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(REVIEW ARTICLE)

ACE Inhibitors vs ARBs in Hypertensive Diabetics: A systematic review of cardiovascular mortality and renal outcomes

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Abstract

Hypertension in individuals with diabetes markedly increases the risk of cardiovascular events and renal complications, making optimal management essential. Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) are widely prescribed as modulators of the renin–angiotensin–aldosterone system (RAAS). This systematic review examined their relative effectiveness in reducing cardiovascular mortality and preserving kidney function among hypertensive diabetic patients. Literature was searched across PubMed, Cochrane Library, and Scopus for randomized controlled trials and meta-analyses published within the last twenty years. Both ACEIs and ARBs were found to lower blood pressure effectively and delay the progression of diabetic nephropathy. ACEIs showed a modest advantage in lowering cardiovascular and all-cause mortality, while ARBs demonstrated comparable renal protective effects with better tolerability in patients intolerant to ACEIs. Evidence also suggests ARBs may provide greater benefit in advanced stages of chronic kidney disease, whereas ACEIs appear more advantageous in primary cardiovascular prevention. These findings emphasize the need for individualized treatment approaches, with ACEIs recommended as first-line therapy when tolerated, and ARBs as suitable alternatives. Further large-scale comparative trials are warranted to refine clinical decision-making and maximize therapeutic outcomes in this high-risk population.

Keywords: Angiotensin converting Enzyme (ACE) inhibitors; Angiotensin receptor blocker; Hypertensives; Diabetics; Cardiovascular mortality; Renal Outcomes

1. Introduction

Hypertension is a leading global health burden and a significant risk factor for cardiovascular morbidity and mortality [1]. The use of renin–angiotensin–aldosterone system (RAAS) inhibitors, particularly angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs), has transformed the management of hypertension, diabetes, and renal complications [2,3]. Although ACEIs and ARBs act through distinct pharmacological mechanisms, both drug classes provide cardiovascular and renal protection [4,5]. However, their comparative effectiveness in hypertensive diabetic patients remains an area of clinical and research interest, especially with respect to cardiovascular mortality and renal outcomes [6,7].

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Several landmark clinical trials, meta-analyses, and real-world studies have evaluated the relative efficacy and safety of ACEIs versus ARBs [8–10]. Some evidence suggests that ACEIs may offer superior cardiovascular protection, while ARBs are generally better tolerated due to fewer adverse effects, such as cough and angioedema [11–13]. This systematic review aims to synthesize current evidence comparing ACEIs and ARBs in hypertensive diabetic populations, with a focus on cardiovascular mortality and renal outcomes.

Objective

To systematically review and compare the impact of ACE inhibitors versus ARBs on Cardiovascular mortality and renal outcomes in hypertensive diabetic patients.

