Research Square

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Renin–Angiotensin System Inhibitors and Longitudinal Kidney and Cardiovascular Outcomes in Patients with Type 2 Diabetes: A Multicenter Common Data Model Cohort Study

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Abstract

Background

While renin–angiotensin system inhibitors (RASi) are the standard of care for diabetic kidney disease (DKD), their long-term effectiveness in patients with type 2 diabetes mellitus (T2DM) across varying degrees of kidney function remains debated.

Methods

We conducted a retrospective, multicenter observational cohort study using a common data model (CDM) from three tertiary hospitals. We identified 18,707 patients with T2DM and stratified them into four cohorts: a DKD-free group and three groups with established chronic kidney disease (CKD) stages 3A, 3B, and 4. Using propensity score matching, we compared RASi users with active controls treated with other antihypertensives. The outcomes were major adverse cardiovascular events (MACEs) and major adverse kidney events (MAKEs). Random-effects meta-analyses were performed to pool incidence rate ratios (IRRs).

Results

In the DKD-free cohort, RASi use was not associated with a reduction in MACEs (IRR 1.079; 95% confidence interval [CI] 0.758–1.538) or MAKEs (IRR 1.014; 95% CI 0.646–1.592). In patients with established CKD, RASi use was associated with an increased risk of MAKEs: CKD stage 3A (IRR 1.429; 95% CI 1.324–1.542), stage 3B (IRR 1.346, 95% CI 1.090–1.663), and stage 4 (IRR 1.312; 95% CI 1.173–1.467). In the RASi groups, kidney events were more frequent, whereas in-hospital mortality was reduced or not significantly different across centers.

Conclusion

In this retrospective, real-world multicenter cohort, RASi therapy was not associated with improved kidney outcomes or a lower risk of MACEs in patients with T2DM, including those with advanced DKD. Given the concurrent signal toward preserved or reduced in-hospital mortality, these findings should inform individualized RASi decisions and close monitoring.

Background

Type 2 diabetes mellitus (T2DM) is a leading cause of chronic kidney disease (CKD) and a major risk factor for cardiovascular disease (CVD). Approximately 30%–40% of patients with T2DM develop diabetic kidney disease (DKD), which is characterized by a decline in the glomerular filtration rate and an increase in albumin excretion over the clinical course.[1, 2] The renin–angiotensin system is among the

key drivers of DKD pathogenesis, promoting intrarenal angiotensin II-mediated glomerular hypertension, inflammation, and extracellular matrix expansion.[3] Clinical studies have shown that pharmacologic renin–angiotensin system inhibitors (RASi), such as angiotensin-converting enzyme inhibitors (ACEi) or angiotensin II receptor blockers (ARB), reduce the progression of albuminuria and attenuate the decline in the estimated glomerular filtration rate (eGFR) in patients with T2DM.[4, 5] This evidence from landmark clinical trials established RASi as the standard of care in patients with DKD to improve kidney outcomes and reduce cardiovascular events, particularly in those with early to moderate CKD. In current practice guidelines, ACEi and ARB are considered first-line antihypertensive options for patients with diabetes and kidney disease and are recommended for their ability to reduce albuminuria and slow the progression of nephropathy.[6, 7]

Controlled randomized controlled trials (RCTs) have shown that RASi improve kidney and cardiovascular outcomes and preserve kidney function in patients with early-stage DKD. However, patients with severely reduced eGFR were largely excluded from these trials, making it unclear whether the same renal and cardiovascular benefits extend to advanced CKD (e.g., stages 4 or 5 non-dialysis). Moreover, emerging evidence from cohort studies, nationwide registries, and other observational designs has occasionally yielded divergent results.[8, 9] Rigorous RCTs often exclude patients with multiple comorbidities or advanced disease and are usually conducted under idealized conditions.[10] Given the gaps in evidence from traditional RCTs, real-world evidence has become crucial for evaluating treatment effects across broader patient populations. Observational studies using real-world data can include large, heterogeneous cohorts that reflect routine clinical practice. In the context of DKD and CKD, real-world analyses enable assessment of RASi effectiveness and safety in patient groups underrepresented in trials, such as those with advanced CKD, older age, or complex comorbidities. To facilitate a real-world, multicenter cohort study, the use of a common data model (CDM) has emerged as a robust approach in observational research.[11, 12] A CDM standardizes disparate hospital databases into a unified format, enabling the pooling and analysis of data across centers with consistent definitions. By leveraging a CDM, investigators can efficiently combine data from multiple centers to create large datasets without the typical heterogeneity that hampers multisite studies.

This study aimed to evaluate the association between RAS blockade and clinical outcomes in patients with T2DM across the spectrum of CKD stages. Therefore, we conducted a multicenter observational study across diverse institutions to evaluate the effect of RASi on DKD using a CDM.

