

Incidence of Idiopathic Ventricular Arrhythmias

A Population-Based Study

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Background—Ventricular tachycardia and premature ventricular complexes (PVCs) most frequently occur in the context of structural heart disease. However, the burden of idiopathic ventricular arrhythmias (IVA) in the general population is unknown.

Methods and Results—We identified incident cases of IVA between 2005 and 2013 from Olmsted County, Minnesota, using the Rochester Epidemiology Project database. For PVC cohorts, we included those with frequent (defined as ≥ 100 PVC/24 hours) symptomatic PVCs. We defined IVA-associated cardiomyopathy as a drop in ejection fraction of $\geq 10\%$ from baseline. Between 2005 and 2013, we identified 614 individuals with incident IVA (229 [37.3%] were male; average age was 52.1 ± 17.2 years). Of these, 177 (28.8%) had idiopathic ventricular tachycardia, 408 (66.5%) had symptomatic PVCs, and 29 (4.7%) had IVA-associated cardiomyopathy. The age- and sex-adjusted incidence rates in 2005 to 2007, 2008 to 2010, and 2011 to 2013 were 44.9 per 100 000 (95% confidence interval [CI], 38.0–51.8), 47.6 per 100 000 (95% CI, 40.8–54.5), and 62.0 per 100 000 (95% CI, 54.4–69.6), respectively. In idiopathic ventricular tachycardia, there was an increase in incidence rate with ages ($P < 0.001$) but not between sexes ($P = 0.12$). The age-adjusted incidence of symptomatic PVC was higher in females than in males (46.2 per 100 000 [95% CI, 40.9–51.6] versus 20.5 per 100 000 [95% CI, 16.8–24.3]; $P < 0.001$). The small number of individuals with IVA-associated cardiomyopathy precluded any formal testing.

Conclusions—The incidence of IVA is increasing. Furthermore, overall incidence increases with age. Although the rate of idiopathic ventricular tachycardia is similar across sexes, women have a higher incidence of symptomatic PVC. (*Circ Arrhythm Electrophysiol.* 2017;10:e004662. DOI: 10.1161/CIRCEP.116.004662.)

Key Words: epidemiology ■ idiopathic VT ■ premature ventricular contraction arrhythmia ■ ventricular arrhythmia ■ ventricular tachycardia

Ventricular tachycardia (VT) and premature ventricular complexes (PVCs) most frequently occur in the context of a structurally abnormal heart, for example, coronary artery disease (CAD), severe valvular heart disease, or low ejection fraction (EF). However, ventricular arrhythmias (VAs) may also occur in individuals with no apparent structural heart disease. These so-called idiopathic VT cases are said to account for 10% of all VT diagnoses.¹ Although the prognosis is typically favorable compared with that of structural heart disease–associated VT, debilitating symptoms and even death have been reported.² Symptoms include fatigue, palpitations, dyspnea, presyncope, syncope

(although rare in PVCs unless in the context of severely depressed cardiac function), and heart failure.^{3–5} Yet, although studies have tried to define the prevalence of idiopathic VA (IVA), data have predominantly originated from referral centers performing ablation procedures.⁶ As such, the burden of IVAs is unknown, and population-based data are scarce. Thus, the purpose of this study was to determine the incidence of IVA from a stable community-based population in South-East Minnesota. We postulated that although relatively infrequent, incident cases of IVA are increasing in frequency, given the increasing use of monitoring devices and device interrogation.

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WHAT IS KNOWN

- Idiopathic ventricular arrhythmias occur in patients with structurally normal hearts.
- The burden of idiopathic ventricular arrhythmias in the general population is unknown.

WHAT THE STUDY ADDS

- The age- and sex-adjusted incidence of idiopathic ventricular arrhythmias is 51.86 per 100 000 (95% confidence interval, 47.72–56.01).
- The incidence increases with age. The incidence of ventricular tachycardia is similar across sexes, while that of PVCs is more common among women.

