



Clinical epidemiology of peritoneal metastases in China: The construction of professional peritoneal metastases treatment centers based on the prevalence rate



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ARTICLE INFO

Article history:

Received 30 May 2022

Received in revised form

22 July 2022

Accepted 21 August 2022

Available online 28 August 2022

Keywords:

Epidemiology

Gastric cancer peritoneal metastasis

Colorectal cancer peritoneal metastasis

Ovarian cancer peritoneal metastasis

Pseudomyxoma peritonei

Malignant peritoneal mesothelioma

ABSTRACT

Objective: To understand the tumor burden of peritoneal metastases (PM) in China, and to guide the construction of professional PM treatment centers in China.

Methods: Based on the cancer statistics by the National Cancer Center of China published in 2016, the prevalence of PM in 2020 was calculated according to the population statistics in China and the survival and mortality rates of various PM.

Results: The prevalence rates of PM in China were as follows: gastric cancer PM 371.0/million, absolute number 523,937; colorectal cancer PM 47.1/million, absolute number 66,482; ovarian cancer PM 97.1/million, absolute number 137,083; pseudomyxoma peritonei 25.1/million, absolute number 35,425; malignant peritoneal mesothelioma 2.6/million, absolute number 3737; the above total was 766,664. According to the annual high-quality treatment volume of 365 cases in each professional PM treatment center, China needs to establish 1194 specialized PM treatment centers. At present, there are 1580 tertiary first-class hospitals in China. Therefore, for every 3 first-class tertiary hospitals in China there should be at least 2 PM treatment centers in full operation.

Conclusions: Considering the large number of PM patients in China and the relatively small number of professional PM treatment centers, more resources should be devoted to the promotion and construction of PM treatment centers.

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1. Introduction

Peritoneal metastases (PM) are defined as the primary or secondary occurrence/progression of malignant tumor in peritoneum. The former includes primary peritoneal carcinoma and malignant peritoneal mesothelioma (MPM), while the latter is commonly referred to as PM from gastrointestinal and ovarian origins [1]. In the past, PM was commonly regarded as the terminal stage of cancer metastasis, and active treatment was not advocated. Most patients only received palliative systemic chemotherapy or debulking surgery, resulting in poor prognosis. Since the late 1990s, with the better understanding of PM pathology and improved treatments in the oncology field, PM has been regarded as a

regional disease with lesions mainly confined to the abdominal and pelvic cavity, and a set of revolutionary treatment strategy has been developed, based on cytoreductive surgery (CRS) plus hyperthermic intraperitoneal chemotherapy (HIPEC). The new strategy of comprehensive treatment significantly improves survival of PM patients, and some patients can even achieve clinical cure [2].

However, the diagnosis and treatment of PM covers a variety of professional fields, requiring medical talents in many fields such as surgical oncology, medical oncology, oncology care, tumor pathology, tumor imaging, and laboratory medicine. As a complex surgical procedure involving many disciplines, CRS + HIPEC can only be performed in experienced centers. There are very few specialized PM treatment centers in China, as a result, many PM patients cannot receive professional diagnosis and treatment. Therefore, it is urgent to promote the construction of PM centers and train professional doctors for PM in China.

This study aims to evaluate the disease burden of PM in China through epidemiological investigation of various PM, and then to guide the construction of specialized PM treatment centers.

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2. Materials and methods

2.1. Incidence

Based on the new cancer statistics by the National Cancer Center of China published in 2016 [3], the incidence of common PM was calculated based on the epidemiological data of gastric cancer, colorectal cancer, ovarian cancer, pseudomyxoma peritonei (PMP), MPM and the population base in China.

2.2. Observation period

According to the survival analysis of various PM, when the survival curve reaches a plateau or the survival rate approaches zero, the remaining patients are cured, or majority of patients have died and no longer need clinical treatment. Therefore, the length of time to reach a plateau or the survival rate approaching zero is used as the observation period for PM patients.

2.3. Annual mortality and cure rate

Considering the lack of PM treatment centers in China, most PM patients received palliative chemotherapy and/or simple debulking surgery instead of specialized CRS + HIPEC treatment. Therefore, in this study, when selecting the survival and mortality data of PM patients, we preferred the data of patients who only received chemotherapy and/or surgery, which is more consistent with the status of diagnosis, treatment and prognosis of PM patients in China.