2. Methods

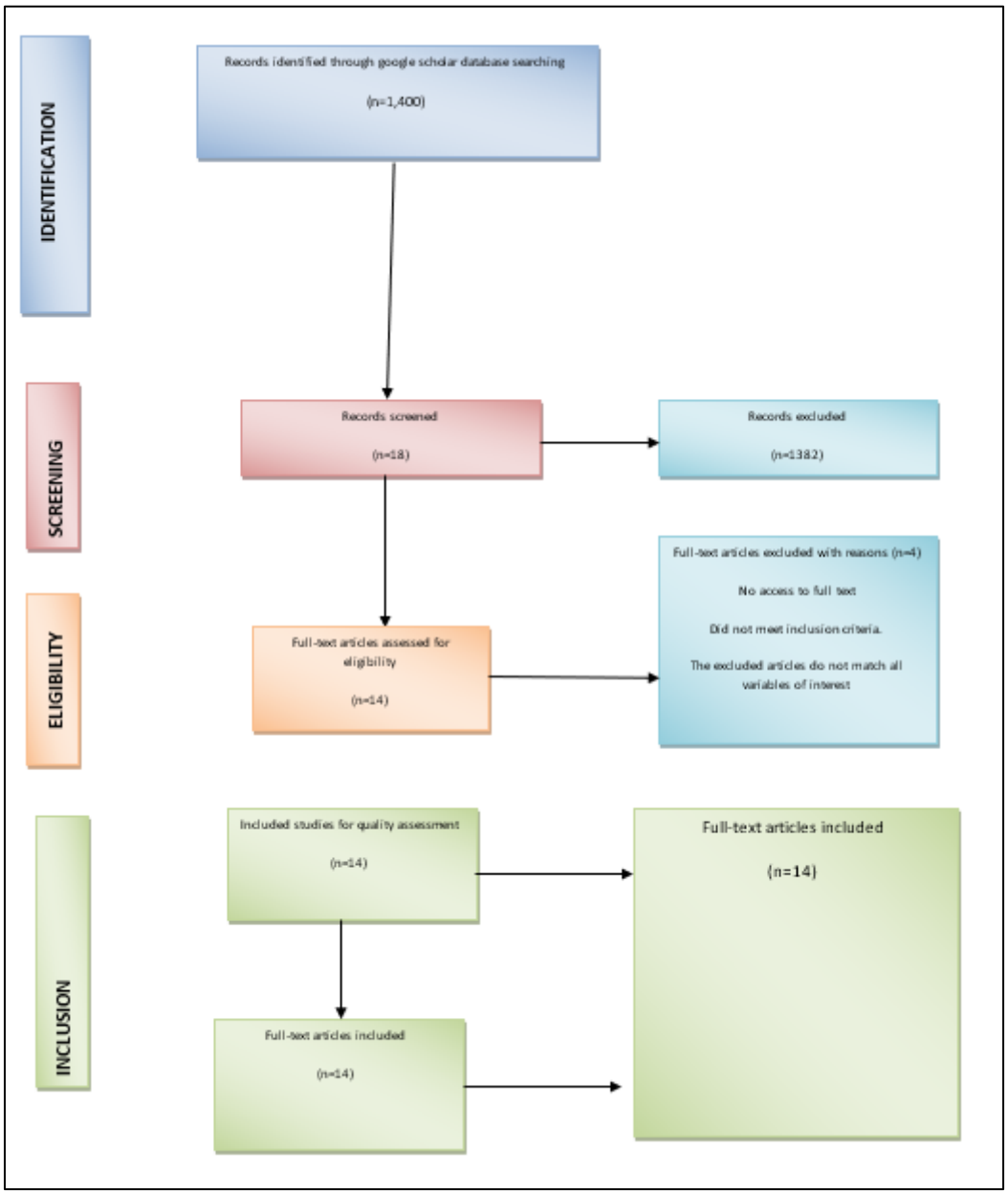

Figure 1 Prisma flow chart

The methodological framework employed in conducting this systematic review is guided by PRISMA 2020, a systematic search of PubMed, Scopus, Web of Science, and Google Scholar was conducted to identify randomized controlled trials (RCTs), meta-analyses, and observational studies comparing ACEIs and ARBs in hypertensive diabetic patients. Studies

published between 2000 and 2025 were included. Outcomes accessed were cardiovascular mortality, major adverse cardiovascular events (MACE), and renal end point such as electrolyte glomerular filtration rate (eGFR) decline, albuminuria, and progression to end stage renal disease (ESRD).

Table 1 PICO Framework

Population (P)	**Adults with both hypertension and diabetes mellitus**
Intervention (I)	ACE inhibitors
Comparison (C):	ARBs
Outcomes (O)	Cardiovascular mortality, major adverse cardiovascular events (MACE), renal outcomes (e.g., eGFR decline, proteinuria, ESRD)

The methodology also includes the development of a research question using the PICO framework, eligibility criteria for study selection, the search strategy applied through Google Scholar, procedures for screening and selection, data extraction methods, and the tools used for assessing the quality and risk of bias in the included studies.

2.1. Eligibility Criteria

The following inclusion and exclusion criteria were used to determine study eligibility:

Table 2 Inclusion and exclusion criteria

Inclusion Criteria	**Exclusion Criteria**
Studies involving adults diagnosed with both hypertension and diabetes	Studies not involving adults diagnosed with both hypertension and diabetes
Comparative studies evaluating ACE inhibitors vs ARBs	Studies not involving a direct comparison of ACE inhibitors and ARBs
Studies reporting cardiovascular mortality and/or renal outcomes (e.g., eGFR, ESRD, albuminuria)	Studies not reporting cardiovascular mortality and/or renal outcomes (e.g., eGFR, ESRD, albuminuria)
Peer-reviewed articles published	Unreviewed articles published
Articles written in English	Articles written in other languages

