Original Article

A Simplified Peritoneal Sarcomatosis Score for patients treated with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy

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Background: With the introduction of cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC), long-term survival can be achieved in selected patients with peritoneal surface malignancy. In patients with peritoneal sarcomatosis (PS), CRS/HIPEC remains a topic of debate. It is important that patient selection and outcome be improved with a tool that better predicts survival in such patients. To this end, we devised a Simplified Peritoneal Sarcomatosis Score (SPSS) adopted from the previously-described peritoneal surface disease severity score (PSDSS).

Methods: Patients were included if they were diagnosed with PS and underwent CRS/HIPEC with intended complete cytoreduction between 2007 and 2017. To calculate SPSS, we recorded symptoms (none =0, present =1), peritoneal carcinomatosis index (PCI) (≤10=0, >10=1), and grade of tumor (low =0, high =1). Thus, SPSS ranged from 0 to 3. SPSS-L (low) included patients with score of 0–1; SPSS-H (high) included patients with scores 2–3. Survival curves were generated using Kaplan-Meier method according to the two tiers of SPSS.

Results: Twenty-five patients were included. Mean age was 51.84±10.75 years. Median follow-up was 18 months. Compared to SPSS-H, SPSS-L patients had a longer median overall survival (OS) (36±16 *vs.* 16±6 months, respectively; P=0.021) and a longer median disease-free survival (DFS) (36±16 *vs.* 16±6 months, respectively; P<0.001). On multivariate analysis, advanced disease (SPSS-H) was an independent predictor of OS (P=0.020) and DFS (P=0.018).

Conclusions: SPSS can be used as a tool for patient selection for surgery, prognosis prediction, and stratification into clinical trials of PS patients.

Keywords: Peritoneal sarcomatosis (PS); cytoreductive surgery (CRS); hyperthermic intraperitoneal chemotherapy (HIPEC); sarcomatosis score; survival

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Introduction

Soft tissue sarcomas are considered uncommon among adult malignancies since they comprise ~1% of the incidence of adult solid tumors (1). About one third of these sarcomas are reported to originate in the abdominal cavity including the retroperitoneum (2). These solid tumors are notorious for their exceptional tendency to recur locally or distantly even after complete surgical resection (3,4).

Perhaps the most common form of recurrence of intraabdominal sarcomas is peritoneal sarcomatosis (PS)

where the tumors disseminate in diffuse seedings and nodules throughout the peritoneal surface (5). Moreover, PS might be present at the time of diagnosis as a primary manifestation of the disease (6).

In either case of PS, primary or recurrent, the prognosis is generally grim with an estimated median OS between 6–14 months (7,8). In addition to their aggressive behavior, sarcomas and PS carry another challenge to the treating physician, which is their poor response to current oncological therapies such as chemotherapy and regional radiation (6).

With the advancement of surgical techniques which address peritoneal surface malignancies (9) and optimization of treatment protocols of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) for peritoneal carcinomatosis (PC), a potential arises for the treatment of PS as well. A consensus was reported in 2008 that CRS/HIPEC in the treatment of PS is an advisable option by the majority of the expert panel if no extraperitoneal disease is evident (10).

Following the maturation milestones of CRS/HIPEC for PC, we learn that patient selection for such an advanced and aggressive intervention is key to achieve the desired improvement in survival, and to define a line where benefit outweighs harm for this complex group of patients based on the extent of disease, performance status, age, and many other factors that can influence the outcome (11-14).

However, studying PS on a similar scale is somewhat difficult given PS has a significantly lower incidence compared to PC. In addition, identifying specific predictors of the surgical outcome is a standing challenge since the majority of the reports stem from small retrospective institutional experiences.

Herein, we aim to analyze our own experience with CRS/HIPEC for PS and use our data to generate a simplified scoring system to stratify the patients based on their disease-related characteristics. This scoring system is an attempt to predict the surgical short- and long-term outcomes, which may, in some instances, guide further treatment based on the specifics of each patient.