Methods

Data Source and Study Design

This study was a retrospective cohort analysis of deidentified electronic health record (EHR) data collected from three major tertiary care hospitals in the Republic of Korea: Seoul National University Bundang Hospital (SNUBH), Seoul National University Hospital (SNUH), and Asan Medical Center (AMC). The data from each institution were standardized to the Observational Medical Outcomes Partnership

(OMOP) CDM version 5, enabling unified analysis across sites.[13, 14] Cohort definitions and analyses were designed and executed using the Observational Health Data Sciences and Informatics (OHDSI) ATLAS platform, which facilitates cohort construction and statistical analysis on the CDM database.

This retrospective, multicenter observational study utilized a comparative cohort design to evaluate the therapeutic effects of RASi across patient groups stratified by baseline kidney function. We identified subjects with T2DM from each participating institution's database using standardized OMOP-CDM version 5 diagnosis codes. To ensure cohort specificity and minimize false-positive selection, diagnostic codes were cross-validated against laboratory data, requiring a hemoglobin A1c (HbA1c) level ≥ 6.5% or a fasting blood glucose concentration ≥ 126 mg/dL. The index date was defined as the date of the initial confirmed T2DM diagnosis, and the observation period extended until the patient’s last recorded hospital visit. Patients were excluded on the basis of the following criteria: 1) a diagnosis of type 1 diabetes; 2) age younger than 18 years or older than 80 years at enrollment; 3) a history of corticosteroid use exceeding 12 weeks or exposure to calcineurin inhibitors to rule out secondary or drug-induced diabetes; 4) a history of malignancy, end-stage kidney disease (ESKD), myocardial infarction, or ischemic stroke prior to the index date; and 5) the absence of any antihypertensive medication prescription within the 6 months preceding or following the index date to confirm the requirement for pharmacological management of hypertension.

Cohort Definition

The index date for each participant was the date of the first clinical encounter confirming a T2DM diagnosis. Within this cohort, two exposure arms were created. Patients who received an ACE inhibitor (ACEi) or an angiotensin II receptor blocker (ARB) at any time from 180 days before to 180 days after the index date and who also had at least one additional prescription for any RASi beyond 180 days post-index were classified into the RASi group. The requirement of a prescription after the 180-day window ensured continued exposure rather than a single, isolated fill. The control group consisted of patients with T2DM who were prescribed antihypertensive agents other than RASi within the same ± 180-day window but did not receive any RASi after 180 days post-index date.

Four parallel cohorts of patients with T2DM were constructed according to kidney disease status at the index date. First, we defined DKD as either a spot urine albumin-to-creatinine ratio ≥ 30 mg/g, a 24-hour albuminuria level ≥ 30 mg, a spot urine protein-to-creatinine ratio ≥ 150 mg/g, a 24-hour proteinuria level ≥ 150 mg, or a Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI eGFR < 60 mL/min/1.73 m^2. The first group, the DKD-free cohort, included individuals whose data at cohort entry revealed no evidence of overt DKD. In addition to the DKD-free cohort, three chronic kidney disease (CKD)–stratified cohorts were defined on the basis of the eGFR at the time the CKD stage (3A, 3B, or 4) was first documented. For each CKD cohort, the exposure definition used a narrower assessment window of ± 90 days around the CKD index date, considering the follow-up interval. All the inclusion criteria and temporal definitions are displayed in Fig. 1.

Definitions of outcomes

Patients in each cohort were followed from the index date until the occurrence of outcome events of interest or censoring. We examined both major adverse cardiovascular events (MACEs) and major adverse kidney events (MAKEs). We defined MACEs as a composite of in-hospital death and ischemic events, including myocardial infarction and ischemic stroke, as determined by diagnostic history. MAKEs were defined as a composite of in-hospital death and the need for renal replacement therapy (RRT) or an eGFR < 15 mL/min/1.73 m2 for more than two consecutive measurements on the basis of the CKD-EPI equation.

Statistical analysis

We employed propensity score matching and survival analysis to compare outcomes between RASi users and controls in each cohort. Propensity scores (PSs) for RASi treatment were calculated using regularized logistic regression (L1-penalized) with ten-fold cross-validation for model tuning. The PS model included baseline covariates such as age, sex, comorbid diagnoses, and concurrent medications (measured before the index date), and laboratory test values were automatically considered via the regularized regression approach. We specifically included baseline medication use and major comorbid diagnoses before the index date. To avoid overlap with outcomes, any events or treatments occurring after cohort entry were excluded from the PS estimation.

