



Peritoneal Surface Oncology in Singapore

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Abstract

Peritoneal surface malignancy is now an established indication for cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. The landscape of treatment in Singapore has evolved through the years, with expanded indications as the experience in the management of this disease improves.

Keywords Cytoreductive surgery · Hyperthermic intraperitoneal chemotherapy · Singapore

Introduction

Peritoneal surface malignancies (PSM) are a group of cancer that are associated with the peritoneum. Rare cancers such as primary peritoneal cancer or malignant mesothelioma can arise from the peritoneum. More frequently, PSM arise from peritoneal metastases where cancer cells spread from different oncologic origins, such as appendiceal, gastrointestinal and gynaecologic malignancies. These cancers were palliatively treated and were often associated with poor prognoses [1]. The implementation of cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) in the 1980s greatly improved the treatment landscape for PSM. This multimodal therapeutic approach involves surgically removing all macroscopic disease following which a heated chemotherapy perfusate is synergistically utilised to eradicate any remaining viable microscopic disease [2]. Treatment of PSM with CRS/HIPEC has been repeatedly shown to improve survival [3–5] and quality of life (QOL) [6, 7], and is accompanied with acceptable morbidity and mortality [3–5, 8, 9].

Peritoneal Surface Malignancies in Singapore

CRS/HIPEC is fast becoming the standard of care for PSM treatment of selected patients across the globe. Similarly,

Singapore has adopted this efficacious therapeutic strategy in our patient care. Presently, there are two tertiary centres that offer CRS/HIPEC to patients with PSM, National Cancer Centre Singapore (NCCS) and National University Cancer Institute Singapore (NCIS). Other institutions, such as Tan Tock Seng Hospital, and private practices have also started to offer this treatment to selected patients on an ad hoc basis.

National Cancer Centre Singapore

Established in 1999, NCCS is the oldest tertiary cancer centre in Singapore. It sees 152,000 patient visits annually and has in its employment, 164 doctors, 377 nursing and allied health professionals and 251 scientists and research staff. Notably, CRS/HIPEC was introduced into Southeast Asia by NCCS. Additionally, it is the single largest cancer institute in the region which performs CRS/HIPEC for various malignancies and is recognised internationally for its success in PSM management. Apart from performing CRS/HIPEC on patients with PSM routinely, the NCCS team has recently launched two phase II clinical trials, establishing novel applications of the technique—prophylactic HIPEC for colorectal cancers at high-risk of developing peritoneal metastases and the use of radical resection and HIPEC for the treatment of retroperitoneal sarcoma.

National University Cancer Institute Singapore

The NCIS is a relatively new tertiary cancer centre in Singapore with a 10-year history. In addition to treatment of PSM using CRS/HIPEC, the NCIS team is currently researching on the use of pressurised intraperitoneal aerosol chemotherapy (PIPAC) as a palliative treatment for patients with advanced cancers with

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peritoneal disease (NCT03172416). PIPAC is a novel treatment strategy for PSM which applies the chemotherapeutic agent as a pressurised aerosol into the abdomen [10, 11].

Healthcare Structure and Insurance Coverage

Singapore's healthcare structure is characterised by a group of savings and insurance programs carefully crafted to ensure individual responsibility and affordable healthcare. MediSave is a savings program that mandates citizens to allocate a percentage of their earnings to a personal account. The savings, conditional to withdrawal limits, can assist in the payment for certain medical costs, such as hospitalisation, radiotherapy and chemotherapy [12]. Exorbitant medical bills can also be covered by the MediShield Life for Singaporeans [13]. Those who continue to struggle financially despite these implementations will be assessed for MediFund assistance [14].

Apart from these initiatives, the Singapore government also provides various subsidies to assist patients. The percentage of subsidies received by each patient is assessed via means testing, which predominantly considers the household income in their assessment of the individual's financial need. This percentage also applies to the type of hospital ward accommodation in public hospitals. Regardless of ward classification, patient care remains priority of the healthcare institutes. Patients, private or not, would be seen by the same doctors and would receive the same medical treatment [15].