3. Results

Table 3 Summary of included articles

SN	STUDY	YEAR	AUTHOR	COUNTRY/REGION	DESIGN/ SAMPLE SIZE	POPULATION	INTERVENTION/COMPARATOR	CARDIOVASCULAR OUTCOME	RENAL OUTCOME	KEY FINDINGS
1	Renin inhibitors vs ARBs for Primary Hypertension	2025	Wang GM, Li LJ, Fan L, Xu M, Tang WL, Wright JM	China and Canada	Systematic review of 11 RCTs; N=6780	Adults with mild primary hypertension (age 52–59, no CV disease)	Aliskiren vs ARBs (losartan, valsartan, irbesartan, telmisartan); duration 4 weeks–9 months	No significant difference in mortality, no MI/stroke data	No ESRD data	Little/no difference in outcomes; short duration studies; need for larger, longer-term RCTs
2	Use of ACEi/ARBs, SGLT2 inhibitors and MRAs Can Help Us Reach the Therapeutic Ceiling in CKD	2024	Pantelis Sarafidis	Greece	Narrative review; references major trials	CKD patients, T2D, albuminuria, hypertension	ACEI, ARBs, SGLT2i (empagliflozin, dapagliflozin), MRA (finerenone) vs placebo/standard care	SGLT2i ↓ CV and all-cause death; ACEI/ARB show no CV benefit in CKD	ACEI/ARB ↓ eGFR decline; SGLT2i ↓ to <0.5 mL/min/1.73m^2 /year; Finerenone beneficial in T2D + CKD	ACEi/ARB foundational; SGLT2i/MRA additive benefit; avoid dual RAS blockade due to safety
3	Diabetic Nephropathy-Based Hypertension Treatment	2023	F. Josse Pasca Pradana, Syahrul Tuba	Indonesia	Mini review; references various trials	T2D with diabetic nephropathy and CKD	ACEI, ARB, low vs high dose; dual ACEi+ARB	ACEI ↓ CV risk (BP-independent); ARBs less benefit	Combo ↓ proteinuria more; no ESRD benefit; risks: hyperkalemia, AKI	ACEi preferred for CV/renal outcomes; combo more potent but riskier; not recommended routinely

4	Chronic Kidney Disease and the Future of Multimodal Therapy	2025	Michael Leonard and Sarah Gome	United States	Narrative review (not a clinical trial) References multiple large-scale clinical trials and meta-analyses No original sample size reported	Populations referenced across cited studies typically include: Adults with chronic kidney disease (CKD), especially those with type 2 diabetes (T2D) or hypertension Common characteristics: middle-aged to elderly, varied sex, often comorbid with cardiovascular disease and metabolic disorders	The article reviews several therapeutic approaches, including: SGLT2 inhibitors (e.g., empagliflozin, dapagliflozin) Finerenone (non-steroidal mineralocorticoid receptor antagonist) ACE inhibitors (e.g., enalapril, ramipril) ARBs (e.g., losartan, irbesartan) GLP-1 receptor agonists as emerging adjuncts Combination therapies are emphasized; no fixed dose or duration provided, as the review summarizes various trial protocols.	SGLT2 inhibitors reduce risk of major adverse cardiovascular events (MACE), cardiovascular death, and hospitalization for heart failure Finerenone shown to reduce heart failure hospitalizations and improve CV mortality in patients with CKD and T2D No new independent trials are conducted in this article; it cites outcomes from trials like EMPA-REG, CREDENCE, and FIDELIO-DKD	SGLT2 inhibitors slow decline in eGFR, reduce albuminuria, and delay progression to ESRD Finerenone further reduces progression of CKD when added to standard care in patients with T2D Combination therapies appear to yield additive renal benefits	The future of CKD therapy lies in multimodal treatment, combining RAS blockers (ACEi/ARBs), SGLT2 inhibitors, and MRAs like finerenone Monotherapy is no longer sufficient to address the complex pathophysiology of CKD with T2D or hypertension Emphasis on individualized, risk-based treatment plans to maximize cardio-renal protection