RASi users were matched 1:1 to control patients on the logit of the PS using a caliper of 0.2, yielding matched cohorts with balanced baseline characteristics. For the matched cohorts, we used Cox proportional hazards models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for each outcome and compared the RASi group with the control group. Survival curves were generated using Kaplan–Meier estimates to visualize time-to-event, and groups were compared using log-rank tests. Because our data were derived from three distinct hospital CDM databases, we performed a random-effects meta-analysis to pool the site-specific HRs into an overall summary effect for each outcome. Heterogeneity across sites was assessed with the I2 statistic.[15] We also conducted sensitivity analyses of the individual components of the composite outcomes to evaluate the robustness of the findings.[16] All analyses were performed in R (version 4.2.3) using the OHDSI collaborative package (https://github.com/ohdsi/cyclops).[17]
Ethical approval

This study was approved by the ethics committees of each institution, and the Institutional Review Board of SNUBH (IRB No. B-1809-493-109), SNUH (IRB No. 1809-062-971), and AMC (IRB No. 2025-0562) waived the requirement for informed consent. This study met the criteria for a waiver of informed consent as outlined in the Bioethics and Safety Act of the Republic of Korea, and all methods used were performed in accordance with the relevant guidelines and regulations.

Results

Baseline Characteristics and Clinical Parameters

The study included 18,707 patients with T2DM who met all predefined inclusion and exclusion criteria across three tertiary centers (SNUBH: 6,089; AMC: 5,911; SNUH: 6,707) prior to matching. In the matched cohorts, patients who received RASi exhibited significantly different baseline profiles from those of the active control group. Across all three institutions, the RASi cohort had significantly higher baseline HbA1c levels, higher albuminuria levels, and higher utilization rates of statins and other antihypertensive agents, reflecting a substantial burden of confounding by indication (Table 1). We performed 1:1 propensity score matching (PSM) to balance these covariates. This process yielded matched cohorts of 1,024 pairs at SNUBH, 1,173 pairs at AMC, and 1,419 pairs at SNUH. After matching, the mean age in the matched cohorts ranged from 62 to 64 years, and the proportion of female patients was approximately 40%. With respect to glucose-lowering therapies, metformin was the most prescribed agent (ranging from 44% to 60%), followed by sulfonylureas and DPP-4 inhibitors.

Table 2 summarizes the mean values of key clinical parameters monitored throughout the observation period. The analysis revealed distinct physiological differences between the treatment arms, consistent with the known pharmacodynamic effects of RAS blockade. Across all three hospitals, patients in the RASi group demonstrated a statistically significant increase in serum creatinine and a corresponding decrease in the eGFR compared with the control group. For instance, in the SNUH cohort, the median eGFR during follow-up was 87 mL/min/1.73 m² (IQR 72–98 mL/min/1.73 m²) in the RASi group versus 89 mL/min/1.73 m² (IQR 77–100 mL/min/1.73 m²) in the control group ($P < 0.01$). A similar pattern was observed at SNUBH (91 vs. 93 mL/min/1.73 m2, $P < 0.01$) and AMC (94 vs. 95 mL/min/1.73 m2, $P < 0.01$). Furthermore, serum potassium levels were consistently higher in the RASi group across all centers ($P < 0.01$). Notably, during the follow-up period, the urine albumin-to-creatinine ratios were consistently higher in the RASi groups than in the control group (e.g., SNUH: 23 mg/g vs. 13 mg/g, P < 0.01).

Clinical Outcomes in the DKD-Free Cohort

To synthesize evidence from the three participating centers (SNUBH, SNUH, and AMC), we conducted a random-effects meta-analysis of the DKD-free cohort. The forest plots for MACEs and MAKEs are presented in Figure 2. For the primary cardiovascular outcome (MACEs, Figure 2-a), the pooled incidence rate ratio (IRR) derived from the random-effects model was 1.079 (95% CI 0.758–1.538). We observed substantial heterogeneity among the institutions ($I^2 = 80\%$, $P < 0.01$). Similarly, regarding the primary kidney outcome (MAKEs; Figure 2-b), the pooled IRR was 1.014 (95% CI, 0.646–1.592) under the random-effects model. Significant heterogeneity was also present in this analysis ($I^2 = 75\%$, $P = 0.02$). Compared with active controls, the use of RASi was not significantly associated with differences in cardiovascular or kidney risk. The individual study results differed notably; the SNUH cohort showed a substantial increase in the risk of adverse kidney events (IRR 1.645, 95% CI 1.056–2.562), whereas the AMC and SNUBH cohorts showed trends toward a protective effect or neutrality (IRR 0.789, 95% CI 0.599–1.039 and IRR 0.848, 95% CI 0.534–1.346, respectively).

