted. Therefore, this thesis provides insight into the occurrence and risk factors of peritoneal metastases from a variety of primary tumors by using nationwide data from the Netherlands Cancer Registry (NCR). Additionally, it presents information on specific treatment strategies, and it reveals the severity of this disease entity. Since this thesis utilizes nationwide data, it enables the evaluation of peritoneal metastases as it is presented in a real-life setting. For instance, this thesis describes that the number of patients with peritoneal metastases from CRC in the Netherlands has increased over the last years. It also depicts on the high number of patients with peritoneal metastases of gastric origin, which was the highest number of peritoneal metastases ever described in literature. Moreover, this thesis reported a very high proportion of peritoneal

metastases in patients with liver cancer, pancreatic cancer and biliary tract cancer.

Altogether, these high numbers of patients diagnosed with peritoneal metastases underscore that peritoneal metastases affect a relevant part of cancer patients. Variations in given treatments were observed among different patient's groups in gastric cancer and CRC, such as between patients with peritoneal metastases that were diagnosed simultaneously with the primary tumor (synchronous) and patients that developed peritoneal metastases later during follow-up after curative intent treatment (metachronous). These distinctions can be helpful in guiding the decision-making process for treatment and follow-up between clinicians and their patients. Furthermore, this thesis exposes the extremely poor prognosis of patients with peritoneal metastases and thereby identifies an important knowledge gap which should encourage future studies to investigate specific treatment options for this patient category.

Substantial effort has been made to improve the management of patients with peritoneal metastases, both globally as well as in the Netherlands. These endeavors comprise a range of trials, including the prevention and early detection of colorectal peritoneal metastases (COLOPEC 1 & 2), the optimization of treatment of colorectal peritoneal metastases by adding perioperative systemic therapy to CRS-HIPEC (CAIRO6), palliative approaches regarding the management of extensive peritoneal metastases in CRC patients (PIPAC I & II and INTERACT I & II), the treatment of peritoneal metastases in gastric cancer with CRS-HIPEC (PERISCOPE-II), as well as the application of CRS-HIPEC for peritoneal metastases in ovarian carcinomas (OVHIPEC 1 & 2). While these trials may not stem directly from this particular thesis, they do underscore this research domain as active, where real-life data hold significant relevance in evaluating treatment strategies and exploring areas with yet limited knowledge.

Target population

In the Netherlands, yearly 3730 patients were diagnosed with peritoneal metastases simultaneously with the primary tumor (years 2019 and 2020). The total amount of patients with synchronous peritoneal metastases is expected to be even higher as small peritoneal metastases are often not diagnosed with current radiological techniques. As such, it is thought that a relevant proportion of patients remains undetected. Moreover, peritoneal metastases also frequently occur at a later moment during follow-up after treatment for their primary tumor.

The findings of this thesis hold relevance for both patients diagnosed with peritoneal metastases and the medical professionals involved in their treatment. The results from this thesis might offer directions for a personalized approach in treating these patients. Besides patients with peritoneal metastases, the results of this thesis are also relevant for patients with colorectal- and gastric cancer without (peritoneal) metastases, as several studies in this thesis provided information on risk factors for the development of peritoneal metastases in nonmetastatic colorectal- and gastric cancer. The risk factors that were identified could improve the clinical decision-making regarding follow-up care in these patients.

Finally, the spread of cancer to the peritoneum is a significant health concern that often is unnoticed or underreported in a broader audience. By raising awareness among policymakers through the findings of this thesis, we can bring attention to this critical issue and advocate for improved healthcare policies, increased funding for research and treatment options, and enhanced support for patients and their families.

Activity

This thesis comprises studies with real-world data (data as presented in a real-life setting) which reflect the actual Dutch population encountered in every day clinical practice. Thereby, the results are informative for a wide range of health care providers and patients worldwide. For example, the number of patients with gastric cancer is a lot higher in Asian countries, thus the epidemiological and clinical information from this thesis on gastric peritoneal metastases is even more relevant in those regions. However, the generalizability of our findings to the population in Asia might be difficult due to the influence of different epidemiological and clinical aspects in those countries as compared to Western countries. The findings of this thesis impose the significant burden of peritoneal metastases as metastatic manifestation on individuals and healthcare systems. Translation of results from these population-based studies into clinical practice ensures that healthcare professionals are provided with up-to-date information to enable the best possible care for patients with peritoneal metastases.