Methods

All patients who underwent CRS/HIPEC for PS by a single surgeon (GIS) between 2007–2017 were included. Patient's data were prospectively maintained in the electronic medical record and retrospectively reviewed under an approved Institutional Review Board (IRB) protocol and used for research purposes with patients' informed consent (NCT02082886). CRS/HIPEC was considered if the patient has PS limited to the peritoneal cavity without evidence of extraperitoneal dissemination, and whose disease was deemed operable on preoperative imaging. A Simplified Peritoneal Sarcomatosis Score (SPSS) was calculated based on 3 characteristics as follows:

(I) Symptoms (absent =0, present =1): pain, obstruction, weight loss, and ascites;

(II) Grade of tumor (low =0, high =1): tumor grade was evaluated according to the three-tiered National Federation of Centers in the Fight against Cancer (FNCLCC) classification. For the purpose of the present study, grade 1 and 2 sarcomas are described as low grade, and grade 3 sarcomas are described as high grade;

(III) Peritoneal carcinomatosis index (PCI) (PCI ≤10=0, PCI >10=1): was used to score the extent of peritoneal involvement at the time of surgery.

Thus, SPSS ranged between 0–3. Patients were considered to have low SPSS (SPSS-L) if they scored 0–1, and high SPSS (SPSS-H) if they scored 2–3. Cox-regression analysis was applied to confirm the SPSS as an independent predictor of survival. Kaplan-Meier method was used to draw overall survival (OS) and disease-free survival (DFS) plots from the time of CRS/HIPEC. P values <0.05 were considered statistically significant throughout the analysis.

Results

Twenty-five patients were included. Mean age was 51.84±10.75 years, and 13 patients were males (52%). Eleven patients (44%) presented with primary PS, whereas 14 (56%) presented as a recurrence of a previously resected intraabdominal sarcoma. Thirteen patients (52%) were asymptomatic at presentation. The dominant histology was liposarcoma (well differentiated, myxoid, pleomorphic, or dedifferentiated) with 15 patients (60%), 4 patients (16%) were diagnosed with leiomyosarcoma, and 6 (24%) had other histologies. *Table 1* summarizes the characteristics of the patients included in the study.

Mean PCI for the group was 11.44±8.67. Twenty-one patients (84%) achieved complete cytoreduction (CC0), and 4 patients (16%) had CC1-3.

The patients were scored per the description of the SPSS; 4, 9, 3, and 9 patients scored 0, 1, 2, and 3, respectively. Thus, 13 patients were considered SPSS-L and 12 were SPSS-H.

SPSS-L patients were comparable to those with SPSS-H

Table 1 Summary of the demographic and perioperative characteristics of the patients with peritoneal sarcomatosis who received cytoreductive surgery and hyperthermic intraperitoneal chemotherapy

Characteristic	N
Age (mean, median)	51.84±10.75, 52
Sex	
Male	13 (52%)
Female	12 (48%)
PCI	11.44±8.67 (median 9)
Complete cytoreduction (CC0)	21 (84%)
Previous treatment (any surgery)	14 (56%)
Progression after CRS/HIPEC	15 (60%)
Follow up (median, months)	18.0
Symptoms	
Asymptomatic	13 (52%)
Symptomatic	12 (48%)
Pathology	
Liposarcoma	15 (60%)
Leiomyosarcoma	4 (16%)
Desmoplastic round cell tumor	2 (8%)
Angiosarcoma	1 (4%)
PEComa	1 (4%)
Malignant fibrous histiocytoma	1 (4%)
Carcinosarcoma	1 (4%)
Grade	
Low	6 (24%)
High	19 (76%)

CRS, cytoreductive surgery; HIPEC, hyperthermic intraperitoneal chemotherapy.

in terms of age, sex, previous treatment (which implies a presentation of primary *vs.* recurrent disease), and the pathology of their PS. However, it was noted that SPSS-L group had a significantly higher rate of CC0 (100% *vs.* 66.7%; P=0.027). *Table 2* shows the comparison between the two groups.

