

The Onset of Arrhythmias in the CKD Continuum: Real-world Insights from a National Cohort

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Introduction

- The AHA Cardiovascular-Kidney-Metabolic (CKM) framework outlines a continuum of risk, starting with metabolic dysfunction and leading to major cardiovascular events.
- However, the role and timing of arrhythmia onset within this trajectory remain poorly understood, and the impact of major arrhythmias has not been reported.
- This real-world evidence (RWE) study is the first to examine arrhythmias onset across the CKM continuum, offering new insights with potential implications for earlier detection, risk stratification, and intervention.

Methods

- We conducted a retrospective RWE study using a large, longitudinal claims dataset of adults with obesity (Symphony Integrated Dataverse - 2018-2024).
- Patients were stratified at baseline according to their CKM risk profile (Table 1).
- Individuals with obesity and no prior CKM risk factors were classified as Stage 1.
- A subset of these patients who then developed arrhythmia were classified as Post-Stage 1 – Target.
- The remaining cohort included individuals with obesity who remained in Stage 1 or who then developed at least one Stage 2 risk factor and were classified as Post-Stage 1 – Control.
- Patients were followed over time to evaluate progression through CKM stages, defined by the development of additional metabolic, kidney, or cardiovascular conditions.
- Arrhythmia onset was tracked at each stage.
- Outcomes of interest included incident arrhythmia, progression to major adverse cardiovascular events (MACE), and transitions across CKM stages.