Training Programs

Understanding the importance of improving and upgrading medical personnel's expertise, the Ministry of Health launched the Health Manpower Development Programme (HMDP) in 2002 [16]. Under this scheme, many clinicians have pursued training and fellowships in local and overseas institutions. Having trained under renowned peritoneal malignancy units, the oncologists in Singapore extend their knowledge and expertise to others by conducting courses for interested participants in the region such as the Peritoneal Malignancy Course [17] and the Asia-Pacific PIPAC Workshop & Symposium on Peritoneal Cancers [18]. Additionally, surgical residents and medical students are often taught by these specialists, complete with opportunities to participate in the management of PSM patients. Fellowships are also offered to local and international clinicians who are keen to gain more experience in PSM treatment in NCCS and NCIS.

The NCCS Experience

The inaugural CRS/HIPEC procedure in Singapore (and Southeast Asia) was conducted in NCCS 17 years ago.

Since then, NCCS remains the leading tertiary centre in Singapore that performs this multimodal treatment strategy, with the largest published experience in CRS/HIPEC in Singapore and the region [19]. As of 23 November 2018, NCCS has performed a total of 335 CRS/HIPEC procedures. Recognising the importance of site-specific centres to provide quality cancer care for our patients, the NCCS Centre for Peritoneal and Pelvic Disease was established in 2011. This brings together dedicated physicians, paraclinical staff and importantly, basic and clinical research personnel in a coordinated approach to understanding and treating this disease entity in a more comprehensive fashion. A corresponding sharp increase in the number of patients treated with CRS/HIPEC in our institution was seen in the same year (Fig. 1). In 2018 alone, 45 cases have been conducted by the dedicated team.

At NCCS, there is a strong advocate for the multidisciplinary treatment approach of patients. PSM patients seen at the NCCS are discussed at weekly multidisciplinary tumour board meetings (MDTM) to establish suitable treatment strategies, facilitating an all-inclusive management for individual patients [20].

Learning Curve

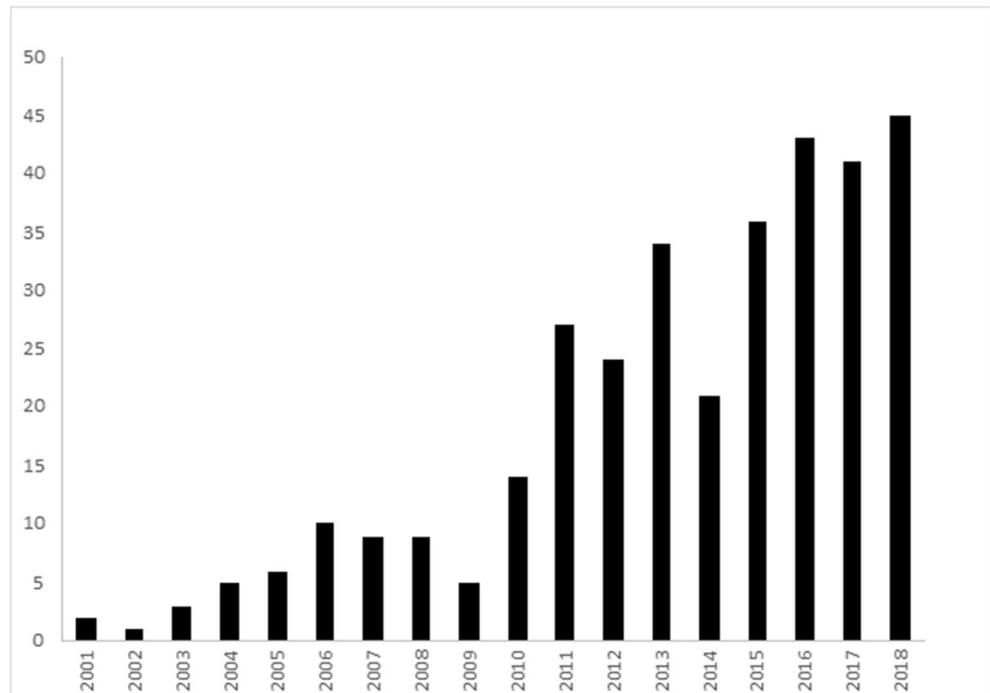
Overcoming the learning curve is a critical feature of achieving improved patient survival and low morbidity in CRS/HIPEC [3–5, 21–23]. Interestingly, a unique biphasic learning curve phenomenon was observed in the NCCS experience [24]. The first 200 CRS/HIPEC cases were subdivided into 4 cohorts of 50 cases each. Fifty CRS/HIPEC cases were noted to be sufficient to achieve technical expertise, where a reduction in the surgical time per peritoneal carcinomatosis index (PCI) score which subsequently remained similar was observed (1.125, 0.49, 0.57, 0.47 h/PCI) [24]. Another 50 cases were conducted before a reduction in rates of severe morbidity (34, 30, 12, 14%) was observed, representative of better selection and perioperative management of patients [24].

