The financial impact of cancer care on renal cancer patients

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Introduction: *Advances in novel treatment options may render renal cell cancer (RCC) patients susceptible to the financial toxicity (FT) of cancer treatment, and the factors associated with FT are unknown.*

Materials and methods: *Eligible patients were ≥ 18 years old and had a diagnosis of stage IV RCC for at least 3 months. Patients were recruited from Princess Margaret Cancer Centre and Sunnybrook Odette Cancer Centre (Toronto, Canada). FT was assessed using the validated Comprehensive Score for Financial Toxicity (COST) instrument, a 12-question survey scored from 0-44, with lower scores reflecting worse FT. Patient and treatment characteristics, out-of-pocket costs (OOP) and private insurance coverage (PIC) were collected. Factors associated with worse FT (COST score < 21) were determined.*

Results: *Sixty-five patients were approached and 80% agreed to participate (n = 52). The median age was 62 (44-88); 20% were female (n = 10); 43% were age ≥ 65 (n = 22); 63% were Caucasian (n = 31). Median COST score was 20.5 (3-44). Factors associated with worse FT were age < 65 (OR 9.5, p = 0.007), high OOP (OR 4.4, p = 0.04) and receiving treatment off clinical trial (in comparison to being on surveillance or on clinical trial) (OR 5.9, p = 0.03), when adjusting for other factors in multivariable logistic regression. However, there was no correlation between annual income or PIC and FT.*

Conclusion: *Financial toxicity in the RCC population is more significant in younger patients and those on treatment outside of a clinical trial. Financial aid should be offered to these at-risk patients to optimize adherence to life prolonging RCC treatments.*

Key Words: financial toxicity, financial burden, financial distress, renal cell cancer

Introduction

In recent years, financial toxicity (FT) in cancer patients has been increasingly studied. Cancer patients with financial concerns may be delayed in seeking treatment and may be more willing to forego treatment.[1] Greater FT can negatively impact treatment adherence and clinical outcomes such as survival and health-related quality-of-life (HRQoL).[2-4] In urologic cancer patients, FT can also lead to higher suicide rates, and urologic oncologists are urged to mindfully engage in FT discussions when making treatment decisions.[5]

Advanced renal cell cancer (RCC) treatment has evolved over the last decade, due to an enhanced understanding of the molecular and immunologic drivers of cancer. The paradigm of metastatic RCC therapies have shifted towards drugs that target particular cancer growth and development pathways.[6,7] Additionally, immunotherapy agents that potentiate lymphocyte

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anti-tumor activity are increasingly incorporated into the treatment paradigm.[8] These treatments have substantially improved outcomes for advanced RCC patients. However, these innovative therapies are accompanied with high costs that are increasingly shifted to patients through insurance copayments, higher deductibles and out-of-pocket expenses.[9]

In order to mitigate FT consequences, health care providers have a responsibility to recognize this as an important issue and deliver high-value cancer care. It is important for the health care team to have an understanding of the financial pressures impacting patients and caregivers. The Comprehensive Score for Financial Toxicity (COST) survey is a tool that was validated to measure FT in advanced cancer patients.[10] Our study aimed to identify underlying factors associated with financial toxicity in advanced RCC patients treated in two cancer centers in Ontario, Canada. Characterizing factors that contribute to financial burden allows health care providers to identify those patients who are most at risk of FT consequences.

Materials and methods

Sample

Patients were eligible if they were over 18 years of age, received a diagnosis of stage IV RCC within the past 3 months and were suitable for consideration for systemic therapy. In order to be enrolled on the study, patients or caregivers were required to speak English. Demographic and treatment characteristics data were collected. Demographic data included self-reported age, sex, family income source, income amount, marital status, postal code, race, country of birth, private insurance coverage (PIC) and out-of-pocket costs (OOP). The OOP question asked patients: "During the past year, about how much did you/your family spend out-of-pocket for your medical care? Include out-of-pocket expenses for prescription drugs, travel, childcare/babysitting, copayments, and deductibles, but do not include health insurance premiums or any costs paid by your health insurance". Data collected on treatment characteristics included type of treatment (surveillance, oral or intravenous therapy) and whether the patient was enrolled in a clinical trial.

Eligible patients were approached consecutively at the Princess Margaret Cancer Centre (PMCC) and Sunnybrook Odette Cancer Centre (SBH). This research study received ethics approval from the University Health Network Research Ethics Board and the Sunnybrook Research Ethics Board. All study participants provided informed consent. Patients were recruited from January to August 2018.

