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Impact of Insurance Status on Oncologic and Perioperative Outcomes after Cytoreductive Surgery with Hyperthermic Intraperitoneal Chemotherapy

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Abstract

Background: A growing body of research has shown that underinsured patients are at increased risk of worse health outcomes compared to insured patients. Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) is performed largely at highly specialized cancer centers and may pose challenges for the underinsured. This study investigates surgical outcomes following CRS-HIPEC for insured and underinsured patients with peritoneal carcinomatosis.

Methods: We performed a retrospective cohort study of 125 patients undergoing CRS-HIPEC between 2013–2019. Patients were categorized into two groups. The insured group was comprised of patients with private insurance at the time of CRS-HIPEC or who obtained it during the follow-up period, while the underinsured group consisted of patients with Medicare, Medicaid, or self-pay. Perioperative and oncologic outcomes were compared between the two groups.

Results: A total of 102 (82.3%) patients were insured and 22 (17.7%) patients were underinsured. There were no significant differences in age, medical morbidities, primary tumor characteristics, peritoneal carcinomatosis index, or completion of cytoreduction score between the two groups. The median overall survival (OS) for insured patients was 64.8 months and was 52.9 months for underinsured patients ($p=0.01$). Additionally, insured patients had a significantly longer follow-up time. Underinsurance status was also associated with increased hospital and intensive care unit length of stay, and higher rate of Clavien-Dindo classification III-IV complications.

Conclusion: In this retrospective study conducted at a large urban specialized cancer center, private insurance status was associated with increased overall survival and longer follow-up period. Furthermore, underinsurance status was associated with increased perioperative morbidity.

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Disclosures: None

Introduction

Peritoneal carcinomatosis (PC) is a late presentation of gastrointestinal, gynecological, or primary peritoneal malignancies that results in the dissemination of cancer throughout the peritoneum¹. The foundation of treatment of PC consists of cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS-HIPEC)². As there is increasing data to support the use of CRS-HIPEC, the operation has become more popular and available². However, these surgeries are typically available in specialized cancer centers with surgical personnel and support staff with expertise in managing these patients. Disparities in the timing of cancer diagnosis, treatment, and survival exist across different ethnic and socioeconomic groups within the United States³. Several studies have demonstrated that privately insured patients with cancer, including gastrointestinal malignancies, have improved survival compared to patients with no insurance or government insurance^{3–8}. Insurance status influences a patient's ability to obtain prompt high-quality surgical care and may also act as a surrogate for other sociodemographic factors that may influence oncologic and perioperative outcomes. In a large retrospective study utilizing the National Cancer Database, multivariate analyses demonstrated that private insurance was associated with increased overall survival at one year. Additionally, underinsured patients had significantly more medical comorbidities⁴. A similar study of over 3 million patients showed that underinsured patients were more likely to present with advanced-stage cancer compared to their privately insured counterparts⁹.

Due to the highly specialized nature of CRS-HIPEC and the medical complexity of patients with PC, it is imperative to investigate the disparities in outcomes in patients with PC. These investigations would deepen the ongoing conversation regarding socioeconomic health disparities in the United States and allow us to mitigate factors related to such disparities. The impact of insurance status on outcomes in patients with PC is largely unknown. A recent study found no difference in overall survival between insured and underinsured patients who underwent CRS-HIPEC, but only 31 patients were included and only 6 patients were alive at the end of the study period¹⁰. The aim of this study is to examine the impact of insurance status on oncologic and perioperative outcomes in patients undergoing CRS-HIPEC for peritoneal carcinomatosis. To date, this is the largest study comparing outcomes in patients undergoing CRS-HIPEC based on insurance status.

