Trends and Social Barriers for Inpatient Palliative Care in Patients With Metastatic Bladder Cancer Receiving Critical Care Therapies

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ABSTRACT

Background: Use of inpatient palliative care (IPC) in the treatment of advanced cancer represents a well-established guideline recommendation. A recent analysis showed that patients with genitourinary cancer benefit from IPC at the second lowest rate among 4 examined primary cancers, namely lung, breast, colorectal, and genitourinary. Based on this observation, temporal trends and predictors of IPC use were examined in patients with metastatic urothelial carcinoma of the bladder (mUCB) receiving critical care therapies (CCTs). **Patients and Methods:** Patients with mUCB receiving CCTs were identified within the Nationwide Inpatient Sample database (2004–2015). IPC use rates were evaluated in estimated annual percentage change (EAPC) analyses. Multivariable logistic regression models with adjustment for clustering at the hospital level were used. **Results:** Of 1,944 patients with mUCB receiving CCTs, 191 (9.8%) received IPC. From 2004 through 2015, IPC use increased from 0.7% to 25.0%, respectively (EAPC, +23.9%; $P < .001$). In analyses stratified according to regions, the highest increase in IPC use was recorded in the Northeast (EAPC, +44.0%), followed by the West (EAPC, +26.8%), South (EAPC, +22.9%), and Midwest (EAPC, +15.5%). Moreover, the lowest rate of IPC adoption in 2015 was recorded in the Midwest (14.3%). In multivariable logistic regression models, teaching status (odds ratio [OR], 1.97; $P < .001$), more recent diagnosis (2010–2015; OR, 3.89; $P < .001$), and presence of liver metastases (OR, 1.77; $P = .02$) were associated with higher IPC rates. Conversely, Hispanic race (OR, 0.42; $P = .03$) and being hospitalized in the Northeast (OR, 0.36; $P = .01$) were associated with lower rate of IPC adoption. Finally, patients with a primary admission diagnosis that consisted of infection (OR, 2.05; $P = .002$), cardiovascular disorders (OR, 2.10; $P = .03$), or pulmonary disorders (OR, 2.81; $P = .005$) were more likely to receive IPC. **Conclusions:** The rate of IPC use in patients with mUCB receiving CCTs sharply increased between 2004 and 2015. The presence of liver metastases, infections, or cardiopulmonary disorders as admission diagnoses represented independent predictors of higher IPC use. Conversely, Hispanic race, nonteaching hospital status, and hospitalization in the Midwest were identified as independent predictors of lower IPC use and represent targets for efforts to improve IPC delivery in patients with mUCB receiving CCT.

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Background

The integration of palliative care into the treatment of advanced cancer represents an established guideline recommendation^{1–3} and has been considered an indicator of quality of care.^{4–11} It is noteworthy that early introduction of palliative care may improve not only quality of life but also survival in patients with advanced cancer,¹¹ and may reduce length of hospital stay and cost.^{12,13} Therefore, equal access to palliative care should be warranted in all patients with metastatic cancer, especially those requiring critical care therapies (CCTs) for treatment-related complications or disease progression.

A recent publication focusing on patients from California during 2010 showed the integration of inpatient palliative care (IPC) in patients receiving CCTs across a variety of metastatic tumor primaries, including genitourinary (GU) cancer.¹⁴ In that report, patients with GU cancer benefited from IPC at the second lowest rate among 4 examined primary cancers (lung, breast, colorectal, and GU).¹⁴ Based on this finding, temporal trends in and social barriers to IPC delivery in patients receiving CCTs were examined in a larger national patient sample and across time. Within the GU category, we focused on metastatic urothelial carcinoma of the bladder (mUCB) because it is associated with poor prognosis, even in contemporary analyses.^{15,16} We hypothesized that, despite occupying the second lowest

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position among other primaries, IPC use rate improved over time in patients with mUCB receiving CCTs. In addition, we tested for potential barriers to IPC delivery in these patients when CCT is delivered.

Patients and Methods

Data Source and Patient Selection

We relied on the Nationwide Inpatient Sample (NIS) database (2004–2015) to assess trends in and predictors of IPC use in patients receiving CCTs. The NIS is a set of longitudinal hospital inpatient databases included in the Healthcare Cost and Utilization Project family, created by the Agency for Healthcare Research and Quality (AHRQ) through a federal–state partnership.¹⁷ The database includes 20% of US inpatient hospitalizations with discharge abstracts from 8 million hospital stays.

