

CKD and CKM Syndrome: Accelerated Progression to Arrhythmias in a National Cohort

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Introduction

- Chronic Kidney Disease (CKD), a key element of the AHA Cardiovascular-Kidney-Metabolic (CKM) framework, is increasingly recognized as an independent risk factor for arrhythmias, especially atrial fibrillation (AF).
- Studies like ARIC and recent guidelines highlight higher arrhythmia risk with declining kidney function, but real-world data on this progression are limited.
- This study examines arrhythmia onset in patients progressing from obesity to CKD.

Methods

- A retrospective real-world evidence study was conducted using the Symphony Integrated Dataverse (2018–2024) to examine arrhythmia development in adults with obesity initially classified as CKM Stage 1—defined by the absence of metabolic or cardiac risk factors at the time of obesity diagnosis (Table 1).

Table 1: CKM profile

Stages	Inclusions
Stage 1: Obesity	<ul style="list-style-type: none"> BMI >27 2 Diagnosis claims >60 days apart for:
Stage 2: Metabolic risk factors and CKD	<ul style="list-style-type: none"> Diabetes and pre-diabetes Hypertension CKD Stages 1-3 Lipidemia Liver dysfunction
Stage 3: Subclinical CVD	<ul style="list-style-type: none"> CKD Stages 4-5 Imaging (R93.1) Coronary Atherosclerosis
Stage 4: MACE and Arrhythmia	<ul style="list-style-type: none"> MACE Arrhythmia

- A subset who progressed to CKD (Stages 1–4) but remained free of cardiac risk factors at CKD onset, were followed longitudinally to evaluate the incidence of major arrhythmias.
- All patients had a minimum of 12 months of baseline (lookback) data and 12 months of follow-up after their initial obesity diagnosis.

Results

- The cohort included 3.5 million adults with obesity (33% male, 67% female; median age 37 years)(Table 2). Of these, 26,478 patients (41% male, 59% female; median age 60 years) progressed to CKD: Stage 1 (7%), Stage 2 (32%), Stage 3 (57%), and Stage 4 (3%).
- After CKD onset, 1,095 patients (4%)(54% male, 46% female; median age 70 years) developed a major arrhythmia—65% AF, 14% supraventricular tachycardia, 16% atrioventricular block, and 3% ventricular tachycardia—within a median of four months (Table 3).
- Between obesity diagnosis and CKD development, 27% developed hypertension, 12% diabetes, and 7% both (Table 4).
- Notably, 70% of all arrhythmia cases occurred in patients with CKD Stage 3.

Table 2: Demographics

Target Arrhythmia	CKM Stage 1 (N=3,516,259)	CKD after Stage 1 (N=26,478)	Major Arrhythmia after CKD (N=1,095)
Median Age	37	60	70
Index Age	18 to 34	44%	8%
	35 to 44	24%	12%
	45 to 54	17%	18%
	55 to 64	10%	23%
	≥65	6%	39%
Sex	Female	67%	59%
	Male	33%	41%
ECI Score Category	Negligible (<2)	93%	88%
	Low (2-5)	5%	8%
	Medium (6-10)	1%	2%
	High (11-15)	1%	2%
	Severe (>15)	0.05%	0.2%

Table 3: Median time to CKD to major arrhythmia by CKD Stage

Stage	Median days from CKD index to arrhythmia index	Patient Breakdown by CKD Stage				
		Any stage	Stage 1	Stage 2	Stage 3	Stage 4
Stage 2: Patients with CKD*	104 Days	1,095	33	276	775	100
AF	87 Days	716	17	159	523	76
Aflutter	87 Days	99	1	34	69	7
AVBk-1	184 Days	115	4	25	85	7
AVBk-2	40 Days	23	1	8	12	2
AVBk-3	7 Days	31	0	9	22	2
AVBk-U	112 Days	7	0	4	3	1
Supraventricular tachycardia	144 Days	154	12	51	97	6
Ventricular tachycardia	87 Days	29	0	6	23	3

*Stage 2: Patients with CKD (Stage 1-4) post-Stage 1 (with no subclinical CVD, non-MACE CVD, and arrhythmia/MACE prior to CKD Stage 1-4)

Table 4: Other metabolic risks before CKD and arrhythmias

	Diabetes before CKD	Hypertension + T2D before CKD	Hypertension before CKD
Overall (N=1,095)	127	76	293
Stage 1	4	2	12
Stage 2	30	20	82
Stage 3	92	52	192
Stage 4	16	10	32

Conclusions

In this real-world cohort, progression from cardiometabolic dysfunction to CKD was associated with a marked rise in new arrhythmias, particularly AF. Early-onset obesity patients who developed CKD had a markedly higher progression to arrhythmia or MACE before age 40. These findings support CKD as a key inflection point in arrhythmia risk and reinforce the CKM framework. Enhanced surveillance for arrhythmias may be warranted as kidney function declines.

Abbreviations AF = atrial fibrillation; Aflutter = atrial flutter; AHA = American Heart Association; ARIC = atherosclerosis risk in communities; AV = atrioventricular; AVBk-1 = AV Block-1; AVBk-2 = AV Block-2; AVBk-3 = AV Block-3; AVBk-U = AV Block-Unspecified; BMI = body mass index; CKD = chronic kidney disease; CKM = Cardiovascular-Kidney-Metabolic; CVD = cardiovascular disease; ECI = Elixhauser comorbidity index; MACE = major adverse cardiovascular events; T2D = Type 2 Diabetes.

References ARIC: <https://www.nhlbi.nih.gov/es/science/atherosclerosis-risk-communities-aric-study>