Clinical Outcomes in the T2DM with CKD Stage 3A, 3B, and 4 Cohorts

We examined outcomes in patients with established DKD stratified by CKD stage. The IRRs for MACEs and MAKEs in each CKD cohort are presented in Figure 3, which compares RASi users with controls and presents pooled estimates across the three sites. We found that the summarized IRRs of MAKEs were high in the matched cohorts with CKD stages 3A, 3B, and 4. For stage 3A, the summarized IRRs of MACEs and MAKEs were 1.140 (95% CI 1.060–1.226) and 1.429 (95% CI 1.324–1.542), respectively. For stage 3B, the IRRs of MACEs and MAKEs were 1.158 (95% CI 0.958–1.399) and 1.346 (95% CI 1.090–1.663), respectively. For stage 4, the IRRs of MACEs and MAKEs were 1.211 (95% CI 0.955–1.536) and 1.312 (95% CI 1.173–1.467), respectively (Figure 3).

Sub-outcome Analysis

We performed a sub-outcome analysis to evaluate the impact of RASi on each component of the primary outcomes. In the DKD-free cohort, RASi use was associated with a significant reduction in in-hospital death at two of the three centers (SNUBH: RR 0.42, 95% CI 0.22–0.77; AMC: RR 0.66, 95% CI 0.49–0.89; SNUH: RR 0.89, 95% CI 0.49–1.59). Mortality–kidney trade-off findings emerged in advanced CKD cohorts, in which we observed a dissociation between kidney outcomes and mortality (Table S1). In the CKD stage 4 cohort, a sub-outcome of kidney endpoints (RRT or eGFR below 15 mL/min/1.73 m^2) was consistently and significantly increased in the RASi group across all centers (SNUBH: RR 1.69, 95% CI 1.20–2.39; AMC: RR 1.76, 95% CI 1.48–2.09; SNUH: RR 1.39, 95% CI 1.12–1.74). In contrast to the kidney endpoints, RASi use was associated with reduced or neutral effects on in-hospital mortality in the CKD stage 4 cohort (SNUBH: RR 0.95, 95% CI 0.51–1.77; AMC: RR 0.55, 95% CI 0.39–0.77; SNUH: RR 1.10, 95% CI 0.66–1.84).

Discussion

This longitudinal, multicenter observational study leverages the strengths of the CDM to reevaluate the effectiveness of RASi across the spectrum of DKD. Our findings indicate that RASi use may not be associated with a significant reduction in MACEs or MAKEs among patients who were DKD-free at baseline. Moreover, in advanced forms of DKD, the traditional renoprotective effect of RASi appeared to diminish. Among patients with CKD stages 3A to 4, RASi use was not associated with improved kidney outcomes. In contrast, previous RCTs in proteinuric DKD have consistently demonstrated that RAS blockade slows nephropathy progression.[4,5] For example, landmark trials such as RENAAL and IDNT have shown that ARB significantly delay the deterioration of kidney function and reduce albuminuria in patients with DKD, in addition to controlling blood pressure.[18] Our real-world study results indicate attenuated or absent renoprotection in multicenter observational cohorts.

The absence of clinical benefit in our DKD-free and advanced DKD cohorts may reflect several factors. First, confounding by indication in routine practice is a consideration. Clinicians preferentially initiate RASi in patients who are perceived to be at higher risk of CKD progression—for instance, those with hypertension and albuminuria—in accordance with established guidelines.[6,7] Consequently, in our DKD-free cohort, RASi users likely had more risk factors at baseline, even after 1:1 PSM. The RASi group had

higher albuminuria levels and lower eGFR values. This selection pattern could bias the outcomes; RASi users start at a higher risk for developing DKD, potentially obscuring any protective effect of the medication. Observational comparisons, even after adjustment, can be influenced by residual confounding and indication bias, which might attenuate the apparent benefits of therapy in real-world data.[19,20] Even among observational real-world studies, two independent retrospective cohort studies reported different conclusions: one reported that compared with other non-RASi agents, ARB provided little or no renoprotective advantage, whereas the other reported that RASi conferred a long-term benefit on the composite kidney outcome.[21,22]

Another factor is that the magnitude of the renoprotective effects of RASi may differ across CKD stages and contexts. Traditional RCTs demonstrating robust nephroprotective effects have primarily enrolled patients with proteinuric DKD and relatively preserved kidney function (often CKD stages 1–3).[9,23] In advanced CKD, multiple processes, such as renal fibrosis, reduced nephron mass, and comorbidities, may limit the impact of RAS blockade. Some evidence suggests that once CKD is advanced, lowering intraglomerular pressure with RASi yields diminishing returns and increases risks, including acute eGFR decline and hyperkalemia.[24,25] Our findings are broadly consistent with emerging evidence and should be interpreted in light of recent high-quality studies. Notably, the results of the STOP-ACEi trial revealed no benefit to routine RASi discontinuation. In that trial, stopping RASi did not improve long-term eGFR decline and was linked to a slightly higher risk of requiring dialysis and more cardiovascular events.[26] In a nationwide study, Fu et al. reported that among patients with an eGFR < 30 mL/min/1.73 m2, continuation of RAS blockade was associated with a substantially lower mortality risk (and fewer major cardiovascular events) than the control treatment.[27] Any decision to continue RAS blockade in patients with advanced CKD requires individualization. Our study stresses the importance of careful monitoring of kidney function and comorbidities in this setting.