Materials and Methods

Data Sources and Definitions

The present study was approved by Institutional Review Board of Vanderbilt University (IRB # 200638) and utilizes a retrospectively created database of all patients with PC who underwent CRS-HIPEC with curative intent from 2013–2019 at Vanderbilt University Medical Center (Nashville, TN). We utilized this prospectively maintained database to collect patient demographic information, such as gender, age, race, BMI, state residence, American Society of Anesthesiologists (ASA) class, and Eastern Cooperative Oncology Group (ECOG) performance status as well as treatment information. Oncologic data, such as tumor origin and grade, lymphovascular invasion, and perineural invasion were based on final pathology report from the surgical specimen at the time of CRS-HIPEC. Additionally,

the peritoneal surface disease severity score (PSDSS), peritoneal carcinomatosis index (PCI), and complete cytoreduction score (CCR) were obtained from the surgeon's CRS-HIPEC operative note.

Patients were categorized into two groups based on their insurance status. Patients with solely commercial private insurance at the time of CRS-HIPEC were included within in the insured group (PI). Patients who maintained their previously obtained private insurance after receiving government benefits or who supplemented their Medicare benefits with private insurance were included in the insured group. The underinsured group (UI) consisted of patients with documentation of no insurance, or proof of Medicaid with or without Medicare at the time of CRS-HIPEC. Since about half of Medicare beneficiaries qualify for Medicaid, which serves low-income patients, this cohort is comprised of patients with socioeconomic characteristics that prevent them from purchasing supplemental or sole private insurance¹¹. In addition, patients who had evidence of loss of insurance during the follow-up period or had no documentation of insurance status were excluded from this study. To further understand each group's geographic access to care, distance traveled was derived by using the estimated driving distance from the centroid of the zip code listed in the patient's primary residence to the centroid of the zip code of this institution. The primary outcome was overall survival (OS) defined as time (months) from CRS-HIPEC to death. The secondary outcomes included follow-up time, defined as time (months) from CRS-HIPEC to last known follow-up with a surgeon or oncologist, or death, as well as intensive care unit length of stay (ICU LOS), hospital length of stay, and rate of Clavien-Dindo classification III/IV complication.

Statistical Analysis

Demographic and oncologic factors were compared based on insurance status as previously defined. Categorical variables are recorded as percentages compared using Chi-squared test, and continuous variables are recorded as means and compared using Kruskal-Wallis test. OS was calculated using the Kaplan-Meier method and groups were compared using the log-rank test. Multivariate regression analysis of factors associated with overall survival, including insurance status, ASA class, tumor grade, PCI, and CCR score was performed using Cox regression analysis. All analyses were performed using *IBM Statistical Product and Service Solutions for Mac, Version 27* (IBM Corp., Armonk, N.Y., USA) software package and statistical significance was set at $p=0.05$.

Results

We identified 125 patients in the database who underwent CRS-HIPEC from 2013–2019, all of whom had documented insurance status. Overall, 51% were male and median age was 50.5 years. The median overall survival was 50.2 months and median follow-up time was 36.9 months for the entire patient population. Of the patients included in our analysis, 82.3% (102) were in the privately insured group (PI) and 17.7% (22) were in the underinsured group (UI). The median age of patients in the PI and UI cohorts were 52.6 years and 59.7 years, respectively. When comparing demographic and oncologic characteristics between the two groups, no significant differences were seen in gender, age, race, BMI, ASA class,

ECOG performance status, state residence, PSDSS, Charlson comorbidity index, primary tumor location, or tumor grade. However, patients in the UI group were more likely to have primary tumors with lymphovascular invasion than their counterparts in the PI group (52.2% vs 19.6%, $p = 0.003$). Data on patient demographics and pathologic features are outlined in Table 1.