Kaplan-Meier survival analysis demonstrated that SPSS-L had a significantly longer median OS compared to SPSS-H (36±16 *vs.* 16±6 months; P=0.021), as well as a longer median DFS (30±14 *vs.* 4±1 months, P<0.001).

Table 2 Comparison between SPSS-L and SPSS-H patients

Characteristic	SPSS-L (N=13) (%)	SPSS-H (N=12) (%)	P
Age	51.61±12.05	52.08±9.69	0.574
Sex			0.418
Male	6 (46.2)	5 (41.7)	
Female	7 (53.8)	7 (58.3)	
CC0	13 [100]	8 (66.7)	0.027*
Previous treatment (any surgery)	6 (46.2)	8 (66.7)	0.265
Pathology			0.950
Liposarcoma	8 (61.5)	7 (58.3)	
Leiomyosarcoma	2 (15.4)	2 (16.7)	
Other	3 (23.1)	3 (25.0)	

*, statistically significant. CC0, complete cytoreduction; SPSS-L, low SPSS; SPSS-H, high SPSS.

Figure 1 demonstrates the Kaplan-Meier plots for OS and DFS in both SPSS-L and SPSS-H groups.

To delineate the role of SPSS by adjustment for possible confounders, a cox multivariate regression was applied to OS and DFS. In both models, SPSS was shown to be an independent predictor of OS and DFS. Interestingly, CC0 was a predictor of DFS as expected but was not a predictor of OS. *Table 3* summarizes the results of the cox regression for OS and DFS.

Discussion

Intraperitoneal sarcomas comprise 18% of all sarcomas (15) and often manifest as PS primarily or after resection as a recurrence. This scenario represents a very challenging theme to the treating oncologist given its obstinance to non-invasive approaches such as radiation and chemotherapy. Currently, the only approach that provided an improved survival for PS is CRS/HIPEC when CC0 is achieved (6,16,17). In the past decade, multiple institutional experiences were reported (16-22) about the impact of CRS/HIPEC on survival in PS and agreed on OS of 24–28 months and DFS of 14–18 months. We have reported that a complete cytoreduction and low PCI score appear to be important factors in the outcome of patient with PS (6). Baratti *et al.* raised the attention that a variability in the outcomes might be attributed to inherent characteristics at presentation, mostly related to histology, and that patient

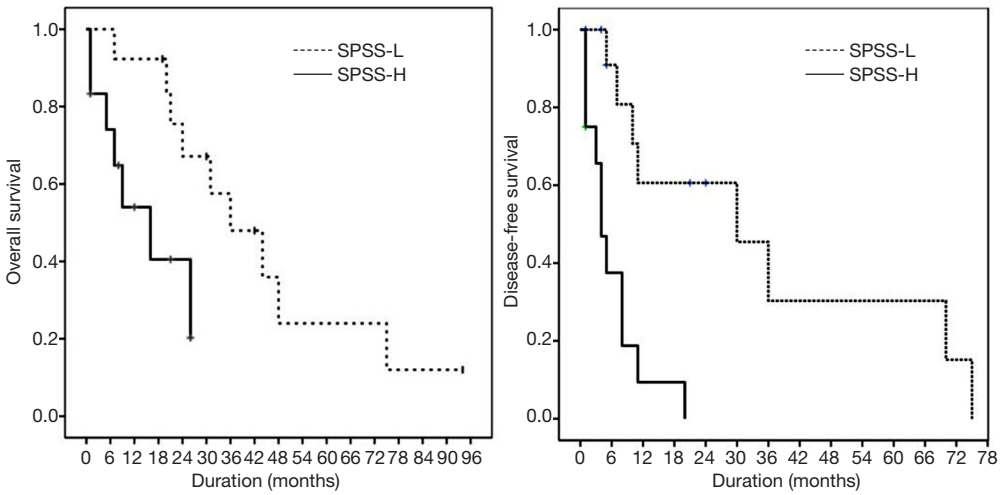

Figure 1 Kaplan-Meier for overall survival and disease-free survival in low SPSS (SPSS-L) and high SPSS (SPSS-H) groups. Median overall survival 36±16 *vs.* 16±6 months (P=0.021). Median disease-free survival 30±14 *vs.* 4±1 months (P<0.001).