In this study, a longitudinal multicenter CDM database was used to analyze treatment effects in real-world practice. By leveraging routine clinical data from multiple centers, we captured a broad, heterogeneous population of patients with T2DM and DKD. This design allows observation of treatment effects in patients with comorbidities and advanced disease, who are typically excluded from RCTs; such an approach may help address an unmet need for evidence in nephrology. Our analysis also examined granular outcomes (MAKEs, MACEs, and in-hospital mortality), providing a specific view of the effects of RASi beyond composite endpoints.

While our study was conducted with data verification and in accordance with a CDM protocol, several limitations must be acknowledged. Given its retrospective and observational design, the potential for selection bias cannot be fully excluded. To address this, we applied PSM across a broad range of confounding variables using a large, multicenter dataset. Nonetheless, the process of cohort construction may have introduced selection bias inherent to real-world retrospective research. Moreover, despite rigorous 1:1 matching, some baseline variables, especially eGFR and albuminuria, remained imbalanced between groups. These residual imbalances may have influenced the interpretation of

outcomes. Higher baseline and follow-up albuminuria levels and lower baseline and follow-up eGFRs in the RASi group may be independently associated with worse clinical outcomes, such as MAKEs.

Our findings suggest that while RASi therapy may improve survival in patients with T2DM, it may not provide sufficient kidney protection, particularly in patients with early and advanced CKD. The dissociation between declining kidney function and improved survival at advanced stages highlights a critical therapeutic window. A multitargeted therapeutic strategy may therefore be needed to more effectively safeguard kidney function and reduce risk in patients with DKD.[28–30] Emerging treatments such as sodium–glucose cotransporter-2 inhibitors, nonsteroidal mineralocorticoid receptor antagonists, and glucagon-like peptide-1 receptor agonists have each demonstrated additional cardiorenal benefits in patients with T2DM and could complement RAS blockade to address the observed dissociation between survival benefit and kidney function decline.

Conclusion

In this multicenter common-data-model cohort study, RASi therapy was not associated with improved kidney outcomes in patients with type 2 diabetes mellitus across the spectrum of chronic kidney disease, including the DKD-free stratum. Although in-hospital mortality was preserved or reduced in two of three centers, the consistent excess of adverse kidney events—particularly in advanced CKD—highlights a clinically important dissociation between cardiovascular and renal effects of RAS blockade. The decision to initiate or continue RASi in advanced diabetic kidney disease should therefore be individualized, with close monitoring of kidney function and electrolytes, and timely use of complementary cardiorenal therapies.

Abbreviations

T2DM
type 2 diabetes mellitus
CKD
chronic kidney disease
CVD
cardiovascular disease
DKD
diabetic kidney disease
RASi
renin–angiotensin system inhibitor
ACEi
angiotensin-converting enzyme inhibitor
ARB
angiotensin II receptor blocker
eGFR

estimated glomerular filtration rate
RCT
randomized controlled trial
CDM
common data model
RAS
renin–angiotensin system
EHR
electronic health record
SNUBH
Seoul National University Bundang Hospital
SNUH
Seoul National University Hospital
AMC
Asan Medical Center
OMOP
Observational Medical Outcomes Partnership
OHDSI
Observational Health Data Sciences and Informatics
HbA1c
hemoglobin A1c
ESKD
end-stage kidney disease
CKD-EPI
Chronic Kidney Disease Epidemiology Collaboration
MACE
major adverse cardiovascular event
MAKE
major adverse kidney event
RRT
renal replacement therapy
PS
propensity score
HR
hazard ratio
CI
confidence interval
PSM
propensity score matching
IQR

interquartile range
IRR
incidence rate ratio
RR
relative risk.

Declarations

Ethics approval and consent to participate

This study was approved by the ethics committees of each institution, and the Institutional Review Boards of Seoul National University Bundang Hospital (IRB No. B-1809-493-109), Seoul National University Hospital (IRB No. 1809-062-971), and Asan Medical Center (IRB No. 2025-0562) waived the requirement for informed consent. This study met the criteria for a waiver of informed consent as outlined in the Bioethics and Safety Act of the Republic of Korea, and all methods used were performed in accordance with the relevant guidelines and regulations, including the Declaration of Helsinki.