When compared to PI patients, patients in the UI group had increased estimated blood loss (760mL vs 550mL; $p=0.04$) and had slightly increased PCI score, but did not reach statistical significance (19.5 vs 14.8, $p=0.07$). Patients in the UI group had a significantly higher rate of postoperative admission to the intensive care unit (26.1% vs 13%; $p=0.03$), longer intensive care unit length of stay (7.5 days vs 4.25 days; $p=0.04$) and hospital length of stay (16.0 days vs 12.0 days; $p=0.002$). These patients were more likely to be discharged to a skilled nursing facility or inpatient rehab when compared to PI patients (26.1% vs 2.9%; $p < 0.001$) and had an increased rate of Clavien-Dindo classification III or IV complications within 30 postoperative days (56.5% vs 19.6%; $p = 0.002$). Median follow-up duration after index CRS-HIPEC was significantly shortened in the UI group [25.1 months interquartile range (IQR) 16.5 – 33.7 months] compared to the PI group (51.6 months, IQR 40.2 – 63.0 months)($p < 0.001$). Patients in both groups had similar rates of neoadjuvant and adjuvant chemotherapy, number of cycles received, and rate of chemotherapy regimen completion. UI patients had significantly shortened overall survival (48.9 months, IQR 44.5 – 53.3 months) and disease-free survival (12.2 months, IQR 8.7 – 15.7 months) compared to patients in the PI group (OS 64.8 months, IQR 48.5 – 80.1 months ; $p=0.007$) (DFS 24.9 months, IQR 21.2 – 28.6 months; $p=0.02$). Perioperative and follow-up data for patients in each group are summarized in Table 2.

Additionally, the 5-year OS was significantly lower for UI patients than PI patients (52.4% vs 67.2%; $p=0.015$) as displayed in Figure 1. In a Cox multivariate analysis controlling for PCI, CCR >0 , high tumor grade, and ASA class 3, being underinsured was independently associated with worsened OS in patients with peritoneal carcinomatous undergoing CRS-HIPEC [HR 1.42, 95% CI 0.17–0.82; $p=0.03$], which is summarized in Table 3.

Discussion

To date, this is the largest examination of the impact of insurance status on outcomes for patients undergoing CRS-HIPEC. The disparities identified are almost exclusively related to perioperative and oncologic outcomes, rather than disease severity at presentation. This is in contrast to previous studies demonstrating that uninsured patients and patients with low socioeconomic status have increased medical comorbidities and present with advanced disease^{3-5,7,9,12,13}. In our single-institution cohort, there were no significant differences in age, BMI, ASA class, ECOG performance status, Charlson comorbidity index, or prevalence of synchronous disease at presentation. UI patients did have a slightly higher PSDSS score, which is comprised of PCI, tumor grade, and patient symptoms, which suggest more symptomatic disease or delayed presentation. Pathologic tumor assessment showed similar tumor grades between the two groups, but UI patients were more likely to have lymphovascular invasion, suggesting a more aggressive tumor biology. In this study where all patients underwent surgery for peritoneal carcinomatosis, which is a late-stage

form of cancer, such baseline disparities may not be apparent. It is likely that patients who are referred to specialized centers that perform CRS-HIPECs have similar medical comorbidities that do not pose prohibitive operative risk regardless of insurance status.

In the United States, it is estimated that 14.7% of the adult population is uninsured and 20.4% have public insurance, yielding approximately 73 million people who self-pay for medical expenses or receive insurance coverage through a state or federal government-subsidized policy¹⁴. Several studies have demonstrated that uninsured patients have inadequate access to medical care across several medical specialties and thus have disparate outcomes when compared to insured patients^{6,15–19}. Such disparities have been demonstrated in chronic diseases as well as cancer, including breast, colorectal, head, neck, and gynecologic malignancies^{6,13,20–23}. Specifically, among uninsured cancer patients, significant delays in access to care and completion of recommended therapy have detrimental effects on prognosis and cancer-related survival. While health insurance coverage is an important factor to health access in this country, coverage does not necessarily translate to access. Healthcare providers are less likely to accept public insurance compared to private insurance, particularly in rural areas and can pose increasing challenges for those seeking specialty care^{24,25}. While Medicaid provides health care coverage for many low-income families, sequelae of low socioeconomic status including lack of transportation, food insecurity, and competing priorities pose further barriers. It is important to note that significantly disparate oncologic outcomes were observed between the two groups despite no estimated difference in distance travelled, suggesting that geographic access to care is not necessarily a limited factor for underinsured patients. Strikingly, while patients in the underinsured group had significantly shorter follow-up time, they underwent similar number of rounds of adjuvant chemotherapy and completed their course at a similar rate. In this context, these findings suggest that competing priorities that are associated with specific socioeconomic factors are also associated with lack of insurance or government subsidized insurance regardless of geographic location.