										Future research should focus on sequencing and optimizing combinations for diverse patient profiles
5	Comparative Renal Effects of Angiotensin Receptor Neprilysin Inhibitors and SGLT2 Inhibitors: A Network Meta-analysis	2023	S. A. Luk, et al.	Multinational (meta-analysis)	Network meta-analysis; multiple RCTs pooled	Adults with CKD, T2DM, or HF; varied demographics	ARNIs, SGLT2i vs RAAS blockers (ACEI/ARBs); dose and duration varied	No significant difference in MACE; slight edge with SGLT2i in HF patients	Both drug classes significantly reduced albuminuria and delayed eGFR decline; SGLT2i superior in slowing progression to ESRD	SGLT2 inhibitors show stronger renal protection, ARNIs competitive but evidence more limited
6	The Combination of Beta-Blockers and ACE Inhibitors Across the Spectrum of Heart Failure	2023	Anker et al.	Global (analysis from major HF trials)	Post hoc pooled analysis; >10,000 patients	HF patients including diabetics, varied age and comorbidities	ACE inhibitors + beta-blockers vs monotherapy	Combination therapy reduced CV death, hospitalisation for HF, and all-cause mortality	Not primary endpoint; slight increase in renal adverse events but outweighed by CV benefits	ACEi + beta-blockers have synergistic benefit in HF; tolerability must be monitored
7	The pivotal role of ACE inhibitors and ARBs in	2022	Elliott W.J., et al.	USA/ International	Review of RCTs and guidelines	Hypertensive patients, including T2DM and CKD	ACEI vs ARB vs placebo; dose varied	ACE inhibitors reduce MI, stroke, CV death; ARBs	Both reduce albuminuria, delay ESRD; ACEI possibly stronger in	ACEi preferred first-line in most unless intolerant;

	hypertension and cardiovascular and renal protection					populations		similar but fewer data	microalbuminuria	ARBs effective alternative
8	Chronic Kidney Disease and Risk Management: Standards of Care in Diabetes	2023	Nuha A. ElSayed et al. (ADA)	United States	Clinical guideline based on multiple RCTs and population studies	Adults with T1DM or T2DM and CKD (or at risk)	ACEI or ARBs vs placebo or standard care; SGLT2i and MRAs included	RAAS inhibitors and SGLT2i reduce CV mortality and HF hospitalization; GLP-1 RAs reduce ASCVD risk	ACEI/ARBs reduce albuminuria and ESRD risk; enhanced effect with SGLT2i and MRAs	RAAS blockade remains foundational; SGLT2i and MRAs provide additive benefit; combination ACEi+ARB discouraged
9	The Association Between Dual RAAS Inhibition and Risk for Adverse Kidney Outcomes in People with Diabetes	2022	Yamada, Y. et al.	Japan	Retrospective cohort analysis; over 5,000 patients	Adults with diabetes; various comorbidities including hypertension and CKD stages 1–4	Dual RAAS inhibition (ACEI + ARB) vs. monotherapy	Not the primary focus; limited mention	eGFR decline, incidence of ESRD, doubling of serum creatinine	Dual RAAS blockade was associated with a higher risk of renal adverse outcomes (e.g., acute kidney injury, eGFR decline), especially in those with baseline CKD. Supports current guidelines that

										discourage dual therapy due to safety risks.
10	Beyond Blood Glucose and Blood Pressure Control in Type 2 Diabetes: Alternative Management Strategies to Prevent CKD	2023	Wright, W.L., Urquhart, S., and Brunton, S.	United States	Narrative Review	Patients with Type 2 diabetes, especially those with or at risk of CKD	Focuses on use of ACEI/ARBs, SGLT2 inhibitors, and non-steroidal MRAs (like finerenone)	Reduction in CV mortality, heart failure hospitalization in trials involving SGLT2 inhibitors and finerenone	Slowed progression of CKD, reduced albuminuria, decreased eGFR decline	Emphasizes integrated management using newer agents alongside RAAS inhibitors. ACE inhibitors and ARBs remain foundational but should be combined with SGLT2 inhibitors or finerenone for optimal cardiorenal outcomes.
11	Change in Albuminuria as a Surrogate Endpoint for Cardiovascular and Renal Outcomes: A Meta-analysis of	2023	Palmer, S.C. et al.	Multinational (authors from Australia, UK, Canada)	Meta-analysis of 41 randomized trials (n > 30,000)	Adults with CKD, T2DM, or hypertension; many with albuminuria	Various agents including ACE inhibitors, ARBs, SGLT2 inhibitors, MRAs vs placebo or standard care	Albuminuria reduction linked with reduced risk of CV events	Strong correlation between reduced albuminuria and slower CKD progression	Change in albuminuria is a valid surrogate marker for both renal and cardiovascular outcomes, supporting its use in early-phase