Methods**Study Setting and Cohort**

This population-based cohort study was conducted within Olmsted County, Minnesota, using the Rochester Epidemiology Project.^{7–10} The study was approved by the Mayo Clinic and Olmsted Medical Center institutional review boards. Even with racial and socioeconomic disparities in Olmsted County compared with the general US population, biological phenomena are generalizable to population at large. The geographic characteristics of this region enable epidemiological studies because Olmsted County is relatively isolated from other urban centers. Furthermore, care to the majority of Olmsted County residents is provided by Mayo Clinic, Olmsted Medical Center, and a few private-care physicians each of whom use a comprehensive medical record system. All medical records of county residents are indexed, thus, enabling retrieval of data while ensuring complete capture of all healthcare-related events occurring in the county for county residents. These sources provide information concerning virtually all the care delivered for Olmsted County residents. The medical records linkage system of the Rochester Epidemiology Project now encompasses 6239353 person-years of follow-up among 502820 unique individuals who attended health care providers at least once between 1966 and 2010 (counting both current and previous residents).

The study period was 2005 to 2013. This period was chosen to reflect the current clinical practice and outcomes associated with idiopathic VT taking into considering the advancements in mapping and ablation that have occurred over the last 2 decades. The cohort consisted of patients aged ≥ 18 years with incident (first-ever) IVA (idiopathic VT, idiopathic PVC, and IVA-associated cardiomyopathy—see below for definitions). Patients with VAs documented prior to 2005 (ie, prevalent cases) were excluded. Asymptomatic patients with frequent PVCs and low EF at presentation during the study period were considered as prevalent cases and were excluded.

Development of the Cohort

Given that our aim was to determine incidence of IVA, Olmsted County residents were reviewed for patients who had received a diagnosis of VA using *International Classification of Diseases*, Ninth Revision codes for VT (427.1) or PVC (427.69). Individuals with a co-existing diagnosis of CAD (*International Classification of Diseases*, Ninth Revision codes 410–415) were excluded from the study.

Trained abstractors reviewed the medical records and collected information on symptoms,¹¹ triggers,¹² and treatment strategies.¹³ Palpitations, dizziness, fatigue, presyncope, syncope, and heart failure symptoms attributable to PVCs at a frequency $>100/24$ hours were considered significant. In clinical practice, symptoms that correlate with ectopy are often reported among patients with fairly low burden ($<500/24$ hours). Taking day-to-day variability of IVA burden into consideration, a threshold of $>100/24$ hours was chosen for the study. Patient-reported triggers for palpitations were abstracted. Medical therapy for VA was grouped according to Vaughan–Williams classification. Baseline demographic and clinical characteristics,

including hypertension, hyperlipidemia, chronic renal disease, diabetes mellitus, thyroid disease, and liver disease were obtained electronically from the medical record using diagnostic codes. Information regarding CAD, including angina presumed to be from CAD, prior myocardial infarction, physiologically significant epicardial CAD (lesion $>70\%$), were abstracted from the medical records. Patients with underlying structural heart disease resulting from CAD, prior myocarditis, adult congenital heart disease, arrhythmogenic right ventricular cardiomyopathy, ion channelopathy, valvular heart disease (\geq moderate valvular lesion), and cardiomyopathies (dilated with EF $<50\%$, infiltrative, or hypertrophic) were excluded after chart review. Data regarding changes in structural function (EF) or size (left ventricular end-diastolic diameter) were obtained by review of M-mode and 2-dimensional echocardiography when available.

Electrocardiographic information based on 12-lead ECG tracings and ambulatory recordings (Holters and event monitors) were obtained. Premature ventricular complexes (PVCs) were defined as wide complex beats (QRS >120 ms) without any preceding atrial activity.¹³ Among patients with frequent supraventricular ectopic beats or atrial fibrillation, aberrancy was determined by typical QRS morphology and preceding long short sequence.¹⁴ PVC burden was determined by dividing the number of ectopic beats by the number of total QRS complexes in 24 hours.

Patients with IVA were divided into 3 cohorts. The definitions of each are as follows:

1. Idiopathic ventricular tachycardia (VT): ≥ 3 sequential wide complex beats arising from the ventricles, rate ≥ 100 beats per minute.¹⁵
2. Symptomatic PVCs: frequent wide complex beats (≥ 100 beats/24 hours) occurring singly or in couplets arising from the ventricles associated with above described symptoms.
3. IVA associated with cardiomyopathy (IVA-CM): drop in EF of $\geq 10\%$ from baseline in the absence of other causes associated with cardiomyopathy.