Study Population

We focused on patients aged ≥ 18 years with a diagnosis of mUCB (ICD-9-CM code 188.0) who received CCTs. All procedures and diagnoses were coded using ICD-9-CM. Procedure codes were used to identify CCTs, specifically invasive mechanical ventilation (ICD-9-CM codes 96.70–96.72), percutaneous endoscopic gastrostomy tube (ICD-9-CM code 43.11), dialysis for acute kidney failure (ICD-9-CM codes 584.5–585.9, and 39.95 to exclude patients receiving chronic dialysis), total parenteral nutrition (ICD-9-CM code 99.15), and tracheostomy (ICD-9-CM codes 31.1, 31.21, 31.29).^{14,18} Only patients with a secondary diagnosis of metastatic disease were included (ICD-9-CM codes 197.x and 198.x). These selection criteria yielded 1,944 patients.

Patient and Hospital Characteristics

Patient age at admission, year of admission, sex, race/ethnicity (white, African American, Hispanic, and other/unknown), Charlson comorbidity index score,^{19,20} and insurance status (private, Medicare, Medicaid, and other [self-pay]) were ascertained from the NIS. For purposes of univariable and multivariable analyses, year of admission was dichotomized in intervals, namely historical (2004–2009) and contemporary (2010–2015). Additional risk variables consisted of hospital region (Northeast, Midwest, South, West), hospital size (small, <200 beds; medium, 200–399 beds; large, ≥ 400 beds), and hospital teaching versus nonteaching status. Teaching institutions had an American Medical Association–approved residency program, were members of the Council of Teaching Hospitals and Health Systems, or had a ratio of ≥ 0.25 of full-time equivalent interns and residents to non–nursing home beds.²¹ Last, inflation-adjusted total hospital charges were defined according to NIS methodology.¹⁷

Definition of Principal Diagnosis and IPC Use

We classified the principal diagnosis using the Clinical Classifications Software codes. Clinical Classifications Software is a classification tool developed by the AHRQ that collapses $>14,000$ ICD-9-CM diagnosis codes and 3,900 ICD-9-CM procedure codes into a smaller set of clinically meaningful categories.^{14,17,18} Use of IPC services was defined by the ICD-9 diagnosis code V66.7^{22–24}; two prior validation studies showed that this code for identification of IPC services in patients with metastatic disease has a sensitivity of 66.3% to 84.0% and specificity of 95.0% to 99.1%.^{22,23} Only hospitals that provided at least one IPC service were included. Therefore, all of the hospitals included in the analysis had access to IPC.

Statistical Analysis and Covariates

To assess contemporary use rates and disparities in IPC use, 3 analytical steps were followed. First, medians with interquartile ranges and frequencies with proportions were reported for continuous and categorical variables, respectively, and the statistical significance of differences was evaluated using Kruskal-Wallis and chi-square tests. Second, estimated annual percentage change (EAPC) was defined in the overall cohort and in subgroup analyses focusing on regions and hospital teaching status. Third, multivariable logistic regression (MLR) models were used to test for predictors of access to IPC services. All multivariable analyses were fitted after adjustment for clustering at the hospital level using generalized estimation equation methodology.²⁵ In MLR models, adjustment variables consisted of age at admission, year of admission, sex, race, Charlson comorbidity index score, hospital teaching status, hospital region, insurance status, hospital size, metastatic sites, primary diagnosis at admission, and type of CCT.

All statistical tests were 2-sided with the level of significance set at $P < .05$. Analyses were performed using R software (version 3.5.1).