Assessment of financial toxicity

Study participants completed the COST questionnaire at a single point in time. The COST questionnaire is a 12-item tool that has been validated for assessing financial toxicity in cancer patients. The survey asks questions on financial satisfaction, concern about income loss, ability to meet monthly expenses, out-of-pocket costs and control over financial situation in relation to cancer care.[11] The COST survey is scored by summing up the individual questions, some of which are reverse scored. The sum is then divided by the number of questions that contributed to the scale (i.e. the number of questions that were answered). This scoring algorithm allowed scorers to address questions with missing answers by only including scores for questions that were answered, and subsequently adjusting total COST score for the unanswered (missing) questions. COST scores range from 0 to 44, with lower COST scores reflecting poorer sense of financial well-being.

Statistical analysis

Patient demographics were analyzed using descriptive statistics and frequency tabulation. Univariable logistic regression was used to test for associations between COST score and the collected variables. Multivariable logistic regression models were built to determine factors associated with worse FT (COST score < 21, the median COST score in our sample). The change in estimate approach was used to fit the multivariable logistic regression model. Variables were selected in a stepwise fashion to include those that changed the parameter estimate of the key predictor variable (such as age) by ≥ 10%, or were deemed clinically important to include (treatment type, OOP). Model fit was assessed using Hosmer-Lemeshow goodness-of-fit statistics. The statistical significance level was set at 0.05 for the model. All statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, USA).

Results

There were 52 patients who participated in this study, out of the 65 patients that were approached (80%). Baseline patient demographics are summarized in Table 1. The median age of participants was 62 (range 44-88), 10 patients (20%) were female and 42 patients (81%) were married. Thirty-one patients (63%) were Caucasian and 11 patients (22.4%) were Asian. The majority of patients were born in Canada (29, 56%). Most of the study participants were employed or receiving pension income (34, 67%), and only 9 participants were receiving

TABLE 1. **Patient demographics and characteristics**

		Number (%) n = 52
Age, years	< 65	29
	≥ 65	22
	Range	44-88
	Unknown	1
Male sex		41 (80.4%)
Female sex		10 (19.6%)
Missing		1
Cancer center	PMCC	23 (44.2%)
	SBH	29 (55.8%)
Ethnicity	White	31 (63.3%)
	Asian	11 (22.4%)
	Other	7 (14.3%)
	Unknown	3
Married	Yes	42 (80.8%)
	No	10 (19.2%)
Country of birth	Canada	29 (55.8%)
	Other	23 (44.2%)
Distance from cancer center	< 28 km	24 (51.1%)
	≥ 28 km	23 (48.9%)
	Unknown	5
Treatment	Surveillance	8 (16.0%)
	Oral therapy	16 (32.0%)
	Intravenous therapy	11 (22.0%)
	Clinical trial	15 (30.0%)
	Unknown	2
Income source – no. (%)	Employed or on pension	34 (66.7%)
	Unemployed	1 (2.0%)
	Other	16 (31.4%)
	Unknown	1
Annual income[a]	< $40,000	16 (37.2%)
	$40,000-80,000	18 (41.9%)
	> $80,000	9 (20.9%)
	Unknown	9
Total OOP expenditures[a]	< $1000	25 (49.0%)
	$1000-5000	21 (41.2%)
	$5000-10,000	4 (7.8%)
	> $10,000	1 (2.0%)
	Unknown	1
Private insurance	Yes	28 (53.8%)
	No	24 (46.2%)

PMCC = Princess Margaret Cancer Centre; SBH = Sunnybrook Hospital; OOP = out-of-pocket; [a]values in 2020 $CAD

income above $80K per year (9, 21%). The majority of patients were had private drug insurance (28, 54%).

Among our entire population, median COST score was 20.5 (range 3-44). Median financial toxicity was similar among patients treated at PMCC and SBH (21 versus 20).

Variables associated with financial toxicity

In the univariable analysis, younger patients and patients with high OOP expenditures (OOP expenditures ≥ $1000) reported increased levels of financial toxicity ($p < 0.05$). The number of study participants under age 65 who reported increased financial toxicity was almost double the number of older patients (62% versus 32%). Sixty-five percent of study participants with high OOP costs reported increased financial toxicity. Figure 1 depicts the percentage of patients reporting increased financial toxicity, by age and OOP category.