Statistical Analysis

All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc, Cary, NC). Categorical variables were expressed as percentages, whereas continuous variables were expressed as mean \pm standard deviation (SD). Comparison of categorical variables was performed using the χ^2 test, whereas comparison of continuous variables was performed with the analysis of variance. All *P* values were 2-sided, and *P* values <0.05 were considered significant. The overall incidence was estimated using the age- and sex-specific population figures in Olmsted County. Yearly incidence rates for each sex was determined by dividing the number of cases within that group by the estimated total Olmsted County resident population of the group for that given year. Population figures for 2000 and 2010 came from the US census data; figures for intercensus years were estimated by using linear interpolation. Rates were adjusted to age or sex distribution of the US white population from 2010. Poisson regression models were used to test for trends over time and across age and sex.

Results

Using billing codes, we identified 2931 individuals satisfying our definition of IVA between 2005 and 2013. Of these, 355 patients were excluded either because of duplicate entries (182 patients) or because of prevalent diagnoses of VT/PVC, that is, prior to 2005 (173 patients). A further 1962 patients were excluded because of identification of structural heart disease or evidence of a supraventricular rhythm with aberrancy. Therefore, 614 patients remained who were suitable for inclusion between 2005 and 2013 (Figure 1).

Baseline Characteristics

Of the 614 patients, 177 (28.8%) had idiopathic VT, 408 (66.4%) had symptomatic PVCs, and 29 (4.7%) had