Consent for publication

The manuscript does not contain any individual person's identifying data, images, videos, or other personal details, nor does it reproduce previously published material from other sources that would require consent for publication.

Availability of data and materials

Individual participant data will not be made available. The following documents are available: the study protocol, statistical analysis plan, and analytic code. Data are to be used only for the aims of the approved proposal. Data access requests should be sent to yongjin.neph@gmail.com, and a data access agreement must be signed.

Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

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Authors' contributions

Conceptualization: YY, SK (Sejoong Kim) Data curation: SK (Seok Kim), SP, JCJ, HJC, JSO, GB Formal analysis: YY, SK (Seok Kim), SY Funding: YY, SK (Sejoong Kim) Investigation: YY, SK (Seok Kim) Methodology: YY, SK (Sejoong Kim) Supervision: SK (Sejoong Kim) Validation: HL, CHJ, JSO, GB Writing–original draft: YY Writing–review & editing: YY, SK (Sejoong Kim) All authors read and approved the final manuscript.

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Figures

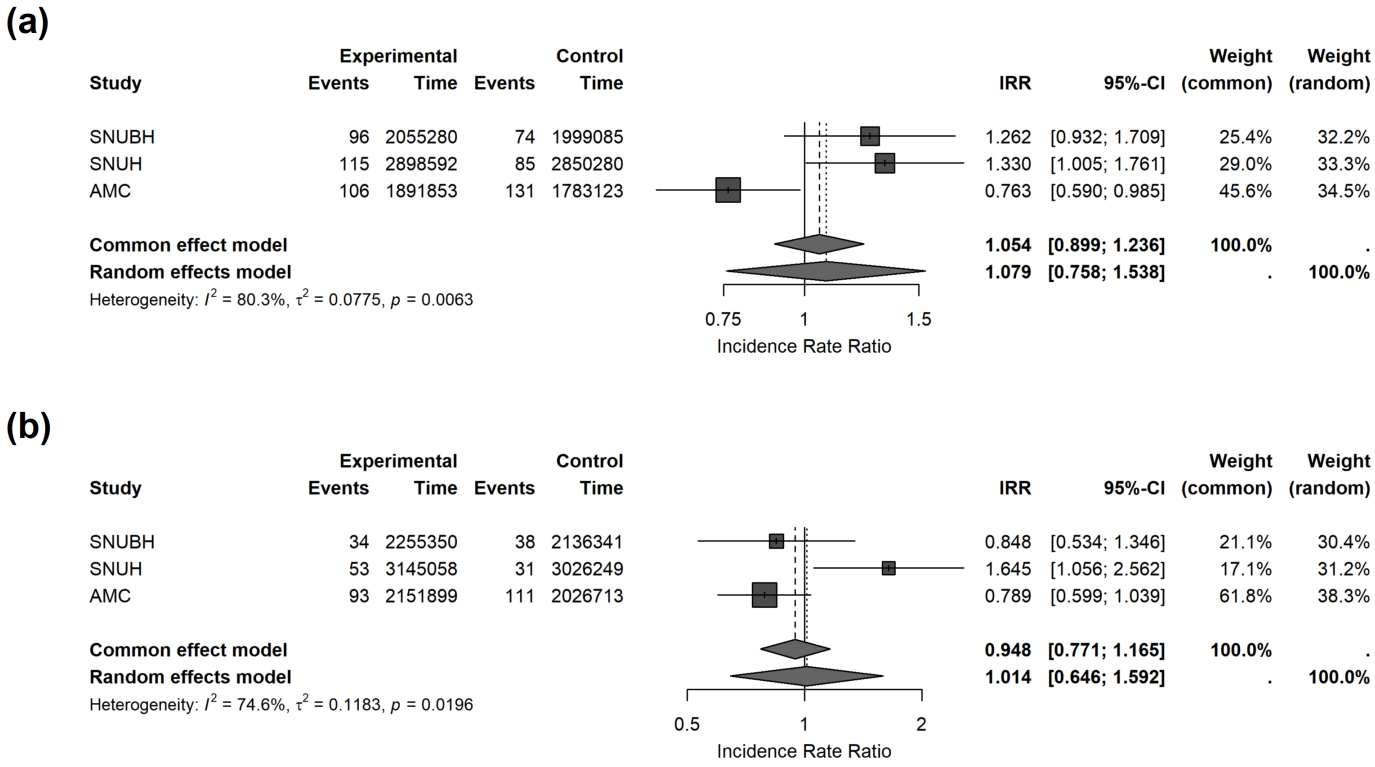


Figure 1

Forest plot summary for the DKD-free cohorts

The incidence rate ratios with 95% confidence intervals for the T2DM groups without DKD are shown. Separate panels present the meta-analysis results for (a) MACEs and (b) MAKEs.