Since overcoming its learning curve, NCCS has achieved zero mortality and an acceptable morbidity of 14.7% high-grade complication rate. These results are comparable to that of other studies, where rates of high-grade morbidity and mortality of 12–43% and 0.9–4.1% respectively have been reported [3, 25–27]. Furthermore, 5-year overall (OS) and disease-free survival (DFS) rates in NCCS were 44.8% and 22.1%, which are similar to that of published literature [3, 5].

Applications of CRS/HIPEC

Majority of the CRS/HIPEC cases seen in NCCS originate from colorectal (34%), ovarian (26%) and appendiceal (25%) tumours (Fig. 2). As with all institutions, CRS/HIPEC was initially conducted for the management of peritoneal disease of gastrointestinal and gynaecological origins [28].

Fig. 1 Annual CRS/HIPEC procedures performed in National Cancer Centre Singapore, 2001–2018

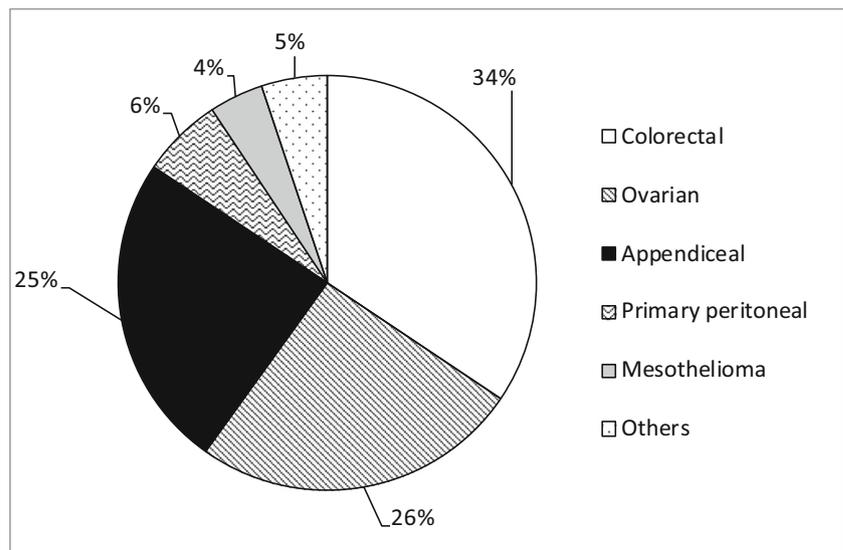


The expertise obtained from an amalgamation of international training programs and the NCCS experience enabled a rapid expansion in CRS/HIPEC applications. To date, the dedicated team in NCCS has performed CRS/HIPEC on unconventional indications, such as peritoneal sarcomatosis, small bowel adenocarcinoma and endometrial adenocarcinoma [29–32]. Additionally, redo-CRS/HIPEC has been applied in selected patients with peritoneal recurrence following an initial CRS/HIPEC procedure [33].

Referral Patterns

As CRS/HIPEC gains awareness in Singapore and the region, an increase in referral numbers for the treatment is also observed. Wang et al. [34] reported increasing trends of referred patients in the NCCS between 2011 to 2015, inclusive of referrals from surgical oncology, medical oncology and even foreign self-referrals. Interestingly, 12.0% of the patients seen were self-referrals from other countries, suggesting that

Fig. 2 Types of primary tumours operated on for CRS/HIPEC in National Cancer Centre Singapore from 2001–2018



Singapore is seen as a cornerstone of CRS/HIPEC in the region. Additionally, the greatest increase in referrals came from the medical oncologists in the institution, a sign of reception to the technique possibly due to positive outcomes from both international and local studies.

Moving Forward

Despite being a small city state, Singapore has earned a reputation for providing quality medical care. By introducing CRS/HIPEC to Southeast Asia, PSM treatment in the region has improved by leaps and bounds. As we continue to strive for improvements, it is necessary to innovate, collaborate and continually improve the expertise of healthcare professionals. Collaborative efforts both local (e.g. Singapore Peritoneal Oncology Study (SPOS) Group) and regional (e.g. Asian Peritoneal Surface Malignancy Group (APSMG)) have since been founded on these grounds.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

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