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Commentary on the Volume-Outcome Relationship in CRS/HIPEC for Peritoneal Carcinomatosis

Stephanie N. Gregory[1], Praveen D. Chatani[1], Henry A. Pitt[1,2*], H. Richard Alexander[1,2]

[1]Department of Surgery, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, USA

[2]Division of Surgical Oncology, Rutgers Cancer Institute of New Jersey, New Brunswick, NJ, USA

[*]Correspondence should be addressed to Henry A. Pitt, Henry.Pitt@rwjbh.org

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Abstract

Background: Peritoneal carcinomatosis historically has a poor prognosis; however, Cytoreductive Surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) have shown improved outcomes. While a volume-outcome relationship is established in oncologic surgeries, its applicability to CRS/HIPEC remains unexplored. This study examines the impact of hospital volume on CRS/HIPEC outcomes.

Methods: Using the national Vizient Clinical Database, this retrospective analysis evaluated 5,165 HIPEC cases from 149 hospitals between January 2020 and December 2022. Hospitals were stratified into tertiles based on procedural volume. Chi-squared analysis and one-way ANOVA assessed the associations between hospital volume and patient demographics, morbidity, mortality, ICU utilization, length of stay, readmission rates, and costs.

Results: No significant differences were found in morbidity (low- 9.4% vs. medium- 7.1% vs. high- 9.0%, $p = 0.71$) or mortality rates across hospital volume tertiles (0.9% vs. 0.6% vs. 0.7%, $p = 0.93$). Postoperative ICU use was higher in low-volume hospitals, yet this factor did not affect the overall length of stay or costs. Hospitals with Magnet nursing status had lower observed mortality (0.5% vs 1.7%, $p = 0.048$), but Magnet status did not significantly affect post-operative complications. CMI was similar between low-, medium-, and high-volume hospitals. While Magnet status and CMI were influential, hospital volume alone was not indicative of patient outcomes. Costs remained consistent across all volumes, indicating a trend toward cost-effective care.

Conclusion: The anticipated volume-outcome relationship for CRS/HIPEC is not supported by this study's findings. Outcomes were more closely related to institutional quality and case complexity rather than procedural volume. These results suggest a reconsideration of the current emphasis on regionalization, advocating for the expansion of high-quality CRS/HIPEC care beyond high-volume centers, potentially increasing accessibility for patients.

Keywords: CRS, Cytoreductive surgery, HIPEC, Hospital volume, Magnet, Operative volume, Peritoneal carcinomatosis, Vizient, Volume-outcome

Introduction

The utilization of Cytoreductive Surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) in the management of peritoneal carcinomatosis represents a significant advancement in the treatment of traditionally challenging malignancies. Historically, peritoneal carcinomatosis was seen as an indicator of terminal disease, with treatments largely focused on palliation and modest life extension [1]. However, evolving surgical techniques and the strategic use of heated intraperitoneal chemotherapy have shifted the treatment paradigm towards more aggressive, curative-intent approaches in selected patients. This evolution has been maintained by a growing body of evidence suggesting that, for certain histologies, such as appendiceal [2], ovarian [3,4], and primary peritoneal neoplasms [5,6] CRS-HIPEC

can offer both extended survival and an improved quality of life.

In oncologic surgery, the concept of a volume-outcome relationship, wherein higher procedure volumes at a facility are associated with better patient outcomes, is well-established for several complex resections including pancreaticoduodenectomies, esophagectomies, colorectal resections, and pulmonary lobectomies [7-9]. Additionally, a recent metanalysis focusing on hospital volume for patients undergoing gastrectomy for gastric cancer reported a 35% lower post-gastrectomy morality rate at hospitals with higher surgical case volume [10]. This study's volume-outcome analysis revealed a plateau in post-gastrectomy mortality rate once a minimum of 100 gastrectomy cases per year were performed at a hospital [10]. Similar to aforementioned study, another study found a reduction in post-esophagectomy mortality by 53% for operations performed in high-volume hospitals compared to their lower-volume counterparts, with a plateau when performing a minimum of 45 esophagectomies per year [11]. Additionally, the SARCUT Study Group demonstrated that cytoreductions for Uterine Sarcomas, a highly complex and low-prevalent procedure, had improved oncologic survival and outcomes when performed at high-volume centers [12].

