

Metformin Use in Relation With Survival Outcomes of Patients With Renal Cell Carcinoma

Jaryl Jun Sheng Cheng,¹ Huihua Li,² Hui Shan Tan,¹ Puay Hoon Tan,³
Lay Guat Ng,⁴ Quan Sing Ng,¹ Chee Keong Toh,¹ Ravindran Kanesvaran,¹
Min-Han Tan¹

Abstract

Metformin is a cheap and widely available diabetic drug that suppresses cancer cell metabolism and proliferation. A total of 290 diabetics with localized and 100 diabetics with metastatic renal cell carcinoma (RCC) were studied. The analysis demonstrated that metformin use was associated with significantly better disease-free survival and cancer-specific survival in localized RCC, but no difference was shown among diabetics with metastatic RCC. Metformin use is correlated with improved survival in patients with localized RCC, but not in metastatic RCC.

Purpose: To examine the effect of metformin use on survival outcomes in patients with renal cell carcinoma (RCC).

Methods: Retrospective analysis of 1528 RCC patients from 2 centers between 1992 and 2012 was conducted. A total of 390 diabetics with confirmed metformin use were included in the final analysis, with a median follow-up of 43.1 months. Primary outcomes were disease-free survival (DFS) and cancer-specific survival (CSS). Cox regression models were performed to evaluate the effects of potential predictors on DFS and CSS, following stratification of patients into local and metastatic disease. **Results:** We identified 290 diabetics with localized and 100 with metastatic RCC. There were no clinicopathologic differences in the profiles of metformin users and non-metformin users. For patients with localized RCC, metformin users had significantly better DFS (hazard ratio, 0.47; $P < .01$) and CSS (hazard ratio, 0.21; $P < .01$) than non-users. There was no difference in CSS between metformin users and non-metformin users in diabetics with metastatic RCC (hazard ratio, 0.78; $P = .286$). Limitations include retrospective design and lack of data on metformin dosage and duration of use. **Conclusions:** Metformin use is correlated with improved survival in patients with localized RCC, but not in metastatic RCC. Future studies should focus on its potential mechanisms and clinical utility.

Clinical Genitourinary Cancer, Vol. 14, No. 2, 168-75 © 2016 Elsevier Inc. All rights reserved.

Keywords: Biguanides, Cancer metabolism, Diabetes, Dimethylbiguanidine, Drug repurposing

Introduction

Metformin is one of the most frequently used first-line diabetic drugs¹ together with sulphonylureas. It has a good safety profile with few adverse side effects in chronic use. As such, its potential utility as an anti-cancer agent is of high interest. It is currently under evaluation as an anti-cancer drug. Studies show that metformin can affect cancer incidence, morbidity, and mortality, including that of prostate, breast, and colorectal cancers in diabetics.²⁻⁸ This is

significant as studies have shown that diabetes is a risk factor for total cancer incidence and mortality, including that of renal cell carcinoma (RCC).^{2,3,9,10}

Despite accumulating evidence of clinical utility in other cancers, there are no published clinical studies systematically examining the effect of metformin on RCC patient outcomes in both localized and metastatic RCC.^{11,12} In the study conducted by Hakimi et al, 784 patients who underwent partial or radical nephrectomy for pathological stage 2 and stage 3 tumors were studied. This study excluded metastatic disease. Multivariate analysis demonstrated that metformin use was not protective with respect to recurrence or cancer-specific survival (CSS) on post-surgical patients with high-risk, localized RCC.¹¹ A second similar study by Psutka et al involved 283 diabetic patients with localized RCC. Again, metastatic disease was excluded. Similar to the study conducted by Hakimi et al, it was found that metformin use was not independently associated with progression-free survival, CSS, or overall survival in post-surgical patients with localized RCC.¹²

¹Department of Medical Oncology, National Cancer Centre Singapore, Singapore

²Department of Health Services Research

³Department of Pathology

⁴Department of Urology
Singapore General Hospital, Singapore

Submitted: Aug 18, 2015; Accepted: Dec 15, 2015; Epub: Dec 21, 2015

Address for correspondence: Min-Han Tan, MBBS, FRCP, PhD, Division of Medical Oncology, National Cancer Centre Singapore, 11 Hospital Drive, Singapore 169610
E-mail contact: minhan.tan@gmail.com