DKD, diabetic kidney disease; MACE, major adverse cardiovascular event; MAKE, major adverse kidney event; T2DM, type 2 diabetes mellitus.

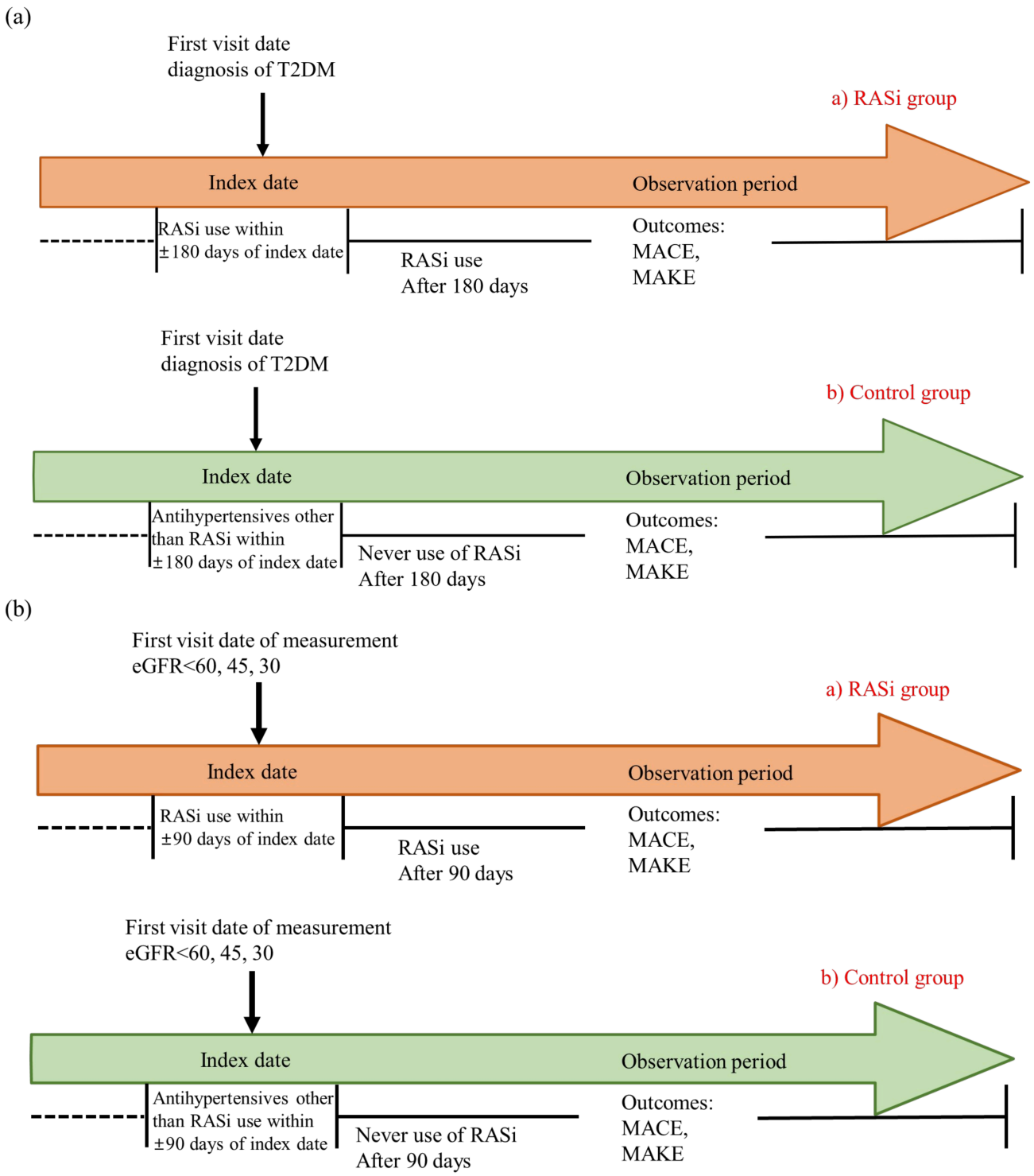


Figure 2

Diagram of cohort construction

(a) Flowchart illustrating how the observational cohort of patients with newly diagnosed T2DM without baseline DKD was defined. (b) Flowchart showing the definition of the observational cohort comprising patients with T2DM and reduced kidney function.

DKD, diabetic kidney disease; MACE, major adverse cardiovascular event; MAKE, major adverse kidney event; RASi, renin–angiotensin system inhibitor; T2DM, type 2 diabetes mellitus.