Interestingly, a retrospective study by El Amari *et al.* showed both improved mortality in specific oncologic procedures in centers with higher volume for that specific procedure, but also lower postoperative mortality for other complex oncologic procedures performed at the same hospital [9]. This association was observed for colectomy, gastrectomy, hepatectomy, esophagectomy, or proctectomy. This relationship has driven initiatives to concentrate certain oncologic surgeries within high-volume centers or "centers of excellence," under the premise that such centralization ensures higher quality care. However, the application of this concept regarding cytoreduction and HIPEC has not been thoroughly investigated, particularly across academic hospitals and cancer centers in the United States.

Establishing a volume-outcome relationship within CRS-HIPEC is important due to the rapid expansion of new HIPEC centers opening across the United States outside of already established "high-volume centers." Several studies investigating the technical proficiency in CRS-HIPEC have identified that a benchmark of approximately 140 to 220 cases is generally required to attain such expertise [13-16]. For a nascent center aiming to establish proficiency within a five-year timeframe, this achievement necessitates conducting between 28 to 44 HIPEC procedures annually [14]. Presently in the United States, such annual case volumes are predominantly confined to a select number of major regional centers with the advocacy for centralizing care supported by its potential to enhance team proficiency, surgical expertise, and overall systems of care.

Vizient Analysis

The author's retrospective study "Does Hospital Operative Volume Influence the Outcomes of Patients After Heated Intraperitoneal Chemotherapy for Peritoneal Carcinomatosis" explores the volume-outcome relationship traditionally upheld in oncologic surgery and addresses the gaps in safety outcomes across HIPEC-performing institutions [17]. Previous research has frequently aligned higher surgical volumes with improved patient outcomes, leading to a healthcare climate that favors the regionalization of complex oncologic procedures to high-volume "centers of excellence." However, the study by Chatani *et al.* [17] disrupts this narrative, by reporting that outcomes were similar among low, moderate, and high-volume institutions.

Chatani and colleagues employed the Vizient Clinical Database, which aggregates data from over a thousand academic medical centers, cancer and community hospitals. This resource enabled a comprehensive evaluation, incorporating de-identified HIPEC cases from January 2020 through December 2022, and captured patient demographics, hospital characteristics, and procedural coding histories. The ICD-10 code '3E0M30Y', which was added into the database in late 2019, was utilized to only include institutions who performed HIPEC. Institutions that did not perform HIPEC were excluded from the study. The robustness of the methodology is evidenced by the inclusion of demographic variables, comorbidities, disease histology, and procedure types, which were compared across hospital volume tertiles to ensure a balanced analytical framework devoid of confounding factors. Importantly, outcomes in Vizient are reported with respect to the index hospitalization. The primary outcome in this study was post-operative observed hospital mortality, while secondary outcomes included postoperative morbidity, ICU utilization and length of stay, hospital length of stay, 30-day readmissions, and total cost [17].

The Vizient study's statistical rigor is evidenced by the deployment of chi-squared analysis for categorical variables and one-way ANOVA for continuous variables, supplemented by post-hoc Tukey tests. This approach permits a nuanced comparison across patient demographics and clinical characteristics stratified into hospital volume tertiles. The Cochran-Mantel-Haenszel test was further utilized to ascertain the association among the volume of specific types of operations and hospital volume tiers.

In the robust sample size of 149 HIPEC-performing hospitals, 5,165 cases were identified over the three-year study period. The distribution of these institutions across the United States—with a higher concentration in the eastern half—mirrors the geographical spread of this emerging treatment paradigm. The hospitals encompassed cancer centers, academic institutions, and community hospitals affiliated with academic centers, thus providing a representative cross-section of healthcare environments.

Key Findings

One key finding was that the incidence of Magnet nursing status differed significantly across the hospital volume tiers, with low-volume centers less likely to hold this designation (**Tables 1** and **2A**). This distinction underscores the variability in institutional accreditation and, potentially, in care standards. However, the study elucidated that no statistically significant variance in morbidity or mortality rates was observed across the low-, medium-, and high-volume centers (**Figures 1A** and **1B**). Complication rates were 9.4%, 7.1%, and 9.0%, respectively (p = 0.71), and mortality rates were 0.9%, 0.6%, and 0.7%, respectively (p = 0.93) [17]. These outcomes challenge the presumption that higher surgical volumes are necessarily a prerequisite for postoperative outcomes in the context of CRS-HIPEC.