Results

Study Population

Between 2004 and 2015, 1,944 patients with mUCB received CCT; of those, 191 (9.8%) received IPC (Table 1). Mean total hospital charges among survivors (ie, patients discharged alive at the end of the hospital stay) were lower in patients who received IPC than in those who did not (\$35,524 vs \$45,047; $P = .04$). Similarly, length of stay among survivors was shorter in patients who received IPC than in those who did not (11 vs 13 days; $P = .002$). IPC services were more frequently delivered to white patients (76.4% vs 70.1%; $P = .06$), in teaching hospitals (68.1% vs 57.4%; $P = .005$), and to patients with liver metastases (20.4% vs 10.0%; $P < .001$). According to principal diagnosis

Table 1. Baseline Patient Characteristics

Variable	Overall	IPC	No IPC	P Value ^a
Total, n (%)	1,944	191 (9.8%)	1,753 (90.2%)	
Age at admission, y				.1
Median	71	70	71	
IQR	62–78	59–78	63–78	
LOS (only survivors), d				.002
Median	13	11	13	
IQR	8–20	6–18	8–20	
THCs (only survivors), mean (SD), \$USD	\$44,359 (\$41,330)	\$35,524 (\$44,440)	\$45,047 (\$41,016)	.04
Year interval, n (%)				<.001
2004–2009	947 (48.7)	37 (19.4)	910 (51.9)	
2010–2015	997 (51.3)	154 (80.6)	843 (48.1)	
Sex, n (%)				.3
Male	1,468 (75.5)	138 (72.3)	1,330 (75.9)	
Female	476 (24.5)	53 (27.7)	423 (24.1)	
Race, n (%)				.06
White	1,374 (70.7)	146 (76.4)	1,228 (70.1)	
African American	195 (10.0)	22 (11.5)	173 (9.9)	
Hispanic	99 (5.1)	7 (3.7)	92 (5.2)	
Other/Unknown	276 (14.2)	16 (8.4)	260 (14.8)	
Charlson comorbidity index score, n (%)				.4
0	1,121 (57.7)	115 (60.2)	1,006 (57.4)	
1	486 (25.0)	40 (20.9)	446 (25.4)	
≥2	337 (17.3)	36 (18.8)	301 (17.2)	
Hospital teaching status, n (%)				.005
Nonteaching	808 (41.6)	61 (31.9)	747 (42.6)	
Teaching	1,136 (58.4)	130 (68.1)	1,006 (57.4)	
Hospital region, n (%)				.08
South	634 (32.6)	72 (37.7)	562 (32.1)	
Midwest	442 (22.7)	42 (22.0)	400 (22.8)	
Northeast	461 (23.7)	32 (16.8)	429 (24.5)	
West	407 (20.9)	45 (23.6)	362 (20.7)	
Insurance status, n (%)				.08
Medicare	1,288 (66.3)	121 (63.4)	1,167 (66.6)	
Medicaid	161 (8.3)	25 (13.1)	136 (7.8)	
Private	418 (21.5)	39 (20.4)	379 (21.6)	
Other	77 (4.0)	6 (3.1)	71 (4.1)	
Hospital size, ^b n (%)				.5
Large (≥400 beds)	1,263 (65.0)	117 (61.3)	1,146 (65.4)	
Medium (200–399 beds)	448 (23.0)	48 (25.1)	400 (22.8)	
Small (<200 beds)	233 (12.0)	26 (13.6)	207 (11.8)	

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Abbreviations: AKF, acute kidney failure; CCT, critical care therapy; GI, gastrointestinal; GU, genitourinary; IMV, invasive mechanical ventilation; IPC, inpatient palliative care; IQR, interquartile range; LOS, length of stay; PEG, percutaneous endoscopic gastrostomy; THCs, total hospital charges; TPN, total parenteral nutrition.

^aBold indicates statistically significant *P* value.

^bBased on number of beds.

Table 1. Baseline Patient Characteristics (cont.)