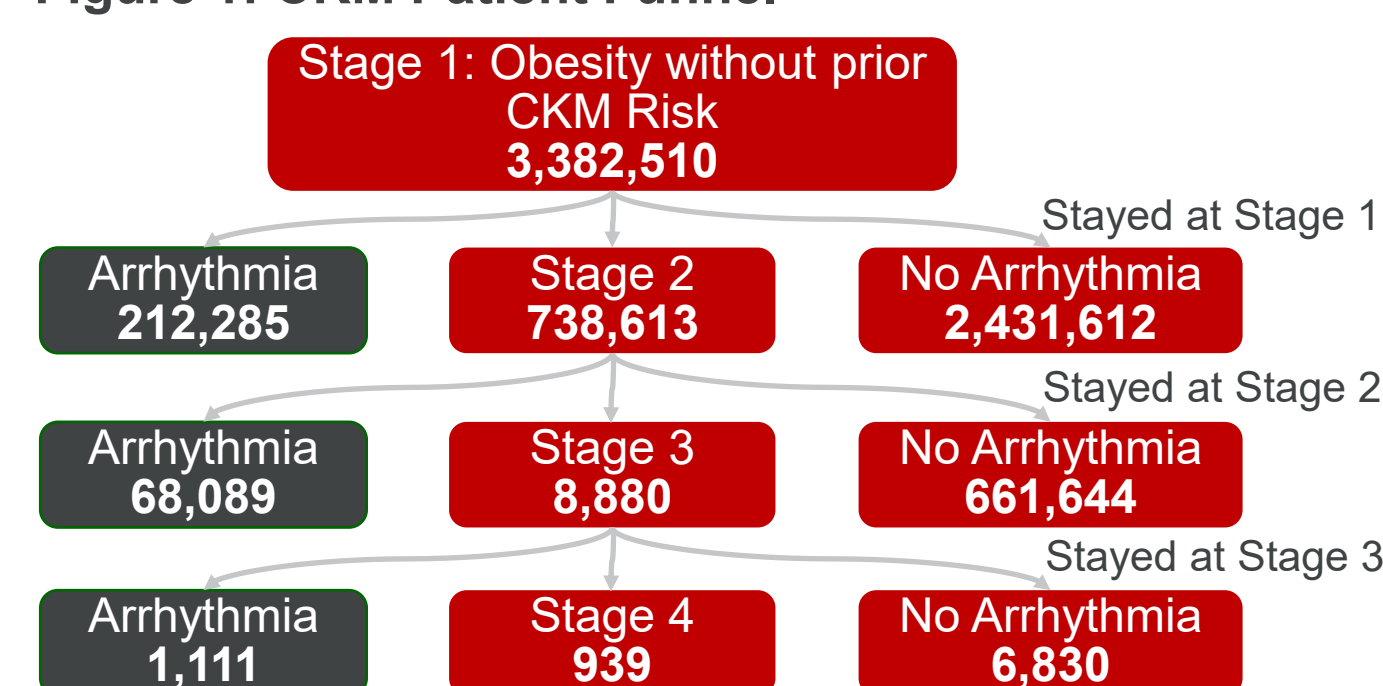
Results

- Among 3,382,510 adults with obesity and no prior CKM risk factors (Stage 1), 212,285 (6.3%) developed incident arrhythmia (Post-Stage 1 – Target), while 3,170,225 (93.7%) did not (Post-Stage 1 - Control). Of this control cohort, 2,431,612 (71.9%) remained in Stage 1 without arrhythmia. The remaining 738,613 (21.8%) progressed to Stage 2 without arrhythmia.
- Of the patients in Stage 2, 68,089 (9.2%) then developed arrhythmias (post-Stage 2 – Target), while 670,524 (90.8%) did not (Post-Stage 2 – Control). Of this control cohort, 661,644 (89.6%) remained in Stage 2 without arrhythmia. The remaining 8,880 (1.2%) patients advanced to Stage 3 without arrhythmia.
- Of the patients in Stage 3, 1,111 (12.5%) then developed arrhythmia (Post-Stage 3 – Target), while 7,769 did not (87.5%) (Post-Stage 3 – Control). Of this control cohort, 939 (10.5%) progressed to Stage 4 with MACE only. Only 6,830 (77%) patients remained in Stage 3 without further progression (Figure 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: <ul style="list-style-type: none"> Diabetes and pre-diabetes
Stage 2: Metabolic risk factors and CKD	<ul style="list-style-type: none"> 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

Figure 1: CKM Patient Funnel



Conclusions

In this large RWE study, arrhythmia frequently emerged early in the CKM disease continuum. These findings highlight the potential value of incorporating arrhythmia surveillance into risk stratification for patients at risk of CKM progression. Further research is needed to determine whether early arrhythmia represents a modifiable inflection point on the path to major adverse cardiovascular events.

Table 2: Demographics

	Target: Arrhythmia	Post-Stage 1 (N=212,285)	Post-Stage 2 (N=68,089)	Post-Stage 3 (N=1,111)
Median Age		38	46	62
Index Age	18-34	41%	24%	3%
	35-44	23%	23%	8%
	45-54	16%	21%	16%
	55-64	11%	17%	31%
	>65	9%	16%	42%
Gender	Female	72%	67%	47%
	Male	28%	33%	53%
ECI Score Category	Negligible (<2)	81%	71%	49%
	Low (2-5)	11%	15%	23%
	Medium (6-10)	4%	6%	12%
	High (11-15)	3%	6%	9%
Severe (>15)	1%	3%	8%	
Control: No Arrhythmia				
		Post-Stage 1 (N=3,170,225)	Post-Stage 2 (N=670,524)	Post-Stage 3 (N=7,769)
Median Age		38	45	61
Index Age	18-34	39%	24%	3%
	35-44	25%	25%	7%
	45-54	18%	23%	18%
	55-64	11%	18%	35%
	>65	6%	11%	37%
Gender	Female	66%	64%	48%
	Male	34%	36%	52%
ECI Score Category	Negligible (<2)	90%	81%	59%
	Low (2-5)	7%	11%	22%
	Medium (6-10)	2%	3%	8%
	High (11-15)	1%	4%	8%
Severe (>15)	0.1%	1%	3%	

Table 3: Median time in days to arrhythmia by type

Median Time in Days	# Patients (N)	AFTER OBESITY DIAGNOSIS					
		Stage 1 to AOI	AOI post-Stage 1 to Stage 2	Stage 2 to AOI	AOI post-Stage 2 to Stage 3	Stage 3 to AOI	Stage 3 to MACE
ONLY AOI to obesity index (No other exclusions)	126,546	20,393	4,174	11,005	489	277	65
All AOI	127	478	364	382	108	152	65
Afib	49	543	422	447	100	190	49
Aflutter	63	638	513	493	72	297	25
AVBik-1	201	449	340	440	90	170	14
AVBik-2	165	536	428	426	112	531	371
AVBik-3	180	644	512	505	36	176	88
AVBik-U	159	583	541	532	17	91	–
SVT	308	431	377	287	127	197	244
VT	311	411	362	272	127	135	229

Abbreviations

AHA = American Heart Association; Afib = atrial fibrillation; Aflutter = atrial flutter; All AOI = all arrhythmias of interest; AVBik-1 = AV Block-1; AVBik-2 = AV Block-2; AVBik-3 = AV Block-3; AVBik-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; RWE = real-world evidence; SVT = supraventricular tachycardia; VT = ventricular tachycardia.



American Heart Association.