Table 1. Descriptive statistics for HIPEC-performing hospitals between January 2020 and December 2023, including patient and disease characteristics. Numbers reflect mean values for hospitals unless otherwise indicated.

	Overall (n = 149)	**Low (n = 113)**	**Medium (n = 25)**	**High (n = 11)**	**P-Value**
Cases	5165	1700	1788	1677	* * * *
Annual Cases (per Hospital)*	6	4	21	47	**<0.001**
Case Mix Index (CMI)	3.0	3.0	2.9	3.0	0.94
% Magnet Nursing Status	71.8	67.2	80.0	100.0	**0.04**
Mean Age (years)	56.5	56.2	57.1	57.7	0.77
% Female	66.0	67.1	63.3	61.6	0.52
% White	77.8	76.1	82.0	84.0	0.29
Histologies					
Foregut	8.0	8.0	6.4	11.9	0.68
Appendiceal	39.3	40.3	38.0	31.7	0.61
Colorectal	18.6	18.0	21.3	17.8	0.73
Mesothelioma	12.2	11.6	13.4	15.1	0.71
Gynecologic	20.4	20.4	19.7	22.5	0.96
Comorbidities					
% Hypertension	44.5	44.8	44.0	43.6	0.98
% Diabetes	14.8	15.4	13.4	12.7	0.73
% Obesity	20.1	19.1	23.5	22.8	0.44
% Weight Loss	11.5	11.1	12.9	12.9	0.76
* Denotes median					

Table 2. Comparison of post-operative outcomes between patients at hospitals (**A**) with and without Magnet nursing status and (**B**) with a case mix index less- or greater-than 3.

(A)	**Non-Magnet (n = 42)**	**Magnet (n = 107)**	**P-Value**
Volume Tertile (% of Tertile)			**0.04**
Low	37 (33%)	76 (67%)	-
Medium	5 (20%)	20 (80%)	-
High	0 (0%)	11 (100%)	-
% ICU Cases	64.3	50.7	**0.04**
Mean ICU Days	3.2	3.1	0.63
Complication Rate (%)	11.4	8.0	0.14
% Deaths (Observed)	1.7	0.5	**0.04**
% Deaths (Expected)	1.3	1.0	0.10

Mortality Index	0.8	0.7	0.82
LOS (Observed)	9.3	9.4	0.82
LOS (Expected)	9.5	9.3	0.74
LOS Index	1.1	1.0	0.37
% 30 Day Readmissions	8.3	4.6	0.10
Mean Total Cost (Observed)	$45,775	$48,645	0.42
(B)	**CMI <3 (n = 92)**	**CMI >3 (n = 57)**	**P-Value**
Volume Tertile (% of Tertile)			0.58
Low	71 (63%)	42 (37%)	-
Medium	15 (60%)	10 (40%)	-
High	6 (55%)	5 (45%)	-
% ICU Cases	45.6	69.4	**<0.01**
Mean ICU Days	2.8	3.6	**0.01**
Complication Rate (%)	5.0	15.5	**<0.01**
% Deaths (Observed)	0.6	1.2	0.24
% Deaths (Expected)	0.9	1.4	**0.01**
Mortality Index	0.8	0.7	0.86
LOS (Observed)	8.0	11.6	**<0.01**
LOS (Expected)	7.9	11.6	**<0.01**
LOS Index	1.1	1.1	0.89
% 30 Day Readmissions	7.2	3.1	0.06
Mean Total Cost (Observed)	$40,621	$59,650	**<0.01**