Variable	Overall	IPC	No IPC	P Value ^a
Metastatic sites, n (%)				<.001
Bone	392 (20.2)	49 (25.7)	343 (19.6)	
Distant nodes	324 (16.7)	26 (13.6)	298 (17.0)	
Lung	154 (7.9)	14 (7.3)	140 (8.0)	
Liver	214 (11.0)	39 (20.4)	175 (10.0)	
Brain	45 (2.3)	5 (2.6)	40 (2.3)	
Adrenal	15 (0.8)	2 (1.0)	13 (0.7)	
Other/Unspecified	800 (41.2)	56 (29.3)	744 (42.4)	
Primary diagnosis at admission, n (%)				<.001
Cancer-related disorders	962 (49.5)	64 (33.5)	898 (51.2)	
Infections	253 (13.0)	44 (23.0)	209 (11.9)	
GU disorders	198 (10.2)	19 (9.9)	179 (10.2)	
Cardiovascular disorders	111 (5.7)	15 (7.9)	96 (5.5)	
Pulmonary disorders	81 (4.2)	12 (6.3)	69 (3.9)	
GI disorders	162 (8.3)	20 (10.5)	142 (8.1)	
Fractures	7 (0.4)	1 (0.5)	6 (0.3)	
Fluid/Electrolyte disorders	36 (1.9)	3 (1.6)	33 (1.9)	
Neurologic disorders	12 (0.6)	2 (1.0)	10 (0.6)	
Other disorders	122 (6.3)	11 (5.8)	111 (6.3)	
Type of CCT, n (%)				.08
IMV	498 (25.6)	64 (33.5)	434 (24.8)	
Dialysis for AKF	332 (17.1)	30 (15.7)	302 (17.2)	
TPN	870 (44.8)	72 (37.7)	798 (45.5)	
PEG	183 (9.4)	20 (10.5)	163 (9.3)	
Tracheostomy	61 (3.1)	5 (2.6)	56 (3.2)	
Discharge disposition (only survivors), n (%)				.001
Home or home healthcare	837 (57.9)	45 (42.9)	792 (59.1)	
Intermediate facilities	600 (41.5)	58 (55.2)	542 (40.4)	
Other/Unknown	9 (0.6)	2 (1.9)	7 (0.5)	
In-hospital mortality, n (%)				<.001
Alive	1,446 (74.4)	105 (55.0)	1,341 (76.5)	
Dead	498 (25.6)	86 (45.0)	412 (23.5)	

Abbreviations: AKF, acute kidney failure; CCT, critical care therapy; GI, gastrointestinal; GU, genitourinary; IMV, invasive mechanical ventilation; IPC, inpatient palliative care; IQR, interquartile range; LOS, length of stay; PEG, percutaneous endoscopic gastrostomy; THCs, total hospital charges; TPN, total parenteral nutrition.

^aBold indicates statistically significant *P* value.

^bBased on number of beds.

at admission, IPC services were more frequently used in patients admitted for infections (23.0% vs 11.9%; $P<.001$), cardiovascular disorders (7.9% vs 5.5%; $P<.001$), or pulmonary disorders (6.3% vs 3.9%; $P<.001$). Conversely, IPC services were less frequently used in patients admitted for cancer-related disorders (33.5% vs 51.2%; $P<.001$). Finally, in-hospital mortality was higher in patients who received IPC than in those who did not (45.0% vs 23.5%; $P<.001$) (Table 1).

After stratification according to regions, the highest overall rate of IPC use was recorded in the South

(11.4%), followed by the West (11.0%), the Midwest (9.5%), and the Northeast (6.9%). Similarly, after stratification according to teaching status, the overall rate of IPC use was higher in teaching hospitals (11.4%) than in nonteaching hospitals (7.5%).

Trends of IPC Use

Overall, IPC use rates in patients with mUCB receiving CCTs increased from 0.7% in 2004 to 25.0% in 2015 (EAPC, +23.9%; 95% CI, +18.5 to +30.4; $P<.001$) (Figure 1). In subgroup analyses stratified according to regions, IPC

Figure 1. Inpatient palliative care delivery rate over time.

use rate increased from 2.6% to 24.1% in the South (EAPC, +22.9%; 95% CI, +14.9% to +33.9%; $P<.001$), from 0% to 34.6% in the West (EAPC, +26.8%; 95% CI, +11.9% to +59.0%; $P=.006$), from 0% to 14.3% in the Midwest (EAPC, +15.5%; 95% CI, +7.8% to +25.8%; $P=.007$), and from 0% to 26.1% in the Northeast (EAPC, +44.0%; 95% CI, +29.2% to +68.7%; $P<.001$) (Figure 2). In additional subgroup analyses stratified by teaching status, IPC use rate increased from 0% to 25.8% in teaching hospitals (EAPC,

+25.0%; 95% CI, +19.4% to +32.0%; $P<.001$) and from 1.4% to 23.1% in nonteaching hospitals (EAPC, +18.9%; 95% CI, +9.6% to +38.4%; $P=.009$) (Figure 3).

