Risk of acute pancreatitis associated with ARBs and ACE inhibitors: a meta-analysis of observational studies

Carlos Alves[1,2], Ana Penedones[1,2], Diogo Mendes[1,2], Francisco Batel-Marques[1,2]

[1] Laboratory of Social Pharmacy and Public Health, Faculty of Pharmacy, University of Coimbra, Coimbra, Portugal.
[2] Clevidence, Porto Salvo, Portugal.

EPH8

OBJECTIVES

- Several observational studies evaluated the risk of acute pancreatitis associated with drugs acting in the Renin–Angiotensin–Aldosterone System, but the results are conflicting.[1-4]
- This meta-analysis is aimed at investigating the risk of acute pancreatitis associated with two classes of Renin-Angiotensin-Aldosterone System inhibitors, the Angiotensin-converting enzyme (ACE) inhibitors and the Angiotensin II receptor blockers (ARBs).

METHODS

- PUBMED and EMBASE were searched from their inception to July 5th, 2024, to identify cohort and case-control studies evaluating the risk of acute pancreatitis associated with either ACE inhibitors or ARB.

- A meta-analysis using a random-effects model was performed to pool odds ratios (ORs) with their 95% confidence intervals (CIs). Between-studies heterogeneity was assessed using the I^2 statistics.

- A sensitivity analysis was conducted to explore the robustness of the initial findings, using two additional methods: a) the Knapp-Hartung method in combination with the Paule-Mandel estimator for the between-study variance; b) a bayesian random-effects meta-analysis.

RESULTS

- Eleven observational studies were retrieved from the literature search, 10 reporting results for ACE inhibitors and 7 reporting results for ARBs.[1-11]

- According to the initial analysis, ACE inhibitors increase the risk of acute pancreatitis (OR 1.33; 95% CI 1.12 – 1.58; I^2 = 93%), but not ARBs (OR 0.82; 95% CI 0.80 – 0.83; I^2 = 0%). Reanalysis of the data according to the Knapp-Hartung method did not significantly change the initial findings.

- The results reported by the bayesian meta-analyses identified an increased risk of acute pancreatitis associated with ACE inhibitors [OR 1.24; 95% credible interval (CrI) 1.00 – 1.59), but not with ARBs (OR 0.81; 95% CrI 0.63 – 1.03).
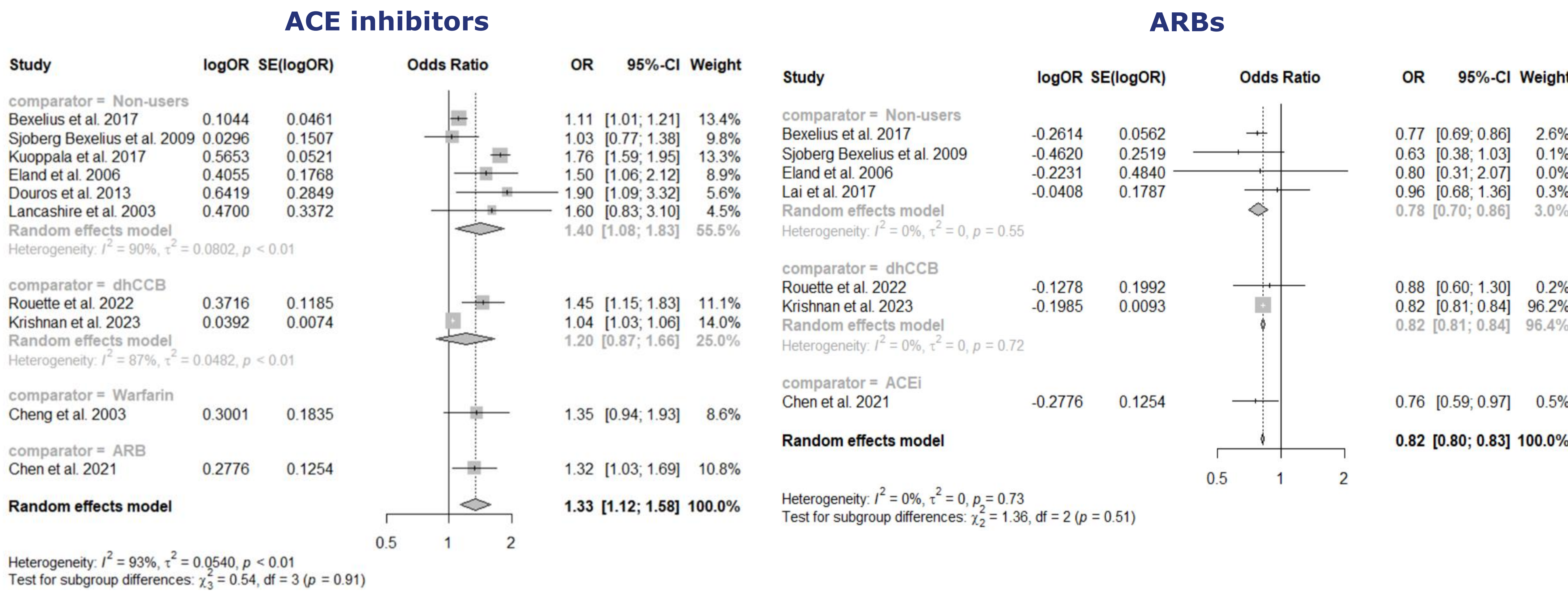