According to the large-scale clinical research data, the annual mortality rates of various PM patients during the observation period were obtained [4–8], which was used to exclude patients who died in the annual cohort, as shown in [Supplementary Table 1](#).

Patients suffering from a certain disease who can achieve a long disease-free survival after treatment are regarded as cured, and the cure rate is the ratio of the number of people cured to the total number of people with the disease in a given time period. In view of the high degree of malignancy and extremely low clinical cure rate of PM except PMP and ovarian cancer PM, the cure rate of PM except PMP and ovarian cancer PM was considered as zero when calculating the prevalence in this study.

2.4. Population data

Based on the latest Chinese population data released by the National Bureau of Statistics of China [9], we obtained the Chinese population base from 2010 to 2020, which were shown in [Supplementary Table 2](#). In view of the different degrees of malignancy and observation periods of each PM, with 2020 as the end point, the number of new cases in each year was calculated based on the incidence of each PM.

2.5. Prevalence rate

The prevalence rate refers to the ratio of the number of cases of a certain disease in a certain population to the total population during the observation period. It represents the absolute number of patients with a certain disease in the population during the observation period. Compared with the incidence rate, it can more realistically reflect the disease burden and guide the further allocation of medical resources. The prevalence calculation method in this study is as follows:

- (1) The number of new PM patients each year is regarded as a cohort. The number of people in each cohort alive by 2020

was calculated based on the annual mortality rate, limited to the observation period of each PM patient;

- (2) The number of surviving patients in each cohort by 2020 was added to the number of new PM patients in 2020, and then the number of cured patients was subtracted to obtain the total number of PM patients in 2020;
- (3) Comparing the total number of PM patients in China in 2020 with the Chinese population in 2020 is the estimated the prevalence of PM patients in China in 2020.

2.6. Calculation of specialized PM treatment centers

As we know, CRS + HIPEC is the principal treatment of PM patients, so we use the approximate annual operation volume of a full-capacity specialized PM treatment center to calculate the number of specialized PM treatment centers currently needed in China. Due to the different malignancy and disease stage of various PM, only a part of the strictly selected patients could be treated with CRS + HIPEC, and the rest of the patients receive systemic chemotherapy or palliative treatment. Based on the statistics of our center from 2018 to 2021 and other long-standing PM centers [10–12] ([Supplementary Table 3](#)), we made the following calculation:

- (1) Total number of PM patients requiring CRS + HIPEC in China = percentage of PM patients suitable for CRS + HIPEC × total number of PM patients.
- (2) Total number of PM centers should be established in China = Total number of PM patients requiring CRS + HIPEC in China ÷ annual operation volume of a full-capacity specialized PM treatment center.

3. Results

3.1. Peritoneal metastases prevalence calculation

3.1.1. Gastric cancer (GC) PM prevalence rate in China

According to statistics from the National Cancer Center of China, the number of new GC patients in China in 2015 was about 679,100 [3]. Epidemiological studies of GC showed that the probability of GC PM was 43% [13]. Therefore, the annual number of new GC PM patients was about 292,013. According to the 2021 China Statistical Yearbook, the total population of China in 2015 was 1383.26 million [9], so the incidence of GC PM in China in 2015 was about 211.1/million.

Published overall survival analyses of GC PM have shown that the survival rate of patients with GC PM is close to zero at 3 years after treatment, and most patients have died within 1 year thereafter [4,14]. Therefore, 3 years (the length of time required to receive clinical treatment) were used as the observation period for patients with GC PM in this study.

Taking 211.1/million as the incidence of GC PM in China, the

Table 1
Calculation of the GC PM prevalence.

Year	2017	2018	2019	2020
New cases of GC PM patients	295,540	296,682	297,668	298,099
1 year (–52%)	141,859	142,407	142,881	143,088
2 year (–82%)	53,197	53,403	53,580	53,658
3 year (–90%)	29,554	29,668	29,767	29,810
Number of cured	0	0	0	0
The total number of patients				523,937
Prevalence				371.0/million

prevalence of GC PM in China was calculated as shown in Table 1. The results showed that the number of patients with GC PM was 523,937, and the prevalence rate was 371.0/million in 2020.

3.1.2. Colorectal cancer (CRC) PM prevalence rate in China

According to statistics from the National Cancer Center of China, the number of new CRC patients in China in 2015 was approximately 376,300 [3]. Based on several CRC epidemiological studies, the incidence rates of simultaneous and metachronous CRC PM were 5.5% and 3.1%, respectively [15–20]. Therefore, the annual number of new CRC PM patients can be calculated to about 31,721. According to the 2021 China Statistical Yearbook, the total population of China in 2015 was 1383.26 million [9]. Therefore, the prevalence of CRC PM in China in 2015 was about 22.9/million.