MLR Models Predicting Use of IPC

In MLR models adjusted for clustering and all available covariates, hospital teaching status (odds ratio [OR], 1.97; 95% CI, 1.37–2.85; $P<.001$), contemporary years interval (2010–2015) (OR, 3.89; 95% CI, 2.63–5.77; $P<.001$), and presence of liver metastases (OR, 1.77; 95% CI, 1.09–2.88; $P=.02$) were associated with higher IPC use in patients with mUCB receiving CCT relative to nonteaching status, historical years interval (2004–2009), and presence of bone metastases, respectively (Table 2). Conversely, Hispanic race (OR, 0.42; 95% CI, 0.18–0.95; $P=.03$) and being hospitalized in the Northeast (OR, 0.36; 95% CI, 0.21–0.87; $P<.001$) were associated with lower IPC use than white race and being hospitalized in the West, respectively.

Regarding primary diagnosis at admission, patients with a primary diagnosis of infections (OR, 2.05; 95% CI, 1.29–3.26; $P=.002$), cardiovascular disorders (OR, 2.10; 95% CI, 1.04–4.22; $P=.03$), or pulmonary disorders (OR, 2.81; 95% CI, 1.35–5.86; $P=.005$) were more likely than patients with cancer-related disorders to receive

Figure 2. Inpatient palliative care delivery rate over time, stratified according to geographic region: (A) Midwest, (B) South, (C) West, and (D) Northeast.

Figure 3. Inpatient palliative care delivery rate over time, stratified according to hospital (A) teaching and (B) nonteaching status.

IPC. Finally, regarding CCT types, no differences in IPC administration were recorded (Table 2).

Discussion

IPC delivery in patients with advanced cancer represents a well-established guideline recommendation.^{1–3} However, in a previous report by Loh et al,¹⁴ the rate of IPC use was among the lowest in patients with metastatic GU cancer receiving CCTs. This observation is worrisome and may indicate suboptimal quality of care in patients with advanced GU malignancies, especially those with a poor prognosis, such as patients with mUCB. Based on this concept, we hypothesized that IPC use increases over time in patients with mUCB receiving CCTs. To address this, we examined the use of IPC in the NIS over a period of 12 years (2004–2015) and also tested for potential predictors of IPC use. These analyses revealed several noteworthy findings.

First, the overall IPC use rate was low at 9.8%. However, the annual rate sharply increased from 0.7% to 25.0% in a highly statistically significant fashion during the study period (EAPC, +23.9%; $P < .001$). This observation suggests improved adherence to North American guidelines and, most important, improved patient care. The previously reported 16.8% rate of IPC use among patients with GU cancer recorded in California in 2010 was higher than the national average of 9.8% recorded in our study among patients with mUCB between 2004 and 2015.¹⁴ Thus, the reference standard reported by Loh et al¹⁴ originated from a state in which the rates of IPC use and possibly the quality of care for this specific patient population are higher than the national average. Indeed, the highest rate of IPC use in 2015 was recorded in the West (34.6%), which includes California. Despite the enthusiasm related to an important absolute and relative increase in IPC delivery across time, our analyses of IPC delivery rates in patients with mUCB receiving CCTs showed a maximum national overall rate of 25.0% in 2015.

This rate is still lower than the highest individual rate of IPC use (28.3%) reported among patients with lung cancer in 2010 within the California state analysis. Therefore, further efforts aimed at educating and sensitizing clinicians involved in the critical care of patients with metastatic prostate cancer nationwide are still needed.

Second, we reported differences in trends over time in the 4 examined geographic regions. Despite the lowest overall rate of IPC use being recorded in the Northeast in both univariable and multivariable analyses, we showed that IPC use sharply increased in more recent years in this region, as shown by the highest EAPC (+44.4%) recorded there among all 4 examined regions. Therefore, this pronounced increasing trend recorded in the Northeast may be interpreted as the increasing adoption of IPC use more recently than in other regions, such as the South or West. Conversely, the lowest IPC use increase and the lowest overall IPC use rate were recorded in the Midwest (EAPC, +15.5%). Taken together, these differences imply that efforts aimed at improving IPC rate delivery may need to be of greater intensity in specific regions, such as the Midwest, where the rate of IPC adoption over time was low.