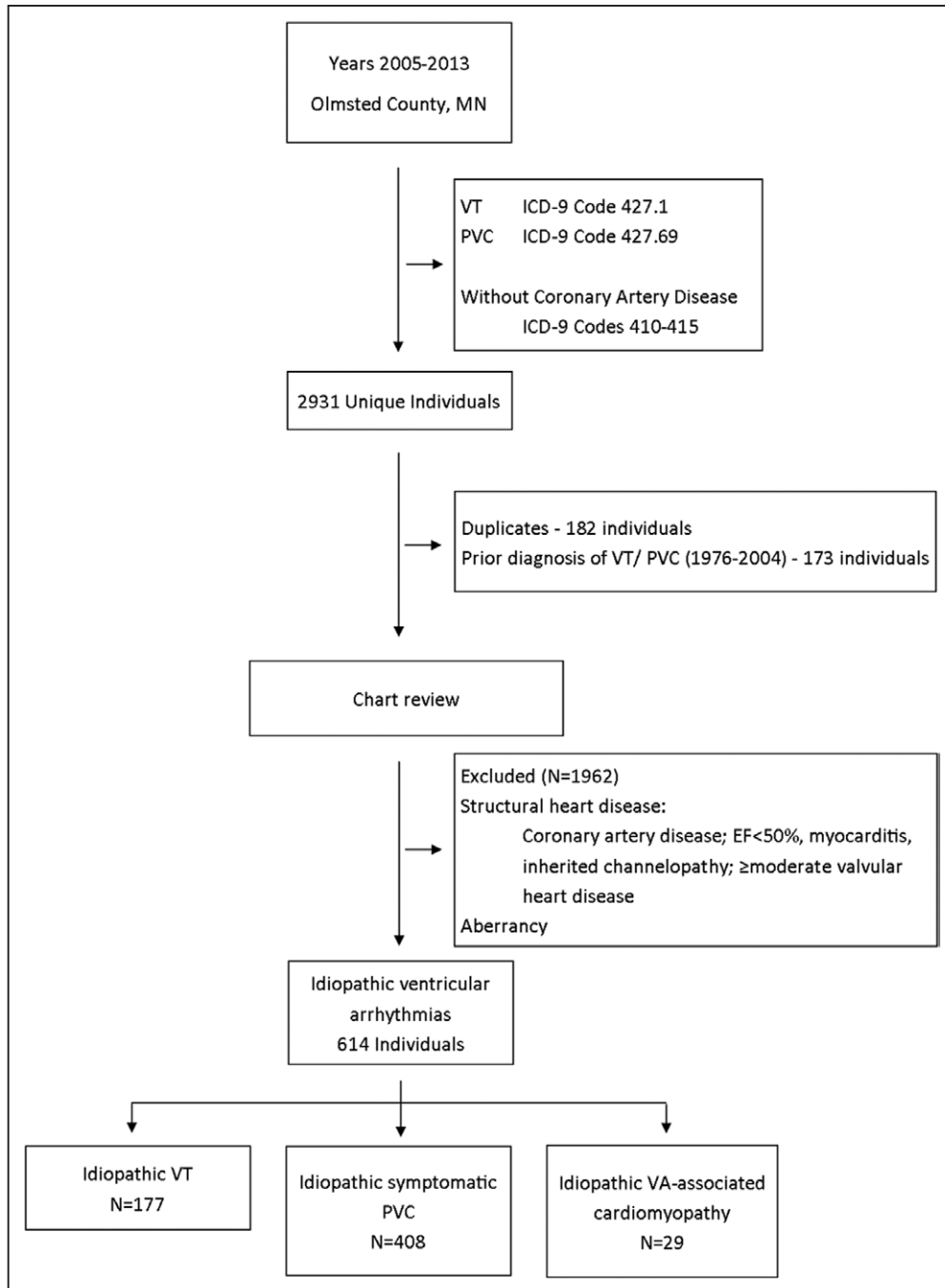


Figure 1. CONSORT flow diagram showing derivation of the idiopathic ventricular arrhythmia cohort. *ICD-9* indicates *International Classification of Diseases-Ninth Revision*; PVC, premature ventricular complex; VA, ventricular arrhythmias; and VT, ventricular tachycardia.

IVA-CM. The average age was 52.1 ± 17.2 years (range 18–93) and 229 (37.3%) were male. Of the overall cohort, 47% had dyslipidemia, 37% had hypertension, 16% had thyroid disease, and 10% had diabetes mellitus. Only 8% had chronic kidney disease or liver disease (Table 1). Significant intergroup differences were seen for age and hypertension. Patients were older and had more comorbidities in the IVA-CM group. As expected, β -blockers and calcium channel blockers were the most frequent medications used (45% of patients). Class I and III antiarrhythmic drugs were used in 5%; however, their use was

less frequent in symptomatic/frequent idiopathic PVC. Ablation was performed in 7.3% of patients (11.9% in idiopathic VT; 2.9% in symptomatic PVC; and 37.9% in IVA-CM).

Average EF and left ventricular end-diastolic diameter were $62.1 \pm 4.9\%$ and 48.7 ± 5.2 mm (normal range 40–54 mm), respectively. Both EF and left ventricular end-diastolic diameter were significantly different between groups ($P=0.004$ and $P=0.03$, respectively), although the actual differences are small in magnitude. Baseline characteristics are summarized in Table 1.

Table 1. Clinical Characteristics According to Ventricular Arrhythmia Type

	Total (N=614)	Idiopathic VT (N=177)	Symptomatic PVC (N=408)	IVA-CM (N=29)	P Value
Age, y	52.1±17.2	59.2±17.6	48.5±15.8	59.2±19.0	<0.001
EF, %	62.1 (4.9)	61.7 (4.8)	62.7 (4.8)	59.8 (9.1)	0.004
LVEDD, mm	48.7 (5.2)	49.5 (6.3)	48.0 (4.3)	50.5 (4.9)	0.03
DM	62 (10%)	21 (12%)	37 (9%)	4 (14%)	0.468
CKD	28 (4%)	10 (6%)	11 (3%)	2 (7%)	0.148
HTN	243 (37%)	84 (47%)	121 (30%)	15 (52%)	<0.001
Hyperlipidemia	312 (47%)	90 (51%)	178 (44%)	17 (59%)	0.110
Hyperthyroid	19 (3%)	5 (3%)	12 (3%)	1 (3%)	0.983
Hypothyroid	88 (13%)	26 (15%)	50 (12%)	2 (7%)	0.453
Liver disease	23 (4%)	8 (5%)	12 (3%)	2 (7%)	0.395
Vaughan–Williams class*					
I	22 (4%)	8 (5%)	6 (1%)	8 (28%)	<0.001
II	254 (41%)	83 (47%)	147 (36%)	24 (83%)	<0.001
III	20 (3%)	11 (6%)	2 (1%)	7 (24%)	<0.001
IV	85 (14%)	34 (19%)	40 (10%)	11 (38%)	<0.001
PVC burden†	5.3±8.1	7.5±9.9	3.8±6	9.1±11	<0.001
Stimulation as trigger‡		14 (7%)	13 (7%)	1 (1%)	<0.001

CKD indicates chronic kidney disease; DM, diabetes mellitus; EF, ejection fraction; HTN, hypertension; IVA-CM, idiopathic ventricular arrhythmia–associated cardiomyopathy; LVEDD, left ventricular end-diastolic diameter; PVC, premature ventricular complex; and VT, ventricular tachycardia.

*Vaughn–Williams Classification is based on the action mechanism of drugs. Note that the numbers of patients treated with medications do not add up to 100%.