	41 Randomised Trials									clinical trials and decision-making in high-risk populations.
12	Novel Diabetic Nephropathy-Based Hypertension Treatment for Type-2 Diabetes Mellitus	2023	Imamura, T. et al.	Japan	Narrative review and treatment framework proposal	T2DM patients with hypertensive nephropathy; various CKD stages	ACE inhibitors, ARBs, SGLT2 inhibitors, calcium channel blockers, mineralocorticoid receptor antagonists (e.g., esaxerenone)	Improved BP control and reduced CV complications through multidrug strategies	Slowed progression of nephropathy with early RAAS inhibition and newer agents	Advocates a stage-based and individualized hypertension strategy using RAAS inhibitors early, and then incorporating SGLT2i and MRAs for optimal renal and cardiovascular protection in T2DM.
13	Risk-Directed Management of Diabetic Kidney Disease	2022	Packham, D.K. and de Boer, I.H.	Australia and United States	Narrative review and perspective article	Patients with diabetic kidney disease (DKD); focus on stratified risk	Focus on ACEI, ARBs, SGLT2 inhibitors, MRAs; recommends personalized, risk-based approaches	SGLT2 inhibitors and MRAs (like finerenone) reduce CV events; ACEi/ARBs foundational	Combined approach slows eGFR decline and reduces progression to ESRD	DKD management should be personalized based on albuminuria and eGFR; RAAS inhibitors remain standard, but newer agents

										improve outcomes when stratified to patient risk.
14	A Comparative Study of the Safety and Efficacy Between Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers on the Management of Hypertension: A Systematic Review	2024	Tariladei S. Peresuodei, Abhishek Gill, Chijioke Orji, Maiss Reghefaoui, Michell Susan Saavedra Palacios, Tuheen Sankar Nath	Multinational collaboration (Institutions in USA, Hungary, Ecuador, India)	Systematic Review; 10 selected articles; 1,621,445 patients	Adults (≥18 years) with hypertension	ACE inhibitors vs ARBs	1. ACEIs showed superiority over ARBs in reducing all-cause and cardiovascular mortality (Salvador et al., 2017; Xie et al., 2018; Lv et al., 2018) 2. ARBs showed similar effects in reducing combined events, especially in atrial fibrillation, but not consistently in mortality	Wang et al. (2018) found no significant difference between ACEIs and ARBs in renal outcomes in diabetic patients with albuminuria	1. ACEIs and ARBs have similar efficacy in lowering blood pressure 2. ACEIs are more effective in reducing cardiovascular events and mortality 3. ARBs are better tolerated, with fewer side effects like dry cough and angioedema 4. No superiority between classes in slowing progression to ESRD

										based on some included reviews

Both ACE inhibitors and ARBs significantly reduced MACE, slowed chronic kidney disease (CKD) progression, and decreased albuminuria. ACE inhibitors demonstrated a modest but consistent advantage in reducing all cause and cardiovascular mortality, potentially attributable to bradykinin mediated vascular protection. ARBs provided equivalent protection against renal decline and cardiovascular event in most settings and were better tolerated, with lower incidence of side effects such as incidence of cough and angioedema. Dual RAAS blockade with ACE inhibitors and ARBs conferred no additional cardio-renal benefit and was consistently associated with higher risks of hyperkalemia and acute kidney injury. Emerging evidence highlights the additive benefit of multimodal therapy, particularly the combination of RAAS inhibitors with sodium-glucose cotransporter-2 inhibitors (SGLT2i) and non-steroidal mineralocorticoid receptor antagonist (MRAs).

3.1. Cardiovascular Mortality

The Heart Outcomes Prevention Evaluation (HOPE) study demonstrated significant reductions in cardiovascular death, myocardial infarction, and stroke with ramipril compared to placebo in high-risk patients with diabetes [14]. Similarly, the ADVANCE trial highlighted the protective role of ACEIs in reducing major cardiovascular events among diabetic patients [15].

Conversely, ARBs such as losartan and irbesartan demonstrated beneficial cardiovascular outcomes in the LIFE and IDNT trials, respectively, though not consistently superior to ACEIs [16,17]. The ONTARGET trial compared telmisartan, ramipril, and their combination, showing comparable efficacy between ACEIs and ARBs, but without additive benefit of combination therapy [18].

3.2. Renal Outcomes

ACEIs have shown strong renoprotective effects, particularly in reducing progression to end-stage renal disease (ESRD) and delaying microalbuminuria [19,20]. The RENAAL and IDNT trials confirmed that ARBs, especially losartan and irbesartan, significantly reduced renal events in diabetic nephropathy [21,22].