Third, we also recorded an important effect of race on the rate of IPC delivery. Specifically, Hispanic patients were significantly less likely to receive IPC, as shown in MLR models (hazard ratio, 0.42; $P = .03$). To the best of our knowledge, we are the first to record disparities in access to end-of-life care among patients with mUCB, and therefore a direct comparison with previous reports cannot be performed. However, racial disparities in access to end-of-life care were identified in other metastatic primaries, such as prostate²⁶ and lung cancer.²⁷

Fourth, we identified hospital teaching status as an important predictor of IPC delivery. IPC delivery rates were higher across teaching hospitals in both univariable (11.4% vs 7.5%; $P < .001$) and multivariable analyses (OR, 1.97; $P < .001$). This difference was persistent across the study

Table 2. Multivariable Logistic Regression Model Predicting Use of Inpatient Palliative Care

Variable	OR (95% CI)	P Value ^a
Teaching status		
Nonteaching	Ref	
Teaching	1.97 (1.37–2.85)	<.001
Year interval		
2004–2009	Ref	
2010–2015	3.89 (2.63–5.77)	<.001
Race		
White	Ref	
African American	0.78 (0.46–1.33)	.4
Hispanic	0.42 (0.18–0.95)	.03
Other/Unknown	0.52 (0.32–0.83)	.007
Hospital region		
West	Ref	
Midwest	0.62 (0.38–1.03)	.07
Northeast	0.36 (0.21–0.62)	<.001
South	0.66 (0.42–1.03)	.07
Metastatic site		
Bone	Ref	
Distant nodes	0.60 (0.34–1.04)	.07
Lung	0.64 (0.32–1.28)	.2
Liver	1.77 (1.09–2.88)	.02
Brain	0.71 (0.27–1.85)	.4
Adrenal	1.21 (0.20–7.30)	.8
Other/Unspecified	0.62 (0.39–0.98)	.04
Type of CCT		
IMV	Ref	
Dialysis for AKF	0.71 (0.41–1.21)	.2
TPN	0.87 (0.58–1.32)	.5
PEG	1.05 (0.58–1.90)	.8
Tracheostomy	0.62 (0.26–1.47)	.2
Primary diagnosis		
Cancer-related disorders	Ref	
Infections	2.05 (1.29–3.26)	.002
GU disorders	1.61 (0.86–3.00)	.1
Cardiovascular disorders	2.10 (1.04–4.22)	.03
Pulmonary disorders	2.81 (1.35–5.86)	.005
GI disorders	1.67 (0.92–3.03)	.08
Fractures	2.14 (0.22–20.90)	.5
Fluid/Electrolyte disorders	1.38 (0.40–4.67)	.6
Neurologic disorders	3.15 (0.76–13.07)	.1
Other disorders	1.25 (0.61–2.55)	.5

Model was adjusted for Charlson comorbidity index score, age at admission, sex, insurance status, and hospital size (number of beds).

Abbreviations: AKF, acute kidney failure; CCT, critical care therapy; GI, gastrointestinal; GU, genitourinary; IMV, invasive mechanical ventilation; OR, odds ratio; PEG, percutaneous endoscopic gastrostomy; TPN, total parenteral nutrition. ^aBold indicates statistically significant *P* value.

period. Specifically, IPC use rates increased, with EAPCs of +25.0% in teaching hospitals and +18.9% in nonteaching hospitals. This association between nonteaching hospitals and lower IPC rates was not identified in California,¹⁴ which may be explained by overall higher rates of IPC delivery in California. Moreover, specific analyses that focused on IPC delivery according to teaching status were not performed in the subgroup of GU cancers in the analysis by Loh et al.¹⁴

Fifth, IPC use in patients with mUCB receiving CCTs was significantly associated with the variables defining metastatic sites and primary diagnosis at admission. Specifically, patients with liver metastases were more likely than those with bone metastases to receive IPC services (OR, 1.77; *P*=.02). This finding may be interpreted as higher IPC use in patients with poor prognosis, because liver metastases have been shown to be associated with the poorest prognosis in patients with mUCB.²⁸ Similarly, patients whose primary diagnosis at admission consisted of infections (OR, 2.05; *P*=.002), cardiovascular disorders (OR, 2.10; *P*=.03), or pulmonary disorders (OR, 2.81; *P*=.005) received IPC at a higher rate than those with cancer-related disorders. The higher rate of IPC use in patients presenting with infections, cardiovascular disorders, or pulmonary disorders as their primary diagnosis at admission (eg, acute myocardial infarction or acute respiratory distress syndrome) can be explained by the highly life-threatening nature of these complaints relative to patients admitted for disorders directly related to cancer, in whom the gravity of individual diagnoses may vary. Our results are in agreement with those of Loh et al,¹⁴ who reported that a higher probability of receiving IPC services was recorded in patients with a primary diagnosis of infection. However, Loh et al¹⁴ did not perform specific subgroup analyses focusing on patients with GU cancer, and therefore valid conclusions about agreement or disagreement between these studies cannot be drawn.