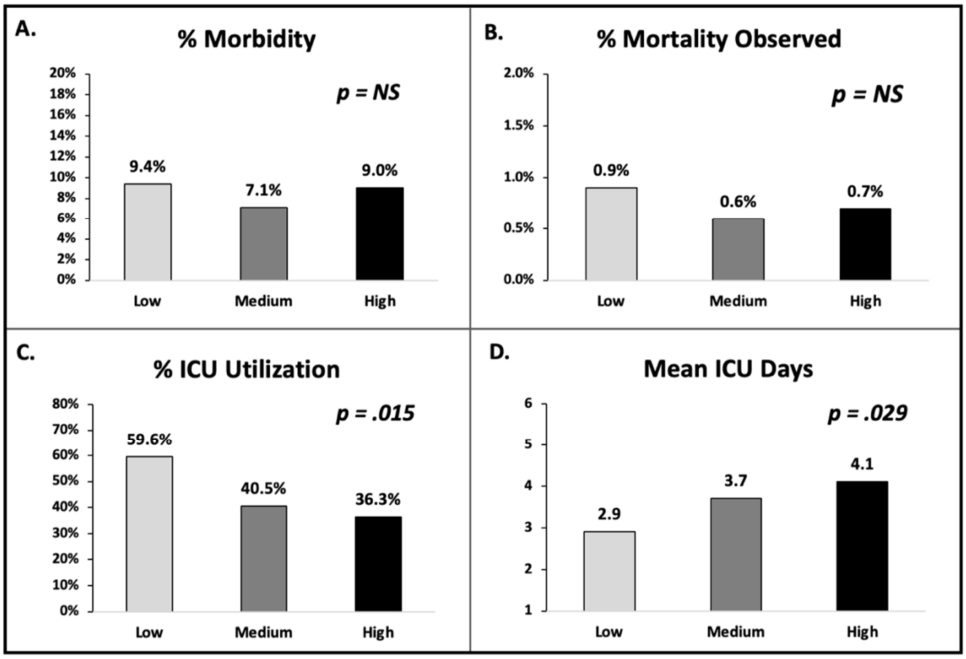

Figure 1. Morbidity, mortality, and ICU utilization per volume-tertile across HIPEC-performing institutions between January 2020 and December 2022.

This analysis was the first to explore ICU usage after CRS-HIPEC (**Figures 1C** and **1D**). Notably, ICU utilization postoperatively did reveal significant differences, with 59.6% in low-volume centers compared to 40.5% and 36.3% in medium- and high-volume centers respectively (p = 0.02) [17]. This finding, however, did not equate to extended ICU stays or increased costs, as shorter ICU length-of-stay was observed at low-volume centers compared to their higher-volume counterparts (2.9 days versus 3.7 and 4.1 days, p = 0.03) [17] (**Figure 2**). ICU utilization and LOS also were related to Case Mix Index (**Table 2B**).

When considering the cost implications, the average total observed cost-per-case was $47,857, congruent across all hospital volume tertiles [17]. Higher costs were associated with more complex cases, as indicated by higher Case Mix Index scores (CMI>3) [17]. This figure reflects a substantial decrease from historical costs of $166,189 reported in the 1990s [18], indicating an evolution towards cost-effectiveness in CRS-HIPEC care delivery. The financial aspect, while not directly correlated with patient volume, signals the shifting economics of healthcare as it relates to complex oncologic operations.

Implications of Results

The current study's results indicate that while certain institutional characteristics, such as Magnet status and higher case mix index (CMI), are associated with variations in outcomes, the central thesis holds that volume alone is not predictive of patient safety outcomes in CRS-HIPEC. The homogeneity in patient demographics and the consistency in outcomes across volume-tertiles reinforces the emerging perspective that high-quality care for peritoneal carcinomatosis can be achieved outside of traditionally designated high-volume centers.

This recognition that outcomes are more intimately tied to the complexity of cases and the capabilities of the institution rather than volume has profound implications for the structuring of oncologic surgical care. Typically, surgeons who train at high-volume "centers of excellence" are recruited to start CRS-HIPEC programs at centers that are low- or medium-volume hospitals. These findings suggest that enhancing institutional capacity, by recruiting specialized surgical expertise and fostering multidisciplinary care teams, could be as pivotal, if not more so, than concentrating procedures at high-volume centers.

Outcomes were reported with respect to the index hospitalization, focusing on postoperative observed hospital mortality as the primary outcome, and extending to secondary outcomes including postoperative morbidity, ICU utilization and length-of-stay, hospital length-of-stay, 30-day readmissions, and total cost. The scope of complications examined was extensive, ranging from in-hospital stroke to *Clostridium difficile* infections, accompanied by a spectrum of Patient Safety Indicators.