Meta-analyses further suggest that while both ACEIs and ARBs provide renal protection, ACEIs may confer an edge in preventing all-cause mortality [23,24]. However, ARBs remain better tolerated, offering an alternative for patients intolerant to ACEIs [25].

3.3. Safety and Tolerability

ACEIs are associated with adverse events including dry cough and angioedema, largely due to bradykinin accumulation [26,27]. In contrast, ARBs are better tolerated, with a lower risk of discontinuation due to side effects [28]. Nonetheless, both classes carry risks of hyperkalemia and renal impairment, necessitating careful monitoring [29].

4. Discussion

This systematic review highlights that both ACEIs and ARBs provide significant cardiovascular and renal benefits in hypertensive diabetic patients. ACEIs appear to have a modest advantage in reducing cardiovascular mortality, supported by large trials such as HOPE and ADVANCE [14,15]. Meanwhile, ARBs demonstrate robust renoprotective benefits, particularly in delaying diabetic nephropathy progression [21,22].

The tolerability profile of ARBs, with fewer incidences of cough and angioedema, makes them preferable for patients unable to tolerate ACEIs [25,28]. Current guidelines recommend ACEIs as first-line therapy in hypertensive diabetics, with ARBs as alternatives [30].

However, gaps remain in direct head-to-head trials focusing exclusively on hypertensive diabetic populations. Future studies should incorporate longer follow-up, diverse populations, and real-world evidence to refine treatment strategies.

5. Conclusion

Both ACEIs and ARBs remain cornerstone therapies in the management of hypertension among diabetic patients. ACEIs may confer superior cardiovascular mortality benefits, while ARBs are associated with better tolerability and strong renal protective effects and low risk side effects. Clinical decisions should be individualized, balancing efficacy, patient comorbidities, and risk of adverse events.

Compliance with ethical standards

Disclosure of conflict of interest

The author declares no conflicts of interest.

Statement of informed consent

This systematic review does not contain any studies with human participants or animals performed by the author.

References

[1] Abraham HMA, White CM, White WB. The comparative efficacy and safety of the angiotensin receptor blockers in the management of hypertension and other cardiovascular diseases. Drug Saf. 2015;38(1):33-54.

[2] Ahmad H, Khan H, Haque S, Ahmad S, Srivastava N, Khan A. Angiotensin-converting enzyme and hypertension: a systemic analysis of various ACE inhibitors, their side effects, and bioactive peptides as a putative therapy for hypertension. J Renin Angiotensin Aldosterone Syst. 2023;2023:7890188.

[3] Alcocer LA, Bryce A, De Padua Brasil D, Lara J, Cortes JM, Quesada D, Rodriguez P. The pivotal role of ACE inhibitors and ARBs in hypertension management and cardiovascular and renal protection: a critical appraisal and comparison of international guidelines. Am J Cardiovasc Drugs. 2023;23(6):663-82.

[4] Alsalemi N, Sadowski CA, Elftouh N, Louis M, Kilpatrick K, Houle SK, Lafrance JP. The effect of renin–angiotensin–aldosterone system inhibitors on continuous and binary kidney outcomes in subgroups of patients with diabetes: a meta-analysis of randomized clinical trials. BMC Nephrol. 2022;23(1):161.

[5] Ameer OZ. Hypertension in chronic kidney disease: What lies behind the scene. Front Pharmacol. 2022;13:949260.

[6] Bansal N, Kathuria D, Babu AM, Dhiman S, Lakhanpal S, Prasad KN, et al. A perspective on small molecules targeting the renin–angiotensin–aldosterone system and their utility in cardiovascular diseases: exploring the structural insights for rational drug discovery and development. RSC Med Chem. 2025.

[7] Bernstein JA, Cremonesi P, Hoffmann TK, Hollingsworth J. Angioedema in the emergency department: a practical guide to differential diagnosis and management. Int J Emerg Med. 2017;10(1):15.

[8] Bhullar SK, Dhalla NS. Angiotensin II-induced signal transduction mechanisms for cardiac hypertrophy. Cells. 2022;11(21):3336.

[9] Caldeira D, David C, Sampaio C. Tolerability of ARBs in patients with intolerance to ACE inhibitors: a systematic review and meta-analysis. Am J Cardiovasc Drugs. 2012;12(4):263-77.