Taken together, our findings showed important absolute and relative increases in IPC delivery among patients with mUCB receiving CCT. However, after stratification according to geographic region, we showed lower uptake of IPC use in the Midwest. Moreover, we identified Hispanic race and nonteaching hospital status as barriers to IPC delivery. Additionally, the presence at admission of specific underlying conditions that have highly life-threatening implications, namely liver metastases, infection, cardiovascular disorders, or pulmonary disorders, was identified as a predictor of higher IPC use rate. These observations indicate that, despite improvements, there is a persistent need for efforts aimed at IPC-focused education and sensitization that should particularly target healthcare providers of Hispanic patients, at nonteaching institutions, and in the Midwest. Moreover, it should be noted that, relative to the study by Loh et al,¹⁴ our study was based on an exponentially larger

patient sample and allowed for a specifically focused analysis of patients with mUCB in addition to temporal analyses and analyses according to the 4 geographic regions. Last, it is also important to note that all multivariable models were performed with additional adjustment for clustering at the hospital level using a generalized estimation equation.^{29,30} This methodology accurately accounted for interhospital variability in IPC use that may have determined the recorded differences in access to IPC. Therefore, our analysis was not affected by residual biases related to severe underuse of IPC services at some institutions.

The decision to use the V66.7 ICD-9 code to discern IPC services was based on recent and solid validation studies.^{22,23,31} Specifically, Feder et al²² performed the largest validation study of this code using the Veterans Health Administration database. They recorded high sensitivity (84%) and very high specificity (98%) that confirm the reliability of this code for IPC use. In consequence, from a clinical standpoint, it is unlikely that patients who received IPC were misclassified. Moreover, the study by Feder et al²² represents the most recent validation of the V66.7 code and largely outperformed previous validation studies in terms of sensitivity (84% vs 66%).^{22,23,31} This finding can also be interpreted as indicative of increasing confidence among clinicians regarding application of this code. Taken together, this evidence underlines the solidity of the ICD-9 code for identifying IPC services and confirms the validity of its use in our analysis. However, these differences in code sensitivity may also reflect variations in billing and coding practices across health systems and the coding input for their respective administrative datasets. Therefore, some residual confounding factors may have remained operational in our analysis.

Our study is not devoid of limitations. First, as is true of previous analyses of IPC use in other cancer databases,^{14,26} our study is based on a retrospective analysis with all of its inherent limitations. Second, we only included specific CCTs, and our findings therefore do not apply to other types of CCTs. Third, IPC was defined according to the V66.7 ICD-9 code, which is characterized by a sensitivity

ranging from 66% to 84%.^{22,23} Therefore, the number of patients who used IPC services may be underestimated. Fourth, we were also unable to adjust for patient characteristics that may have contributed to reported differences in IPC use rates, such as performance status; American Society of Anesthesiologists physical status; differences in laboratory values and opioid use; and presence or absence of exposure to chemotherapy, androgen deprivation, or radiotherapy. Fifth, the NIS database does not allow identification of the exact time when patients were referred for IPC services during their hospital stay. Similarly, we cannot code sequences of interventions or explore the correlation between use of IPC and escalation in procedural intervention. In addition, only inpatient data are available in the NIS database. Thus, we could not examine post-discharge management. These factors should ideally be included when analyses focusing on IPC use in advanced cancers are performed.

Conclusions

IPC use in patients with mUCB receiving CCTs sharply increased between 2004 and 2015. The presence of liver metastases and infections or cardiopulmonary disorders at admission were independent predictors of higher IPC use. Conversely, Hispanic race, nonteaching hospital status, and hospital location in the Midwest were identified as independent predictors of lower IPC use and represent targets for efforts aimed at improving IPC delivery in patients with mUCB receiving CCTs.

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