The univariable analysis also found a trend towards increased financial toxicity in patients who were on systemic therapy off clinical trial, and patients who were not receiving employment or pension income ($p = 0.05$). There was no association between sex, ethnicity, marital status, country of birth, distance from cancer center, annual income or private insurance status and financial toxicity in the univariable analysis (all $p > 0.05$). The results of these univariable analyses are described in Table 2.

After adjusting for potential confounders in the multivariable model, the following variables were associated with worse financial toxicity: age < 65, on treatment off trial and high OOP expenditures. The odds of reporting increased financial toxicity were 9.5 times higher in younger patients compared to patients greater than 65 years old ($p = 0.007$). Similarly, the

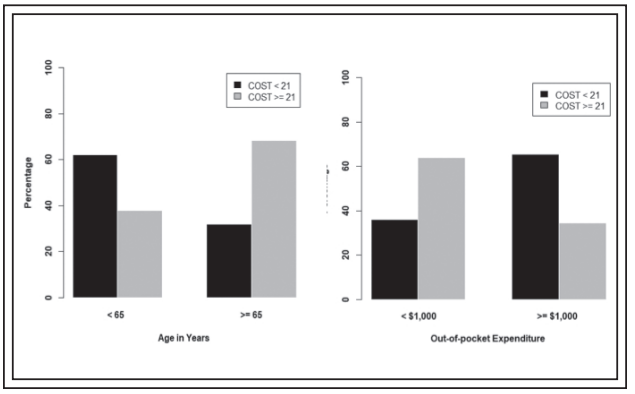

Figure 1. Percentage of patients reporting increased financial toxicity (COST < 21) by age and OOP category.

TABLE 2. **Univariable analysis of factors associated with worse financial toxicity (COST < 21)**

	Odds ratio	95% CI	Univariable p
Age			
<65	3.51	(1.09-11.29)	0.04
≥ 65 (reference)	-		
Distance from cancer center	1.09	(0.35-3.43)	0.88
Treatment			
On systemic therapy off trial (oral or intravenous therapy)	3.19	(1.00-10.17)	0.05
On surveillance or clinical trial (reference)	-		
Employed or on pension			
No	3.43	(0.99-11.93)	0.053
Yes (reference)	-		
Annual income			
< $40,000	-0.51	(0.10-2.57)	0.38 (global p)
$40,000-80,000	1.33	(0.25-7.01)	
> $80,000 (reference)	-		
Total OOP expenditures			
< $1000 (reference)	-		
>= $1000	3.36	(1.06-10.59)	0.04
Private insurance			
No	1.00	(0.34-2.98)	1.00
Yes (reference)	-		

PMCC = Princess Margaret Cancer Centre; SBH = Sunnybrook Hospital; OOP = out-of-pocket

TABLE 3. **Multivariable analysis of factors associated with worse financial toxicity (COST < 21)**

	Adjusted odds ratio	95% CI	Multivariable p
Age			
< 65	9.48	(1.83-49.20)	0.007
≥ 65 (reference)	-		
Treatment			
On systemic therapy off trial (oral or intravenous therapy)	5.92	(1.24-28.12)	0.03
On surveillance or clinical trial (reference)	-		
Total OOP expenditures			
< $1000 (reference)	4.40	(1.04-18.61)	0.04
>= $1000	-		

PMCC = Princess Margaret Cancer Centre; SBH = Sunnybrook Hospital; OOP = out-of-pocket

odds of reporting increased financial toxicity were 5.9 times higher in patients receiving chemotherapy off clinical trial (p = 0.03). Table 3 describes the results of the multivariable analysis.

Discussion

In our multicenter study, we identified factors associated with financial distress in advanced renal cell cancer patients. Increased financial toxicity was associated with younger patients, patients with high OOP costs and patients receiving treatment off clinical trial. Similar levels of financial toxicity were reported in patients treated at PMCC and SBH, the two largest cancer centers in Ontario. In a cost-constrained health care system, it appears that patient level factors have a greater impact on reported financial burden than treatment center.