Figure 1. Meta-analysis of the risk of acute pancreatitis associated with ACE inhibitors and ARBs.

Abbreviations: ACE, angiotensin-converting enzyme; ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blocker; CI, confidence interval; dhCCB, dihydropyridine calcium channel blockers; OR, odds ratio; SE, standard error.

CONCLUSIONS

The results from this meta-analysis suggest ACE inhibitors increase the risk of acute pancreatitis, confirming the results reported by some observational studies published over the years. No new increased risk was found for ARBs.

REFERENCES: 1) Bexelius TS, et al. Angiotensin II receptor blockers and risk of acute pancreatitis - a population based case–control study in Sweden. BMC Gastroenterol 2017;17:36. 2) Rouette J, et al. Renin–Angiotensin–Aldosterone System Inhibitors and Risk of Acute Pancreatitis: A Population-Based Cohort Study. Drug Saf 2022;45:65–74. 3) Douros A, et al. Drug-induced acute pancreatitis: results from the hospital-based Berlin case-control surveillance study of 102 cases. Aliment Pharmacol Ther 2013;38:825–34. 4) Kuoppala J, et al. ACE inhibitors and the risk of acute pancreatitis—a population-based case–control study. Pharmacoepidemiol Drug Saf 2017;26:853–7. 5) Cheng RM, et al. Association between ACE Inhibitors and Acute Pancreatitis in the Elderly. Annals of Pharmacotherapy 2003;37:994–8. 6) Sjöberg Bexelius T, García Rodríguez LA, Lindblad M. Use of Angiotensin II Receptor Blockers and the Risk of Acute Pancreatitis: A Nested Case-Control Study. Pancreatology 2009;9:786–92. 7) Eland IA, et al. Antihypertensive medication and the risk of acute pancreatitis: The European case-control study on drug-induced acute pancreatitis (EDIP). Scand J Gastroenterol 2006;41:1484–90. 8) Lai S-W, et al. No association between losartan use and acute pancreatitis in hypertensive patients. European Journal of Hospital Pharmacy 2017;24:120–3. 9) Chen R, et al. Comparative First-Line Effectiveness and Safety of ACE (Angiotensin-Converting Enzyme) Inhibitors and Angiotensin Receptor Blockers: A Multinational Cohort Study. Hypertension 2021;78:591–603. 10) Krishnan A, et al. 575 Risk of acute pancreatitis with the use of reninangiotensin-aldosterone system inhibitors: a multicenter matched cohort study. Gastroenterology 2023;164:S104. 11) Lancashire RJ, Cheng K, Langman MJS. Discrepancies between population-based data and adverse reaction reports in assessing drugs as causes of acute pancreatitis. Aliment Pharmacol Ther 2003;17:887–93.

DISCLOSURES: The authors have no conflicts of interests that are relevant to the content of this work.

CLEVIDENCE

FACULDADE DE FARMÁCIA
UNIVERSIDADE Ð COIMBRA
1290