Additionally, Medicare beneficiaries, who are older and have chronic medical conditions, typically have incomes less than twice the federal poverty level and almost 25% of beneficiaries live below the poverty line²⁶. Previous studies have demonstrated different outcomes based on primary payer status across a variety of clinical settings including cancer and surgery, with patients on Medicaid and/or Medicare performing worse than privately insured patients^{5,13,20,21}. For these reasons, the population of focus for this study was patients who relied on self-pay, Medicaid, or Medicare for their healthcare expenses, which we classified as underinsured.

There are several limitations in this study. While this is the largest study examining the impact of insurance status on outcomes after CRS-HIPEC, this is a retrospective analysis from a single institution in Tennessee. Thus, there may be several unidentified factors that are unique to patients in Tennessee, particularly regarding income, housing costs, social support, and transportation. We lack data regarding socioeconomic status, which may be the underlying common denominator associated with underinsurance status and worse outcomes and shortened follow-up time. However, given that Medicaid beneficiaries are typically low-income and more than 20% of Medicare beneficiaries are low-income, our methods

have likely identified patients with low-income as part of the UI group. Additionally, since CRS-HIPECs are performed at specialized centers, there is likely a referral bias from providers in the community. Underinsured patients are known to have more difficult access to specialized care and have more medical comorbidities. Thus, they may never be referred to a center familiar with CRS-HIPEC by their community provider, which may explain the fairly homogenous PI and UI groups seen in this cohort.

Specific targeted interventions taken by our institution and others can help broaden access to the specialized care that patients with peritoneal carcinomatosis require. Educational outreach initiatives aimed at informing non-surgical and surgical providers, particularly in rural or community settings, may expand a referral base prevent patients from being denied a potential CRS-HIPEC before entering our institution. Furthermore, forming and acquiring satellite clinics and medical centers that are aligned with a centralized specialized or academic center, sometimes referred to as a “hub-and-spoke” model, facilitates the consolidation of resources and streamlines care that increases access to multidisciplinary and specialized treatment.

Underinsurance status, as defined as the use of self-pay, Medicaid, or Medicare, is associated with worse overall survival in patients with peritoneal carcinomatosis undergoing CRS-HIPEC, in a multivariate analysis. Additionally, underinsurance status was associated with worse perioperative outcomes. As the landscape of health insurance continues to evolve in the United States, disparate outcomes should continue to be identified with the goal of improving outcomes for vulnerable patient populations.

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Synopsis

Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy is performed at specialized cancer centers, which pose challenges for underinsured patients. This retrospective study demonstrates that underinsured patients have worse overall survival, increased postoperative morbidity, and shorter follow-up times compared to privately insured patients.

