The impact of angiotensin-converting enzyme inhibitors on lung cancer and non-lung cancers compared with angiotensin II receptor blockers

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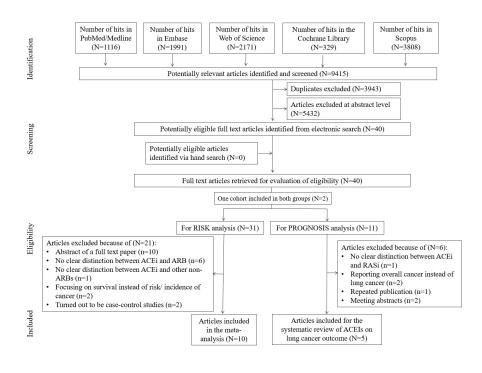
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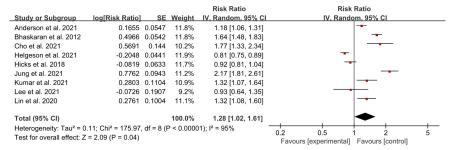
Abstract

Aim: Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs) have been reported to manifest controversial relationships with cancer, and recent focus concerning the tumorigenic effect of ACEIs mainly falls on lung cancer. We compared ACEIs with ARBs for their impact on the risk and prognosis of lung cancer and non-lung cancers, respectively. *Methods:* A meta-analysis was performed to explore the impact of ACEIs on the risk of lung cancer and non-lung cancers, while a systematic review was performed to further analyze ACEIs' influence on the prognosis of lung cancer. Terms concerning ACEIs and cancer were searched, and 10 cohort studies were included for risk analysis, while 5 cohort studies were included for analyzing the prognosis of lung cancer. *Results:* Initial pooled result revealed that ACEIs prescription is associated with an observed increase on the risk of lung cancer (RR 1.28, 95% CI 1.02-1.61), colorectal cancer (RR 1.46, 95% CI 1.13-1.87) and hepatic cancer (RR 2.00, 95% CI 1.01-3.94) when compared with ARBs, but further sensitivity analyses suggested the results unsolid, thus neither the development of lung cancer nor non-lung cancers could be proved associated with ACEIs prescription. However, systematic review suggested that ACEIs prescription is associated with an improved lung cancer prognosis. *Conclusion:* There has been no adequate evidence to demonstrate that ACEIs are associated with a higher incidence of lung cancer or non-lung cancers, but an improved prognosis of lung cancer was observed in patients taking ACEIs. Large-scale RCTs are needed and underlying mechanisms need further exploration.

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	Experimental		Control		Risk Ratio		Risk Ratio	
Study or Subgroup 1.2.1 Colorectal Cance		Total	Events	Total	weight	M-H. Random, 95% CI	M-H. Random. 95% Cl	
		000005	004	100111	44 50/	4 40 14 00 4 001	-	
Bhaskaran et al. 2012 Cho et al. 2021		269235		108414	11.5% 10.0%	1.19 [1.06, 1.33]		
	61	4210	474	55645		1.70 [1.31, 2.22]		
Jung et al. 2021 Subtotal (95% CI)	111	5915 279360	2155	185199 349258	10.9% 32.4%	1.61 [1.33, 1.95] 1.46 [1.13, 1.87]	-	
Total events	1304	279300	3013	349230	32.4%	1.40 [1.13, 1.07]	-	
Heterogeneity: Tau ² = 0		- 11 00 -		0.0041	2 - 0.00/			
Test for overall effect: Z			1 = 2 (P =	0.004); 1-	62%			
Test for overall effect. Z	= 2.55 (F	= 0.003)						
1.2.2 Breast Cancer								
Bhaskaran et al. 2012	1631	269235	780	108414	11.7%	0.84 [0.77, 0.92]	-	
Cho et al. 2021	8	4210	204	55645	4.9%	0.52 [0.26, 1.05]		
Subtotal (95% CI)		273445		164059	16.7%	0.75 [0.50, 1.12]		
Total events	1639		984					
Heterogeneity: Tau ² = 0	.05; Chi ² =	= 1.79, df	= 1 (P = 0).18); l ² =	44%			
Test for overall effect: Z								
1.2.3 Prostate Cancer								
Bhaskaran et al. 2012	2325	269235	700	108414	11.7%	1.34 [1.23, 1.45]	-	
Cho et al. 2021	28	4210	244	55645	8.3%	1.52 [1.03, 2.24]		
Siltari et al. 2018	4342	34700	2794	20365	11.9%	0.91 [0.87, 0.95]	•	
Subtotal (95% CI)		308145		184424	32.0%	1.19 [0.86, 1.66]	-	
Total events	6695		3738					
Heterogeneity: Tau ² = 0			f = 2 (P <	0.00001)	; l ² = 97%			
Test for overall effect: Z	= 1.06 (P	= 0.29)						
1.2.4 Hepatic Cancer								
Cho et al. 2021	28	4210	266	55645	8.3%	1.39 [0.94, 2.05]	<u> </u>	
Jung et al. 2021	93	5915		185199	10.6%	2.76 [2.24, 3.41]		
Subtotal (95% CI)	55	10125	1004	240844	19.0%	2.00 [1.01, 3.94]		
Total events	121		1320			2.00 [1.01, 0.04]		
Heterogeneity: Tau ² = 0		= 9.49. df		0.002): l ² :	= 89%			
Test for overall effect: Z			. (0070			
Total (95% CI)		871075		938585	100.0%	1.30 [1.06, 1.60]		
Total events	9759		9055					
Heterogeneity: Tau ² = 0			df = 9 (P	< 0.00001	1); I ² = 96%	6	0.2 0.5 1 2 5	
Test for overall effect: Z	- 0 FC (D	= 0.01					0.0 1 2 3	