Table 3 Cox multivariate regression analysis for predictors of overall survival and disease-free survival in peritoneal sarcomatosis

Variable	Overall survival		Disease-free survival	
	Hazard ratio (CI)	P	Hazard ratio (CI)	P
Age	0.960 (0.890–1.035)	0.285	0.991 (0.913–1.077)	0.839
Sex		0.114		0.814
Male	Referent		Referent	
Female	2.587 (0.796–8.413)		0.860 (0.200–3.696)	
SPSS		0.020*		0.018*
SPSS-L	Referent		Referent	
SPSS-H	5.435 (1.313–22.509)		6.756 (1.392–32.799)	
CC0	0.762 (0.078–7.446)	0.815	13.922 (1.710–113.340)	0.014*
Previous resection	0.397 (0.086–1.926)	0.236	1.416 (0.299–6.702)	0.661
Pathology				
Liposarcoma	Referent		Referent	
Leiomyosarcoma	1.445 (0.297–7.022)	0.648	5.017 (0.660–38.113)	0.119
Other	2.927 (0.538–15.931)	0.214	7.342 (1.31–41.148)	0.023*

*, statistically significant. CC0, complete cytoreduction; SPSS-L, low SPSS; SPSS-H, high SPSS.

selection might be advised in this patient population (16). Hence, we aimed to establish a scoring system that would predict the long-term outcomes of CRS/HIPEC in PS based on disease-specific characteristics. In 2009, Pelz and colleagues proved the utility of the peritoneal surface disease severity score (PSDSS) in the prognosis of patients with PC from colorectal origin (23) and was subsequently adopted by the American Society of Peritoneal Surface Malignancies (ASPSM) for stratification of patients with PC from colorectal and ovarian origins (24,25). PSDSS was built on three characteristic pillars; presence of symptoms, radiologic PCI, and histology of the disease, with a significant discrimination in OS between the proposed stages.

In this work, we implement a similar scoring system into PS in a simplified form using our PS population which had comparable OS and DFS to those reported in the literature (26 and 12 months, respectively). Indeed, stratifying patients based on the SPSS into SPSS-L and SPSS-H created an apparent contrast in OS and DFS between the two groups. Since PCI is integrally higher in the SPSS-H group, incomplete cytoreduction would represent a possible confounder that would influence survival. After adjustment for all factors, the multivariate regression analysis proved SPSS to be an independent predictor of OS and DFS. Interestingly, CC0 was only a predictor of DFS but not OS. Given the high tendency of this disease to recur locally, regionally, or remotely, this finding suggest that the improved OS might not be attributed to the complete cytoreduction itself, but rather to the indolent and lenient progression of this disease in this group of patients.

The shortcomings of this study revolve around the small sample size, which cannot be overcome for the rarity of PS cases amenable to CRS and HIPEC. We attempted to limit the bias caused by the small number by confining the stratification to two groups (SPSS-L *vs.* SPSS-H), and we used a simplified scoring model to avoid the exaggerated complexity that might render this system impractical. Moreover, our PCI score is reported based on the intraoperative evaluation, unlike the PSDSS which was based on preoperative imaging. In our model, this shortcoming can be overcome by considering preoperative radiologic PCI if, based on the institutional volume and experience, correlated adequately with the operative index.

Conclusions

SPSS is a simplified scoring system for PS derived from the PSDSS. It demonstrates an evident survival discrimination between SPSS-L and SPSS-H patients, suggesting that it may be used as tool for patient selection for surgery, prognosis prediction, and stratification into clinical trials in PS.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: This study is conducted under an approved IRB protocol and patients' informed consent and the protocol's name is Edward-Elmhurst Healthcare IRB#1 and its registration number is 0003456.

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