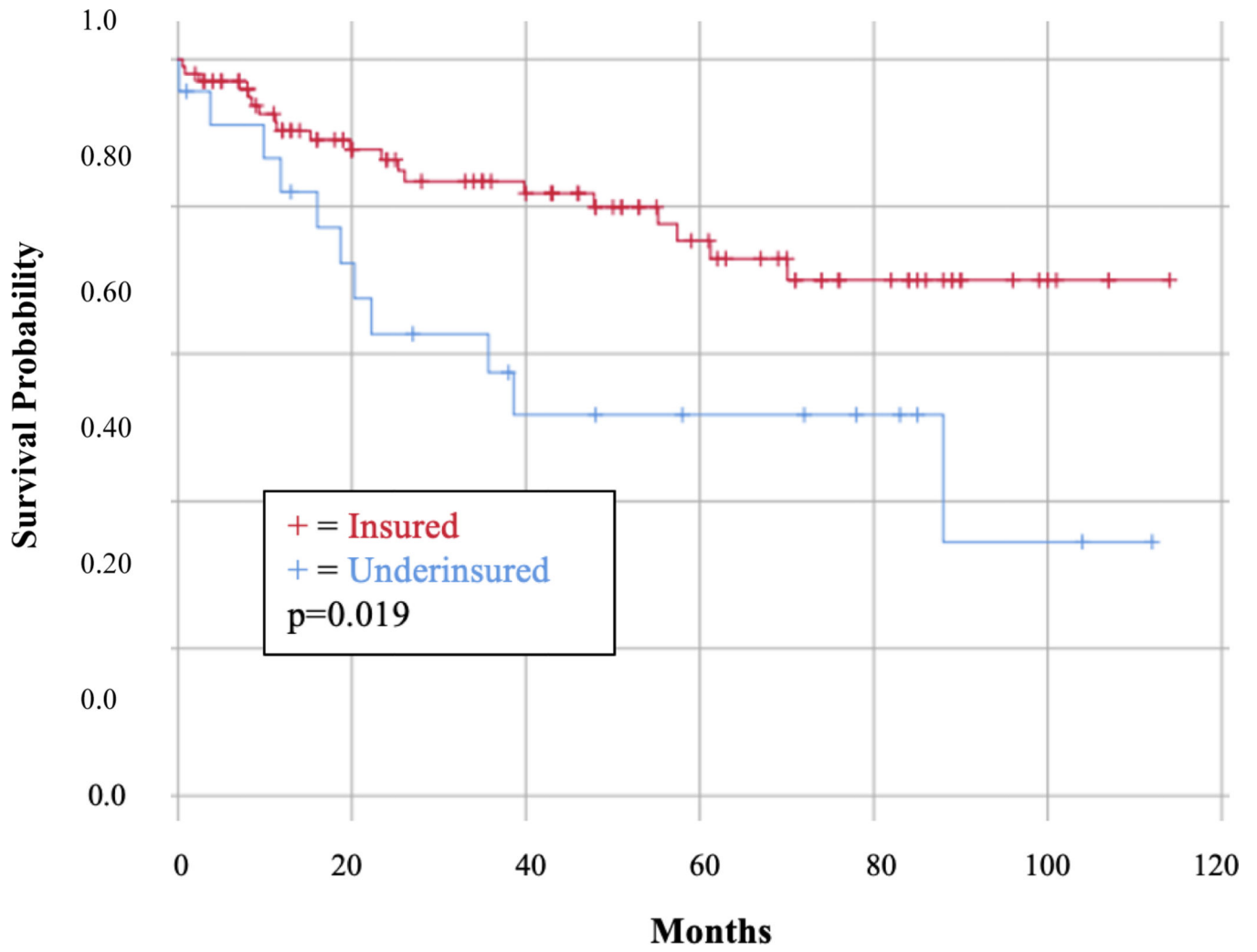


Figure 1:
Overall Survival by Insurance Status

Table 1:

Demographics and Oncologic Characteristics among Insured and Underinsured Patients

