

Statin Use and its influence on Survival Outcomes in patients with Renal Cell Carcinoma: A Systematic Review and Meta-analysis

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Introduction

- Statin use has been associated with improved survival outcomes in various cancers.
- However, studies evaluating the association between statin use and outcomes in renal cell carcinoma (RCC) produced conflicting results.
- A systematic review and meta-analysis were performed to investigate the association between statin use and survival of patients with RCC.

Research Question or Hypothesis

- Does statin use improve survival outcomes in patients with RCC?

Methods

- A systematic review and meta-analysis.

Study Design

- This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.
- The PubMed, MEDLINE, EBSCOhost, Cochrane library, Google Scholar were searched using MeSH and keywords.
- Observational studies exploring the association between statin use in RCC patients of any clinical stage were included.
- Studies published in non-English languages, had missing data on survival outcomes, case reports, case series, commentary, editorial, or letter to the editor were excluded.
- Data extractions were performed independently by two reviewers and discrepancies were resolved by consensus.
- We pooled hazard ratios with 95% CI for OS, PFS, CSS, DFS and RFS using random-effects models.
- Heterogeneity was assessed by the χ^2 test and expressed by the I^2 index.
- The risk of bias in studies was assessed using Newcastle-Ottawa Scale for observational studies and publication bias using funnel plot and Egger's test.
- Analysis was conducted using RevMan 5.4 and STATA 14.2 software.
- A p-value of <0.05 was considered statistically significant.

Table 1. Characteristics of the included studies

Study	Study Design	Country	No. of patients	Age (mean)	Men (%)	Race/Ethnicity	Main treatment	Stage	Statin Use	No. Statin Users	Median Follow up (months)	Outcomes Reported
Lee 2013	RC	Multinational	416	59	69	White	Interferon and temsirolimus	IV	Concurrent	34	17.9	OS and PFS
Nielsen 2012	RC	Denmark	295925	69	96	White	Radical/partial nephrectomy	I-IV	Regular	18721	31.2	CSS
Choi 2013	RC	Korea	315	61.3	62.6	Asian	Radical/partial nephrectomy	I-III	Concurrent	21	40	PFS, RFS
Krane 2014	RC	USA	339	61.8	NR	Multi ethnicity	Robot-assisted partial nephrectomy	I-III	Concurrent	104	19.7	PFS, PFS
Hamilton 2014	RC	USA	2608	61.2	65.1	Multi ethnicity	Radical/partial nephrectomy	I-IV	Concurrent	699	36	OS and PFS
Viers 2015	RC	USA	2357	63	67	Multi ethnicity	Radical/partial nephrectomy	I-III	Regular	630	93.6	OS, CSS, and PFS
Kaffenberger 2015	RC	USA	916	60.8	65	Multi ethnicity	Radical/partial nephrectomy	I-IV	Concurrent	270	43.5	OS and CSS
Haddad 2015	RC	USA	850	57.1	57.9	Multi ethnicity	Radical/partial nephrectomy	I-III	Concurrent	342	25	OS, CSS, RFS and PFS
McKay 2016	RC	Multinational	4736	71.2	73.2	Multi ethnicity	Target therapy	IV	Concurrent	513	30	OS and PFS
Nayag 2016	RC	Canada	893	57.4	64.3	Multi ethnicity	Radical/partial nephrectomy	I-III	Concurrent	259	47	OS, PFS, CSS, DFS and RFS
El-Bafal 2017	RC	USA	26107	63.2	53.6	Multi ethnicity	Radical/partial nephrectomy	I-IV	Concurrent	6908	32	OS
Neumann 2019	RC	Germany	388	64.2	66.8	White	Radical/partial nephrectomy	I-III	Concurrent	207	57.9	OS
Boegemann 2020	PC	Germany	557	67	71.8	Multi ethnicity	Target therapy	IV	Concurrent	130	40	OS and PFS
Heide 2020/2019	RC	Multinational	104	62	66	White	Radical/partial nephrectomy	I-III	Concurrent	41	35.4	CSS and OS
Fiala 2021	RC	Czech	343	64.5	74.3	White	Target therapy	IV	Concurrent	78	19.9	OS and PFS
Santoni 2022	RC	Multinational	304	NR	74	White, Hispanic	Immunotherapy and/or target therapy	IV	Concurrent	93	35.8	OS and PFS
Berquist 2017	RC	USA	283	57.5	66.1	Multi ethnicity	Radical/partial nephrectomy	I-III	Concurrent	180	68	OS, CSS, and PFS
Lee, 2014	RC	USA	155			Multi ethnicity	Radical/partial nephrectomy		Regular	92	68	OS, CSS, and PFS
Gayed 2014	RC	USA	63	61*		Multi ethnicity	Targeted therapy		Concurrent	34	22	CSS

Figure 1

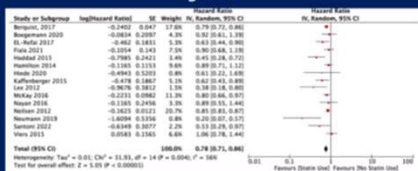


Figure 3

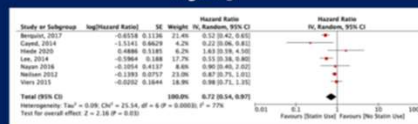


Figure 2

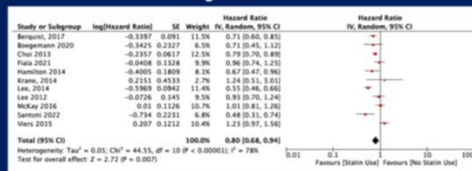
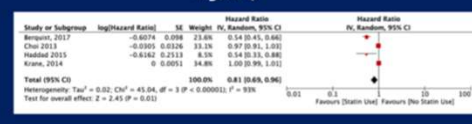


Figure 4



Meta-analysis of the effect of statin use on overall survival Fig. (1), PFS Fig. (2), CSS Fig. (3) and RFS Fig. (4) in patients with RCC

Results

- Patients mean age ranged between 57.1 to 69 years, and the proportions of men ranged between 56.3 and 74.3%.
- The mean follow-up durations was between 12 to 94.6 months.
- A total of 19 cohort studies involving 337,459 RCC patients were included in this meta-analysis (Table 1).
- Statin use was associated with a better OS (HR: 0.78, 95%CI: 0.71, 0.86, $p < 0.00001$; $I^2 = 56%$); (Fig. 1); PFS (HR: 0.80, 95% CI: 0.86, 0.94, $p = 0.007$; $I^2 = 78%$) (Fig. 2); CSS (HR: 0.72, 95% CI: 0.54, 0.97, $p = 0.03$; $I^2 = 77%$) (Fig. 3), and RFS (HR: 0.81, 95% CI: 0.69, 0.96, $p = 0.01$; $I^2 = 93%$) (Fig. 4).
- The Subgroup analyses showed similar OS in patients with both surgical and non-surgical treatments.
- Patients with stage I-III and stage IV also had improved OS.
- Significant heterogeneity was observed in all analyses except for estimating OS for non-surgical treatments and estimating PFS for stage IV tumor.
- No apparent publication bias based on the funnel plots and Egger's test ($p > 0.05$).

Conclusions

- Statin use was associated with improved overall survival in patients with RCC.
- Although, all the studies included were retrospective cohort, prospective clinical studies should be considered to validate these results.
- Our findings suggest that statins may be used as a potential adjuvant therapy for patients with RCC.

Disclosures

Authors have no financial or other conflicts of interest to declare



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