The results illuminate the nuanced landscape of CRS-HIPEC patient care, where no marked disparities in morbidity or

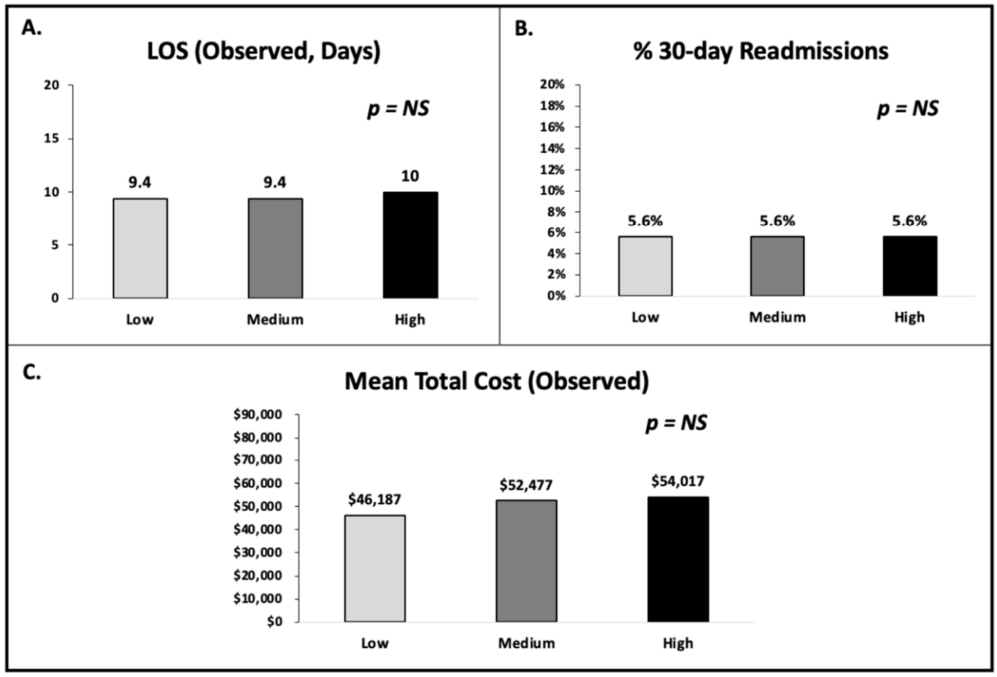

Figure 2. Hospital length-of-stay, readmission rates, and total observed cost per volume-tertile across HIPEC-performing institutions between January 2020 and December 2022.

mortality were observed across varying hospital volumes. Interestingly, the study also revealed that low-volume centers had a predilection for higher postoperative ICU utilization, which did not, however, translate into longer hospital stays or increased care costs. This observation suggests that while operational practices, such as ICU admissions, vary, they do not necessarily impact the efficiency or effectiveness of patient care in the context of CRS-HIPEC.

In terms of limitations, the study acknowledges its retrospective nature and reliance on database information, which may lack the granularity required to capture the full spectrum of postoperative complications or longer-term mortality rates. Unlike databases such as the National Cancer Database (NCDB) or SEER-Plus, the Vizient database does not permit the analysis of overall survival – a critical endpoint in oncological research. Although a multivariate analysis was not conducted within the scope of the original manuscript, the study did investigate several demographic and clinical variables, which are elucidated in the Key Findings section. Moreover, the analysis underscores the need for further investigation into postoperative care practices, particularly ICU utilization, to comprehensively understand and optimize patient care pathways.

Conclusions

The commentary encapsulated here advocates for a measured re-evaluation of the current healthcare delivery models for CRS-HIPEC, informed by empirical evidence rather than historical precedence. As the field continues to mature, reconciliation of these findings with the longitudinal outcomes of patients and the dynamic economics of healthcare to ensure equitable, high-quality care for all patients, regardless of institutional volume will be important.

The findings carry substantial implications for healthcare policy and practice. They challenge the extant rationale for the centralization of complex surgical procedures and suggest that equivalent standards of care are attainable in lower-volume institutions, provided they possess the necessary infrastructure and expertise. This proposition holds significant promise for broadening patient access to these life-extending treatments, reducing the logistical and financial burdens associated with travel to high-volume centers, and potentially alleviating capacity strains on such centers.

In conclusion, the study by Chatani and associates represents a substantive addition to the literature on surgical oncology, particularly in the domain of peritoneal carcinomatosis management. The analysis of Vizient national data champions a shift in perspective that elevates the importance of case complexity management and comprehensive institutional capabilities over the conventional emphasis on surgical volume. The implications of this work may reverberate through future healthcare policy, shaping guidelines and influencing the broader distribution of specialty surgical services. However, a need exists for continued research that builds upon these findings, delving into the long-term patient outcomes and health system implications of CRS-HIPEC care delivery.

Conflicts of Interest

The authors have no conflicts of interest.

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Author Contributions

All authors contributed equally to writing, editing, and reviewing the manuscript.

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