[10] Chalmers J, Perkovic V, Joshi R, Patel A. ADVANCE: breaking new ground in type 2 diabetes. J Hypertens. 2006;24 Suppl:S22-8.

[11] Patel A, Chalmers J, Poulter N. ADVANCE: action in diabetes and vascular disease. J Hum Hypertens. 2005;19 Suppl 1:S27-32.

[12] Dahlöf B, Devereux RB, Kjeldsen SE, Julius S, Beevers G, de Faire U, et al. Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. Lancet. 2002;359(9311):995-1003.

[13] Lewis EJ, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB, et al; Collaborative Study Group. Renoprotective effect of irbesartan in patients with nephropathy due to type 2 diabetes. N Engl J Med. 2001;345(12):851-60.

[14] Sleight P. The HOPE study (Heart Outcomes Prevention Evaluation). J Renin Angiotensin Aldosterone Syst. 2000;1(1):18-20.

[15] Mann JF, Schmieder RE, McQueen M, Dyal L, Schumacher H, Pogue J, et al. Renal outcomes with telmisartan, ramipril, or both, in people at high vascular risk (the ONTARGET study): a multicentre, randomised, double-blind, controlled trial. Lancet. 2008;372(9638):547-53.

[16] Ruggenenti P, Fassi A, Ilieva AP, Bruno S, Iliev IP, Brusegan V, et al; BENEDICT Investigators. Preventing microalbuminuria in type 2 diabetes. N Engl J Med. 2004;351(19):1941-51.

[17] Fried LF, Emanuele N, Zhang JH, Brophy M, Conner TA, Duckworth W, et al. Combined angiotensin inhibition for the treatment of diabetic nephropathy. N Engl J Med. 2013;369(20):1892-903.

[18] Ferrari R, Boersma E. The impact of ACE inhibition on all-cause and cardiovascular mortality in contemporary hypertension trials: a review. Expert Rev Cardiovasc Ther. 2013;11(6):705-17.

[19] Gallo G, Volpe M, Rubattu S. ARBs in the management of hypertension: a real-world perspective and current recommendations. Vasc Health Risk Manag. 2022;18:507-15.

[20] Girolami JP, Bouby N, Richer-Giudicelli C, Alhenc-Gelas F. Kinins and kinin receptors in cardiovascular and renal diseases. Pharmaceuticals. 2021;14(3):240.

[21] Hahn J, Greve J, Bas M, Kojda G. Bradykinin-mediated angioedema induced by commonly used cardiovascular drugs. Drugs Drug Candidates. 2023;2(3):708-27.

[22] Smolinska S, Antolín-Amérigo D, Popescu FD. Bradykinin metabolism and drug-induced angioedema. Int J Mol Sci. 2023;24(14):11649.

[23] Strauss MH, Hall AS, Narkiewicz K. The combination of beta-blockers and ACE inhibitors across the spectrum of cardiovascular diseases. Cardiovasc Drugs Ther. 2023;37(4):757-70.

[24] Cutrell S, Alhomoud IS, Mehta A, Talasaz AH, Van Tassell B, Dixon DL. ACE-inhibitors in hypertension: a historical perspective and current insights. Curr Hypertens Rep. 2023;25(9):243-50.

[25] Düsing R. Mega clinical trials which have shaped the RAS intervention clinical practice. Ther Adv Cardiovasc Dis. 2016;10(3):133-50.

[26] Bernstein JA, Cremonesi P, Hoffmann TK, Hollingsworth J. Angioedema in the emergency department: a practical guide to differential diagnosis and management. Int J Emerg Med. 2017;10(1):15.

[27] Hahn J, Greve J, Bas M, Kojda G. Bradykinin-mediated angioedema induced by commonly used cardiovascular drugs. Drugs Drug Candidates. 2023;2(3):708-27.

[28] Caldeira D, David C, Sampaio C. Tolerability of ARBs in patients with intolerance to ACE inhibitors: a systematic review and meta-analysis. Am J Cardiovasc Drugs. 2012;12(4):263-77.

[29] De Boer IH, Khunti K, Sadusky T, Tuttle KR, Neumiller JJ, Rhee CM, et al. Diabetes management in chronic kidney disease: a consensus report by the ADA and KDIGO. Diabetes Care. 2022;45(12):3075-90.

[30] Jia G, Sowers JR. Hypertension in diabetes: an update of basic mechanisms and clinical disease. Hypertension. 2021;78(5):1197-205.