Published CRC PM survival analysis studies have shown that the survival rate of CRC PM patients after treatment is almost zero after 4 years of follow-up, and most patients have died within 1 year thereafter [5]. Therefore, this study took 4 years (the length of time required to receive clinical treatment) as observation period for CRC PM patients.

Taking 22.9/million as the incidence of CRC PM in China, the prevalence of CRC PM in China was calculated as shown in Table 2. The results showed that the number of patients with CRC PM was 66,482, and the prevalence rate was 47.1/million in 2020.

3.1.3. Ovarian cancer (OC) PM prevalence rate in China

According to statistics from the National Cancer Center of China, the number of newly diagnosed OC patients in China in 2015 was about 52,100 [3]. Epidemiological studies of OC showed that 75% of OC patients are in advanced stages when they are first diagnosed, and 75% of these patients with advanced OC have PM [21]. Therefore, it can be calculated that the annual number of new OC PM patients is about 29,306. According to the 2021 China Statistical Yearbook, the total population of China in 2015 was 1383.26 million [9], so the incidence of OC PM in China in 2015 was about 21.2/million.

Published overall survival curves for OC PM showed that the analysis curves reached a plateau after 7 years of follow-up, and almost all recurrences have occurred by that time [6,22,23]. Therefore, this study used 7 years (the length of time required to receive clinical treatment) as the observation period for patients with OC PM. OC PM patients had not experienced relapse at year 7 were regarded cured, and the published 7-year progression free survival (PFS) was therefore considered the clinical cure rate. Reported 7-year-PFS of OC PM is 6.3%–22.1% [22,23]. For the purpose of calculating the prevalence rate of OC PM, this study selected 6.3% as the conservative cure rate of OC PM.

Taking 21.2/million as the incidence of OC PM in China, the prevalence of OC PM was calculated as shown in Table 3. The results showed that the number of patients with OC PM was 137,083, and the prevalence rate was 97.1/million in 2020.

Table 2
Calculation of the CRC PM prevalence.

Year	2016	2017	2018	2019	2020
New cases of GC PM patients	31,884	32,063	32,184	32,291	32,338
1 year (–39%)	19,449	19,558	19,632	19,698	19,726
2 year (–75%)	7971	8016	8046	8073	8085
3 year (–87%)	4145	4168	4184	4198	4204
4 year (–93%)	2232	2244	2253	2260	2264
Number of cured	0	0	0	0	0
The total number of patients					66,482
Prevalence					47.1/million

3.1.4. Pseudomyxoma peritonei (PMP) prevalence rate in China

A national epidemiological survey of PMP in Norway and England, which recorded the incidence of PMP during the 10-year period from 2009 to 2018, showed that the average incidence in both countries was 3.2 per million during the 10-year period [24]. At present, there are few epidemiological investigations of PMP in China. Therefore, this study regards 3.2 per million as the estimate of PMP incidence in China.

Published studies have shown that the survival curve of PMP patients treated with CRS + HIPEC reached a plateau after 10 years of follow-up, and the vast majority of registered relapsed patients have occurred by that time [7,25,26]. Therefore, 10 years (The length of time required to receive clinical treatment) were used as the observation period for PMP patients in this study. In addition, Patrick-Brown T et al. reported that the conservative 10-year cure rate of PMP patients was about 47% [24].

Taking 3.2/million as the incidence of PMP in China, the prevalence of PMP in China was calculated as shown in Table 4. The results showed that the number of people with PMP was 35,425, and the prevalence rate was 25.1/million in 2020.

3.1.5. Malignant peritoneal mesothelioma (MPM) prevalence in China

At present, the epidemiological data of MPM in the world are quite different, and there is almost no relevant data in China before 2000. Zhao et al. [27] conducted an epidemiological survey of MPM in China from 2000 to 2013, and it showed that the age-standardized incidence of MPM in 2013 was 1.71/million.

van Kooten JP et al. [8] retrospectively analyzed 629 MPM patients registered at the National Cancer Center in the Netherlands from 1993 to 2018, and it showed that the survival rate of MPM patients who received chemotherapy and/or surgery was close to zero after 3 years of follow-up. Therefore, this study used 3 years (The length of time required to receive clinical treatment) as the observation period for MPM patients.