Our study in advanced lung cancer patients found that patients younger than 65 years old and those with high OOP costs reported increased financial toxicity.[12] These similar findings are likely due to the nature of drug coverage in the Ontario public health care system. Universal coverage of all oral prescription medications exists for patients over 65 years of age, unlike younger patients who are left to rely on insurance plans or other resources to access these therapies. Unfortunately, younger patients with a cancer diagnosis may also be more susceptible to additional financial stressors such as less savings and job loss. Loss of occupation may result in loss of insurance. Unlike the lung cancer population, the present study did not find an association between lack of private insurance coverage and increased financial toxicity in the renal cell population. However, there was an association between patients with high OOP costs reporting increased financial burden (p = 0.04). These differences may be due to the smaller sample size in the RCC study.

Oral anticancer treatments continue to play a large role in renal cell cancer treatment. Treatment options and sequencing of therapies are largely dependent upon patients' International Metastatic Renal Cell Carcinoma Database Consortium Risk Group and histological subtype. Recent trials have demonstrated the efficacy of first-line combination immunotherapy therapy, using nivolumab and ipilimumab PD-1/CTLA-4 inhibition, and immunotherapy plus oral vascular endothelial growth factor (VEGF) inhibitor combinations, which include pembrolizumab plus axitinib, avelumab plus axitinib, and atezolizumab plus bevacizumab.[7,8,13-15] Real world evidence regarding treatment sequencing is continually evolving in the context of this rapidly changing treatment landscape. The drug access, funding, and reimbursement structure of each jurisdiction has a large impact on care practices and treatment sequencing. Current evidence indicates that the majority of patients receive a VEGF-based therapy (axitinib, cabozantinib, everolimus and lenvatinib, pazopanib, sunitinib) in the second-line, following first-line combination therapy.[16-18] In patients previously treated with a VEGF-based therapy, the multi-tyrosine kinase inhibitor, cabozantinib, has demonstrated superior efficacy to the mammalian target of rapamycin (mTOR) inhibitor, everolimus.[19] Finally, single-agent nivolumab has been established as a superior therapy to everolimus in patients, who have received at least one VEGF-based therapy and remains a treatment option later in the sequencing of treatment in many patients.[20]

The cost of these newer oral targeted agents is dramatically different than traditional cytotoxic chemotherapy costs. For example, Nazha et al reported that the median cost of treating metastatic RCC patients with up to 2 lines of targeted therapy is over $56,000.[21] In order to manage this monetary burden, many public and private payers are increasingly implementing cost sharing measures that shift more of the financial responsibility to patients.[22] Prior research has shown that nonelderly adults are more prone to the high OOP costs of cancer treatment.[23] We found that more than half of the patients in our study (> 51%) reported OOP expenditures that exceeded $1000 in the past year, with approximately 10% reporting OOP costs more than $5000. Although these medical care costs may include other expenditures such as travel and childcare, it is conceivable that prescription drug expenses comprise a significant portion of these costs.

As greater focus is placed on the economic burden of cancer, cost discussions are becoming a critical component of care. The health care team has increased responsibility to deliver high-value care, which means favoring treatments that maximize clinical benefit while minimizing financial impact on the patient. Zafar et al studied 300 cancer patients and found that 57% of patients who had engaged in a cost discussion with their oncologist reported reduced OOP expenses as a result of that discussion.[24] Physicians can benefit from more information on how to approach these cost discussions, and a greater recognition of how susceptible patients is at the start of therapy. Ultimately, it is important to note that tackling these financial challenges requires access to resources provided by the entire health care team including social workers, nursing, pharmacists and medication reimbursement specialists.

Some study limitations should be noted. Our study sample size was small, which can limit generalizability. Additionally participants were recruited solely from academic centers. This may present a selection bias because factors associated with financial toxicity may vary in the community setting. Due to the cross-sectional nature of our study design, we did not capture data on the evolution of financial toxicity as patients progressed through treatment, and future work can explore this. As a metastatic RCC patient progresses through their cancer journey, knowledge of when the financial stressors are most likely to peak is important to help understand the best time to intervene.

Conclusion

Our study in advanced renal cell cancer patients found that increased financial toxicity was reported in patients less than 65 years old, patients with high OOP costs and those receiving treatment outside of a clinical trial setting. Clinician sensitivity to these financial burdens can be targeted to this subset of patients. Interventions such as explicit cost and value of treatment discussions should occur at the patient-provider level to mitigate financial distress in these patients. Targeting financial aid to patients younger than 65 can optimize treatment adherence to life prolonging RCC treatments. □

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