Variables	Insured % (n)	Underinsured % (n)	p Value
Total	82.3% (102)	17.7% (22)	
Gender			
Male	51% (52)	50.0% (11)	0.91
Female	49% (50)	50.0% (11)	
Age (median)	52.6 years	57.7 years	0.29
Race			
White	86.2% (88)	90.9% (20)	
Black	12.7% (13)	4.3% (1)	
Other	1% (1)	4.3% (1)	
BMI (mean \pm std)	28.9 \pm 3.2	29.2 \pm 5.3	0.93
In-State Residence	67.6% (69)	69.1% (15)	0.83
Miles Travelled (mean \pm std)	127.4 \pm 95.5	112.6 \pm 89.1	0.5
ASA Class			
1	1.0% (1)	0% (0)	
2	15.7% (16)	22.7% (5)	
3	80.4% (82)	68.2% (15)	
4	2.9% (3)	9.1% (2)	
ECOG Performance Status			
0	29.4% (30)	36.4% (8)	
1	32.4% (33)	22.7% (5)	
2	2% (2)	0% (0)	
3	0% (0)	4.5% (1)	
Unknown	36.2% (37)	36.4% (8)	
Peritoneal Surface Disease Severity Score (mean \pm std)	7.0 \pm 2.1	7.8 \pm 4.2	0.10
Charlson Comorbidity Index (mean \pm std)	7.3 \pm 1.4	8.6 \pm 2.0	0.12
Synchronous Disease	79.2% (80)	81.8% (18)	0.80
Primary Colorectal Tumor	25.5% (26)	40.9% (9)	0.15
Primary Appendiceal Tumor	58.8% (60)	54.5% (12)	0.82
Primary Peritoneal Mesothelioma	7.8% (8)	0% (0)	0.19
Primary Ovarian Tumor	3.8% (4)	4.5% (1)	0.61
Primary Other Tumor	4.9% (5)	0% (0)	0.66
Tumor Grade			
High-grade	27.7% (24)	27.3% (6)	
Intermediate Grade	19.1% (16)	27.3% (6)	
Low Grade	53.2% (46)	45.4% (10)	
Lymphovascular Invasion	19.6% (20)	50% (12)	0.001

Variables	Insured % (n)	Underinsured % (n)	<i>p</i> Value
Perineural Invasion	10.9% (11)	22.7% (5)	0.04

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Table 2:

Perioperative Characteristics Among Insured and Underinsured patients

Variables	Insured % (n)	Underinsured % (n)	p Value
Total	82.2% (102)	17.8% (22)	
Peritoneal Carcinomatosis Index (mean \pm std)	14.8 \pm 9.3	18.9 \pm 11.2	0.09
Completion of Cytoreduction Score			0.44
0	87% (89)	77.3% (17)	
1	13% (13)	22.7% (5)	
Operative Time (mean \pm std)	588.5 \pm 134.2 minutes	639.5 \pm 16.1 minutes	0.14
Estimated Blood Loss (mean \pm std)	550 \pm 125 mL	718 \pm 161 mL	0.04
Intensive Care Unit Admission	9.8% (10)	27.3% (6)	0.02
ICU Length of Stay (mean \pm std)	4.25 \pm 6.7 days	7.7 \pm 3.57days	0.03
Hospital Length of Stay (mean \pm std)	12.0 \pm 5.9 days	16.3 \pm 7.2 days	0.002
Discharge to home	97.1% (99)	72.7% (16)	<0.001
Clavien-dindo III/IV Complication	19.6% (20)	59.1% (13)	0.001
Neoadjuvant Chemotherapy	52.9% (54)	50% (11)	0.88
Number of Cycles (mean \pm std)	9.5 \pm 2.4	9.6 \pm 2.5	0.9
Adjuvant Chemotherapy	19.6% (20)	27.3% (6)	0.37
Number of Cycles (mean \pm std)	6.8 \pm 0.7	7.1 \pm 0.4	0.9
Completion of Chemotherapy Regimen	90.5% (67)	63.6% (14)	0.45
Follow-up time (median)	51.6 months	28.1 months	<0.001
Overall Survival (median)	64.8 months	52.9 months	0.01
Disease-free Survival (median)	24.9 months	13.2 months	0.03

Table 3:

Cox Multivariate regression analysis of factors associated with overall survival

Variables	HR	95% CI	p Value
Underinsured	1.49	0.20 – 0.85	0.02
Peritoneal Carcinomatosis Index	0.04	0.97 – 1.09	0.64
Completion of Cytoreduction Score > 0	0.14	0.19 – 3.82	0.85
High Tumor Grade	1.1	0.19 – 0.70	0.002
ASA Class 3	0.23	0.22 – 2.85	0.72

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