Taking 1.71/million as the incidence of MPM in China, the prevalence of MPM in China was calculated as shown in Table 5. The results showed that the number of people with MPM was 3,737, and the prevalence rate was 2.6/million in 2020.

3.2. Estimation of specialized PM treatment centers

According to above calculations, the prevalence rates of various PM in China are as follows: GC PM 371.0/million, absolute number 523,937; CRC PM 47.1/million, absolute number 66,482; OC PM 97.1/million, the absolute number 137,083; PMP 25.1/million, the absolute number 35,425; MPM 2.6/million, the absolute numbers 3737; and the above total was 766,664.

Based on the statistics of our center and other PM treatment centers [10–12], the overall percentage of PM patients who can be treated with CRS + HIPEC was about 57%, and the disease-specific percentages were PMP 81%, MPM 70%, OC PM 67%, GC PM 53%, and CRC PM 52%, respectively (Table 6). The median operation time of CRS + HIPEC reported by the Chinese PM treatment center was 595 min [28], and the annual high-quality treatment volume of each specialized PM center was calculated as 365 patients at the maximum. Therefore, China needs to establish 1194 specialized PM treatment centers (Table 6), which can meet the medical requirements of PM patients.

4. Discussion

This study estimated the disease burden of PM in China, based on the above calculation of the prevalence rates of various PM. The results showed that the population of PM patients in China is

Table 3
Calculation of the OC PM prevalence.

Year	2013	2014	2015	2016	2017	2018	2019	2020
New cases of OC PM patients	28,986	29,181	29,325	29,517	29,682	29,795	29,894	29,937
1 Year (-6%)	27,247	27,430	27,566	27,746	27,901	28,007	28,100	28,141
2 Year (-22%)	22,609	22,761	22,874	23,023	23,152	23,240	23,317	23,351
3 Year (-43%)	16,522	16,633	16,715	16,825	16,919	16,983	17,040	17,064
4 Year (-55%)	13,044	13,131	13,196	13,283	13,357	13,408	13,452	13,472
5 Year (-63%)	10,725	10,797	10,850	10,921	10,982	11,024	11,061	11,077
6 Year (-70%)	8725	8754	8798	8855	8905	8939	8968	8981
7 Year (-73%)	7826	7879	7918	7970	8014	8045	8071	8083
Number of cured	1826	1838	1847	1860	1870	1877	1883	1886
The total number of patients								137,083
Prevalence								97.1/million

Table 4
Calculation of the PMP prevalence in China.

Year	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
New cases of PMP patients	4291	4317	4350	4375	4405	4426	4455	4480	4497	4512	4519
1 Year (-8%)	3948	3972	4002	4025	4053	4072	4099	4122	4137	4151	4157
2 Year (-14%)	3690	3713	3741	3763	3788	3806	3831	3853	3867	3880	3886
3 year (-20%)	3433	3454	3480	3500	3524	3541	3564	3584	3598	3610	3615
4 year (-22%)	3347	3367	3393	3413	3436	3452	3475	3494	3508	3520	3525
5 Year (-26%)	3175	3195	3219	3238	3260	3275	3297	3315	3328	3339	3344
6 Year (-29%)	3047	3065	3089	3106	3128	3142	3163	3181	3193	3204	3209
7 Year (-31%)	2961	2979	3002	3019	3040	3054	3074	3091	3103	3113	3118
8 Year (-33%)	2875	2892	2915	2931	2951	2965	2985	3002	3013	3023	3028
9 Year (-35%)	2789	2806	2828	2844	2863	2877	2896	2912	2923	2933	2937
10 Year (-37%)	2703	2720	2741	2756	2775	2788	2807	2822	2833	2843	2847
Number of cured	2017	2029	2045	2056	2070	2080	2094	2106	2114	2121	2124
The total number of patients											35,425
Prevalence											25.1/million

Table 5
Calculation of the MPM prevalence in China.

Year	2017	2018	2019	2020
New cases of MPM patients	2394	2403	2411	2414
1 Year (-75%)	599	601	603	604
2 Year (-83%)	407	409	410	410
3 Year (-87%)	311	312	313	314
Number of cured	0	0	0	0
The total number of patients				3737
Prevalence				2.6/million

exceptionally large, of which GC PM accounts for the largest proportion, followed by secondary OC PM and CRC PM.

