Receiving Immunotherapy for the Treatment of Advanced Renal Cell Carcinoma Associated with Higher Burden of Illness, Coagulopathy, and Cardiac Arrythmia.

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Abstract

In recent years, immunotherapy (IT) has emerged as a fundamental treatment for metastatic renal cell carcinoma (mRCC). Nevertheless, the adverse events and expenses associated with IT have not been thoroughly delineated. The aim of our study is to measure association between the utilization of IT in patients with mRCC and the overall costs, coagulopathy, and arrhythmia

A cross-sectional analysis was conducted utilizing the National Inpatient Samples database to identify and examine patients who were hospitalized with mRCC. The study examined association between the utilization of IT in mRCC and the burden of illness (BOI)—total charges, and length of stay (LOS), coagulopathy, and arrhythmia through generalized linear models (glm).

We examined 230 of the 28,535 patients with mRCC who were receiving IT. Patients receiving IT had mean [SD] age of 54.50 [8.67] vs. 65.80 [12.18] non-IT. White patients made up 81.0% of the IT recipients. 82.6% of IT beneficiaries were non-Medicaid or non-Medicare. IT patients' mean total charges were $260,905 [134,956.18] vs. $72,343 [$91,457.79] for non-IT patients, with a difference in LOS of stay of 4.98 [1.94] versus 6.28 [6.67] for non-IT patients. IT-treated mRCC patients reported a coagulopathy rate of 26.1% and an arrhythmia rate of 37.0%. In the adjusted glm, after controlling for variables, the use of IT was associated with higher total charges (7.67; 95% CI: 4.86 – 12.09). Further, coagulopathy (aOR = 5.61; 95% CI: 2.40 – 13.14) and arrhythmia (aOR = 4.34; 95% CI: 2.20 – 8.55) was associated with IT.

mRCC patients who received immunotherapy had a higher likelihood of coagulopathies and arrhythmia which impacted total charges. While IT has played a vital role in treating mRCC in recent years, this is the first instance where real-world evidence on adverse events and expenses associated with IT is being examined. The findings may have substantial implications for new supportive care in this population

Introduction

Immune checkpoint inhibitors (ICIs) are revolutionizing the approach to cancer treatment. Nevertheless, the utilization of immune checkpoint inhibitors (ICIs) has led to a proportional rise in immune-related adverse effects (irAEs). ICIs could disrupt the balance of the immune system and decrease the tolerance of T-cells. Consequently, blocking immunological checkpoints might cause autoreactive T-cells to become activated, leading to the development of diverse immune-related adverse events (irAEs) that resemble autoimmune disorders. Common adverse effects include gastrointestinal toxicity, endocrine toxicity, and dermatologic toxicity. Neurotoxicity, cardiotoxicity, and pulmonary toxicity are few but have the potential to cause death. Adverse effects such as gastrointestinal toxicity, dermatologic toxicity, and hypophysitis are more frequently observed with anti-CTLA-4 drugs. Our study's objective is to quantify the relationship between mRCC patients' use of IT and their total expenses, coagulopathy, and arrhythmia.

Methods

The National Inpatient Sample (NIS) database was used. We utilized both univariate and multivariate survey-weighted generalized linear models to assess the association between IT and clinical outcomes– – cardiac arrythmias, coagulopathies and burden of illness (length of stay, and total charges) while controlling for patients' characteristics. A cross-sectional analysis was conducted to identify and examine patients who were hospitalized with mRCC. The study examined association between the utilization of IT in mRCC and the burden of illness (BOI)—total charges, and length of stay (LOS), coagulopathy, and arrhythmia through generalized linear models (glm). All analyses were two-tailed, and statistical significance was defined as P<0.05.

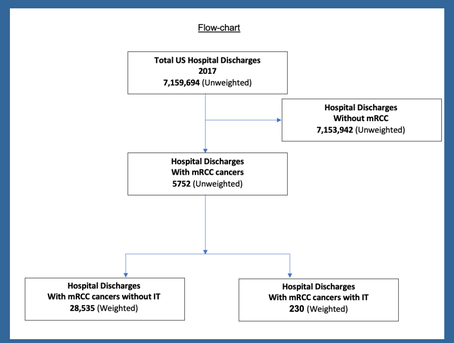

Table 1. Baseline characteristics of Patients hospitalized in 2017 with metastatic renal cell carcinoma with and without immunotherapy.