Table 1 Characteristics of Renal Cell Carcinoma Patients

Descriptor	Localized RCC			Metastatic RCC		
	Metformin-Using Diabetics (n = 131)	Non-Metformin-Using Diabetics (n = 159)	P Value	Metformin-Using Diabetics (n = 53)	Non-Metformin-Using Diabetics (n = 47)	P Value
Age, mean (SD)	59.0 (10.9)	59.8 (10.2)	.56	63.2 (10.5)	60.6 (9.7)	.20 ^b
Gender, %			.31			.66
Male	87 (66.4)	115 (72.3)		37 (69.8)	35 (74.5)	
Female	44 (33.6)	44 (27.7)		16 (30.2)	12 (25.5)	
Race, %			.80			.67
Chinese	92 (76.7)	120 (80.0)		38 (74.5)	39 (83.0)	
Indian	12 (10.0)	13 (8.7)		5 (9.8)	3 (6.4)	
Malay	16 (13.3)	17 (11.3)		8 (15.7)	5 (10.6)	
Follow-up time, months ^a	62.4 (0.6, 261.7)	54.0 (0.4, 336.6)	—	12.3 (0.6, 284.8)	8.5 (0.5, 96.5)	—
BMI, kg/m ^{2a}	26.8 (17.5, 45.1)	25.2 (17.0, 41.5)	.14	24.1 (19.3, 33.0)	23.7 (17.2, 32.9)	.45 ^b
Chronic renal failure, %			.0002			.52
No	91 (90.1)	92 (69.7)		33 (82.5)	34 (89.5)	
Yes	10 (9.9)	40 (30.3)		7 (17.5)	4 (10.5)	
Hypertension, %			.61			.0013
No	20 (19.2)	22 (16.4)		5 (11.1)	18 (42.9)	
Yes	84 (80.8)	112 (83.6)		40 (88.9)	24 (57.1)	
Grade of RCC at diagnosis, %			.07			.91
1	16 (13.1)	10 (7.1)		1 (5.0)	2 (7.7)	
2	69 (56.6)	70 (49.6)		7 (35.0)	7 (26.9)	
3	24 (19.7)	46 (32.6)		6 (30.0)	10 (38.5)	
4	13 (10.7)	15 (10.6)		6 (30.0)	7 (26.9)	
Vascular invasion at diagnosis, %			.88			1.0
No	79 (78.2)	102 (77.3)		6 (28.6)	7 (25.0)	
Yes	22 (21.8)	30 (22.7)		15 (71.4)	21 (75.0)	
Lymphovascular invasion at diagnosis, %			1.0			1.0
No	98 (88.3)	121 (89.0)		8 (50.0)	9 (47.4)	
Yes	13 (11.7)	15 (11.0)		8 (50.0)	10 (52.6)	
Stage of RCC at diagnosis, %			.97			—
I	77 (60.2)	93 (59.6)		—	—	
II	10 (7.8)	14 (9.0)		—	—	
III	41 (32.0)	49 (31.4)		—	—	
IV	0 (0)	0 (0)		53 (100.0)	47 (100.0)	
Nephrectomy done, %			.26			.69
No	8 (6.1)	5 (3.1)		30 (56.6)	29 (61.7)	
Yes	123 (93.9)	154 (96.9)		23 (43.4)	18 (38.3)	
Subtypes of RCC, %			.72			.43
CCRCC	116 (88.5)	138 (86.8)		43 (81.1)	41 (87.2)	
Non CCRCC	15 (11.5)	21 (13.2)		10 (18.9)	6 (12.8)	
Use of TKI as first line agent, %			—			1.0
No	—	—		41 (77.4)	36 (76.6)	
Yes	—	—		12 (22.6)	11 (23.4)	

Download English Version:

<https://daneshyari.com/en/article/2752017>

Download Persian Version:

<https://daneshyari.com/article/2752017>

[Daneshyari.com](https://daneshyari.com)