PM is a heavy disease burden in China. More than 70% of patients with gastrointestinal cancer are in clinical stage III or above when they are first diagnosed, and have a high risk of developing PM. PM is also an inevitable outcome in the development of OC. However, just like other forms of tumor metastasis, PM remains a long-standing and formidable problem in cancer treatment. Recently, the international oncology community has recognized that PM is a regional cancer metastasis. For some carefully selected

cases, active comprehensive treatment can not only effectively control the progression of the disease, but also may achieve clinical cure. As the core treatment technology system for the treatment of various PM, CRS + HIPEC has been actively promoted globally, and has become the standard treatment strategy for selected PM patients. At present, more and more clinical studies have shown that CRS + HIPEC can significantly prolong the overall survival and improve the quality of life for selected GC PM [29], CRC PM [30], OC PM [31], PMP [7], MPM [32] and other PM patients.

Currently, although some centers in China have adopted the new concept and comprehensive treatment of PM, the overall situation is far from adequate compared with the international advances. It is mainly manifested in two aspects: (1) The correct understanding of PM is scarce, lagging far behind the international level, this also leads to the inadequate treatment technology of PM and poor treatment effect of patients; (2) The systemic and standardization of the diagnosis and treatment process is insufficient, for example, patient selection, surgical methods and clinical evidence are still disputes, resulting in poor reliability of clinical research and difficult to be generally recognized by international peers. The promotion of PM-related knowledge and technology systems and the construction of specialized PM treatment centers

Table 6
The number of PM patients and specialized PM treatment centers needed in China in 2020.

PM	Number cases	Percentage of patients for CRS + HIPEC	Number of patients for CRS + HIPEC	PM treatment centers needed
GC PM	523,937	53%	277,687	761
CRC PM	66,482	52%	34,571	95
OC PM	137,083	67%	91,846	252
PMP	35,425	81%	28,694	79
MPM	3737	70%	2616	7
Sum	766,664	57%	435,414	1194

can effectively change this situation, so that more PM patients can benefit from treatment.

In 2015, the “Expert Consensus on Cytoreductive Surgery and Intraperitoneal Hyperthermia Chemotherapy for the Treatment of Peritoneal Surface Tumors” was first published in China, which detailed the diagnostic strategy of PM patients and the standard clinical pathway of CRS + HIPEC [2]. Since then, many consensus documents have been published in China, including the diagnosis and treatment of PMP and MPM, the application of intraperitoneal hyperthermic perfusion chemotherapy, the diagnosis and treatment of CRC PM, and the diagnosis and treatment of gynecological tumor-derived peritoneal metastasis [33–37]. With the promotion of CRS + HIPEC treatment strategy in China, some tertiary hospitals began to establish specialized PM centers. However, the number is far from meeting the needs of Chinese PM patients. According to the 2021 China Health Statistics Yearbook [38], there are currently 2996 tertiary hospitals, including about 1580 tertiary first-class hospitals. As CRS + HIPEC treatments are technically difficult, such surgeries can only be performed in tertiary-level hospitals in China. As a result, for every 3 first-class tertiary hospitals in China there should be at least 2 PM treatment centers in full operation. Therefore, establishing large number of specialized PM treatment centers is the key to solving this “old, big and hard” problem of PM in China.

The disadvantage of this study is the survival and mortality data cited are not Chinese clinical research data when calculating the prevalence of various PM, so we can only make a preliminary estimate of the disease burden of various PM in China.

5. Conclusion

PM burden is a heavy problem in China, and the specialized PM treatment centers currently available in China cannot meet the increasing needs in China. To cope with this urgent problem, we still have a long way to go in promoting specialized PM treatment centers with CRS + HIPEC as the core treatment technology.

Funding

General Program of the National Natural Science Foundation of China (No. 82073376).

Declaration of competing interest

The authors report no conflict of interest.

CRediT authorship contribution statement

Rui Yang: Study concepts, Study design, Data acquisition, Quality control of data and algorithms, Formal analysis, and interpretation, Statistical analysis, Manuscript preparation. **Yan-dong Su:** Data analysis and interpretation, Manuscript preparation, Manuscript editing. **Ru Ma:** Data analysis and interpretation, Manuscript preparation, Manuscript editing. **Yan Li:** Study concepts, Study design, Manuscript review, Manuscript preparation.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejso.2022.08.023>.

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