	Metastatic Renal Cell Carcinoma Without Immunotherapy (Weighted)	Metastatic Renal Cell Carcinoma With Immunotherapy (Weighted)	P value
n	28305	230	
AGE (mean [SD])	65 (12.18)	54 (8.67)	<0.001
Female	9245.0 (32.7)	65.0 (28.3)	0.2
RACE (%)			0.55
White	19570.0 (71.5)	170.0 (81.0)	
Black	3115.0 (11.4)	10.0 (4.8)	
Hispanic	2885.0 (10.5)	20.0 (9.5)	
Others	1815.0 (6.6)	10.0 (4.8)	
Expected primary payer (%)			<0.001
Medicare	15700.0 (55.5)	40.0 (17.4)	
Medicaid	3040.0 (10.8)	10.0 (4.3)	
Private insurance	8265.0 (29.2)	175.0 (76.1)	
Self-pay, No charge and other	1270.0 (4.5)	5.0 (2.2)	
Median household income (based on current year)			0.103
0-25th percentile	7530.0 (27.0)	30.0 (13.3)	
26th to 50th percentile	7325.0 (26.2)	95.0 (42.2)	
51st to 75th percentile	6915.0 (24.8)	45.0 (20.0)	
76th to 100th percentile	6145.0 (22.0)	55.0 (24.4)	
Patient Location: NCHS Urban-Rural Code (%)			0.29
"Central" counties of metro areas of >=1 million population	8010.0 (28.4)	75.0 (32.6)	
"Fringe" counties of metro areas of >=1 million population	6900.0 (24.4)	35.0 (15.2)	
Counties in metro areas of 250,000-999,999 population.	5655.0 (20.0)	45.0 (19.6)	
Counties in metro areas of 50,000-249,999 population &	2580.0 (9.1)	40.0 (17.4)	
Micropolitan counties & Not metropolitan or micropolitan counties.	5105.0 (18.1)	35.0 (15.2)	
Admission type (%)			
Elective	5710.0 (20.2)	170.0 (73.9)	<0.001
Weighted Elixir score mean (SD))	24.66 (8.10)	22.78 (5.63)	0.02
Length of Stay (mean (SD))	6.28 (6.67)	4.98 (1.94)	<0.001
Total Charge (mean (SD))	$72342.73 (91457.76)	$260904.65 (134956.18)	<0.001
In-hospital Mortality (%)	2175.0 (7.7)	0.0 (0.0)	0.22
Cardiac arrhythmias (number (percentage))	5740.0 (20.3)	85.0 (37.0)	0.003
Coagulopathy (number (percentage))	6080 (6.9)	70.(27.5)	<0.001

Abbreviations: SD, Standard deviation; NCHS, National Center for Health Statistics; $, United States' Dollar. LOS: Length of Stay.
Note: All frequencies and percentages are weighted

Results

We analyzed a sample of 230 out of the total 28,535 patients with metastatic renal cell carcinoma (mRCC) who were undergoing immunotherapy (IT) treatment. The patients who received IT treatment had a mean age of 54.50 years with a standard deviation of 8.67, while the patients who did not receive IT treatment had a mean age of 65.80 years with a standard deviation of 12.18. The recipients of IT recipients were predominantly white, accounting for 81.0% of the total. The majority (82.6%) of IT beneficiaries did not receive Medicaid or Medicare. The average total expenses for IT patients were $260,905 [134,956.18], whereas non-IT patients had average charges of $72,343 [$91,457.79]. The length of stay for IT patients was 4.98 [1.94] days, compared to 6.28 [6.67] days for non-IT patients. The incidence of coagulopathy in patients with IT-treated mRCC was 26.1%, while the incidence of arrhythmia was 37.0%. In the adjusted generalized linear model (GLM), after accounting for other variables, the IT was found to be linked with increased total charges. The estimated effect size (Coeff) was 7.67, with a 95% confidence interval ranging from 4.86 to 12.09. In addition, the presence of coagulopathy (adjusted odds ratio [aOR] = 5.61; 95% confidence interval [CI]: 2.40 – 13.14) and arrhythmia (aOR = 4.34; 95% CI: 2.20 – 8.55) was found to be linked with IT. An unadjusted analysis revealed that Private insurance was the primary payer during the IT, and Whites received a greater number of IT compared to Blacks and Hispanics. Furthermore, there is a greater rate of optional admission among individuals who have received IT qualifications.
Cardiotoxicity caused by immune checkpoint inhibitors (ICIs) is infrequent, occurring in less than 1% of cases. However, when it does occur, it is typically severe and has the potential to be life-threatening. Patients may exhibit symptoms such as cardiac fibrosis, cardiac arrest, autoimmune myocarditis, cardiomyopathy, heart failure, pericardial involvement, and vasculitis. This study is the inaugural investigation into the correlation between cardiac and coagulopathy in immunotherapy for cancer patients.

Conclusions

Immunotherapy-treated mRCC patients were more likely to have coagulopathies and arrhythmias, which increased overall costs. Even though IT has been a key component of the treatment of mRCC in recent years, this is the first time that actual data on unfavorable outcomes and costs related to IT is being looked at. The results might have a big impact on how this population receives new supportive care.

References

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