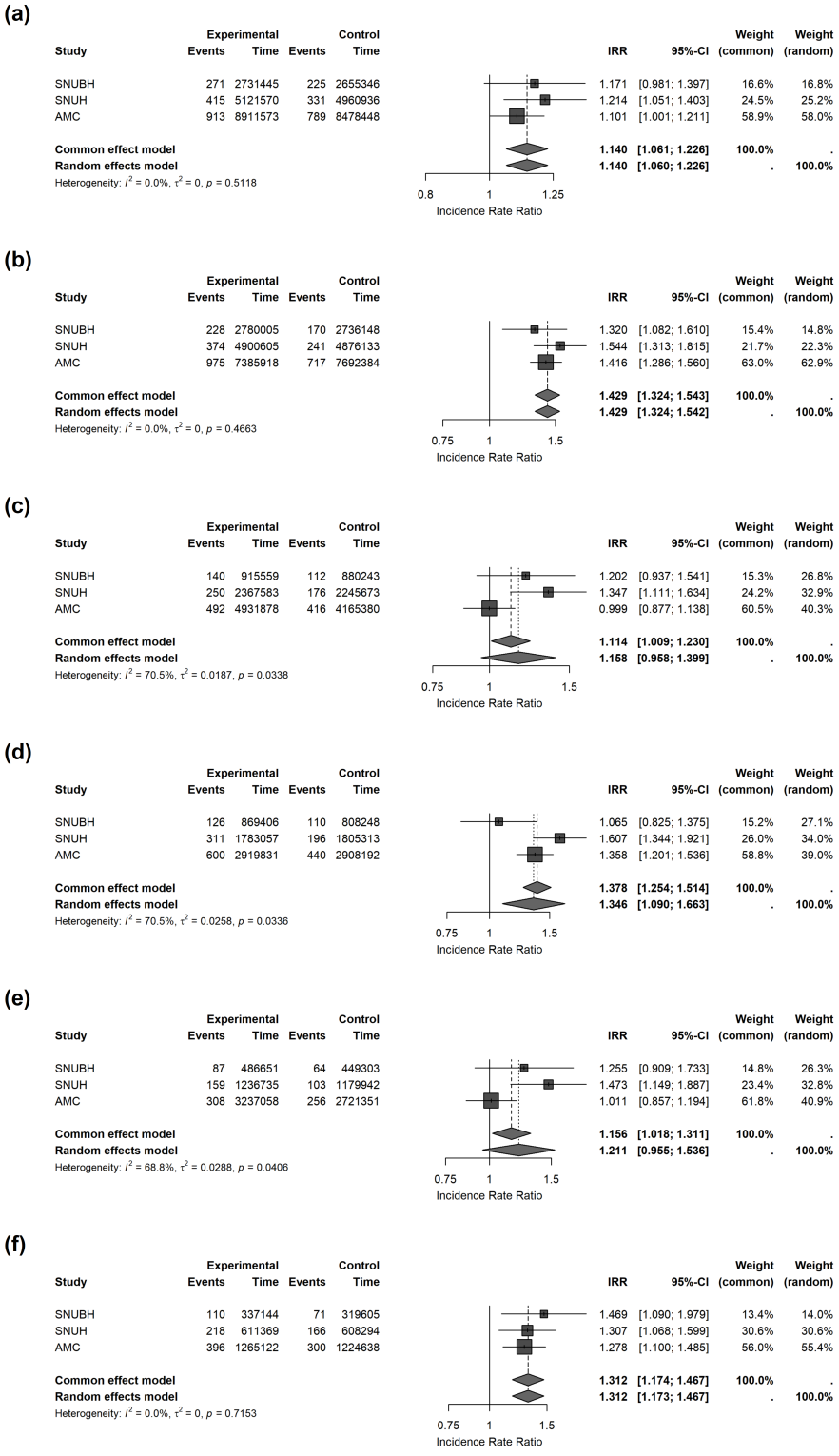


Figure 3

Forest plot summary for cohorts with impaired kidney function

The incidence rate ratios with 95% confidence intervals for patients with T2DM stratified by CKD stage (CKD 3A, 3B, and 4) are shown. The panels represent (a) MACEs in CKD stage 3A, (b) MAKEs in CKD stage 3A, (c) MACEs in CKD stage 3B, (d) MAKEs in CKD stage 3B, (e) MACEs in CKD stage 4, and (f) MAKEs in CKD stage 4.

CKD, chronic kidney disease; MACE, major adverse cardiovascular event; MAKE, major adverse kidney event; T2DM, type 2 diabetes mellitus.

Supplementary Files

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- tableS1.docx