†PVC burden=PVC count/total number of beats expressed as percent.

‡Stimulation includes exercise, pain, and caffeine.

Overall Incidence

The crude incidence rates of IVA, idiopathic VT symptomatic PVC, and IVA-CM are shown in Table 2 and Figure 2.

The overall age- and sex-adjusted incidence of IVA was 51.9 per 100 000 (95% confidence interval [CI], 47.7–56.0). This predominantly consisted of symptomatic PVCs,

Table 2. Incidence Rate of Idiopathic Ventricular Arrhythmias

	Overall Cohort (N=614)	Idiopathic VT (N=177)	Symptomatic PVC (N=408)	IVA-CM (N=29)
Overall crude incidence rate	48.10 (41.75–55.41)	13.85 (11.92–16.09)	31.93 (27.72–36.78)	2.27 (1.52–3.27)
Males	36.65 (31.81–42.22)	15.52 (12.59–18.93)	18.88 (15.69–22.69)	2.24 (1.22–3.76)
Females	58.97 (51.19–67.93)	12.25 (9.71–15.19)	44.42 (38.56–51.17)	2.30 (1.29–3.80)
2005–2007	41.34 (35.43–48.20)	12.71 (9.49–16.65)	26.42 (22.25–32.02)	
2008–2010	44.05 (38.06–50.92)	12.42 (9.30–16.27)	29.52 (24.68–35.28)	
2011–2013	58.13 (50.46–66.97)	16.29 (12.74–20.53)	39.36 (33.81–45.78)	
Age-adjusted incidence rate	52.05 (47.90–56.01)	15.79 (13.45–18.13)	33.72 (30.42–37.02)	2.55 (1.61–3.48)
Males	42.43 (36.83–48.03)	19.18 (15.29–23.06)	20.54 (16.77–24.31)	2.72 (1.27–4.17)
Females	61.97 (55.74–68.20)	13.31 (10.37–16.24)	46.22 (40.87–51.57)	2.44 (1.20–3.68)
Age- and sex-adjusted	51.86 (47.72–56.01)	15.80 (13.46–18.15)	33.51 (30.23–36.80)	2.55 (1.61–3.48)
2005–2007	44.91 (38.04–51.78)	14.90 (10.80–18.99)	27.52 (22.26–32.78)	
2008–2010	47.62 (40.76–54.49)	13.91 (10.15–17.68)	31.32 (25.80–36.84)	
2011–2013	62.01 (54.37–69.65)	18.41 (14.14–22.69)	40.84 (34.73–46.95)	

Rates per 100 000 (95% CIs). CI indicates confidence interval; IVA-CM, idiopathic ventricular arrhythmia–associated cardiomyopathy; PVC, premature ventricular complex; and VT, ventricular tachycardia.

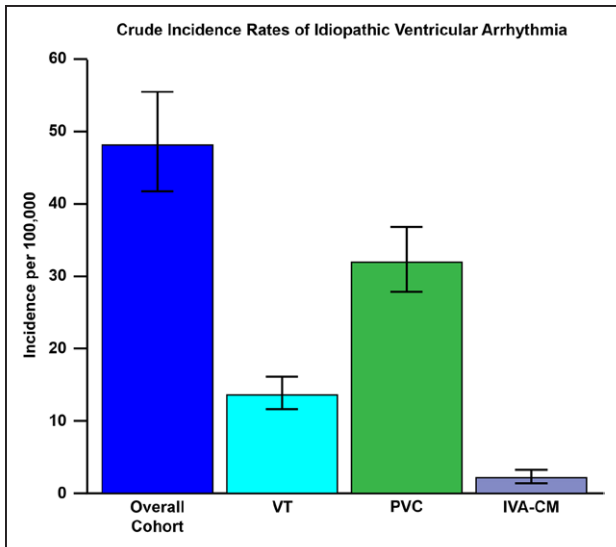


Figure 2. Crude incidence rates of idiopathic ventricular arrhythmia overall and according to subgroups. IVA-CM indicates idiopathic ventricular arrhythmia-associated cardiomyopathy; PVC, premature ventricular complex; and VT, ventricular tachycardia.

with an age- and sex-adjusted incidence rate of 33.5 (95% CI, 30.2–36.8) per 100 000. Of note, the age-adjusted incidence of VA overall was greater in females than in males (62.0 per 100 000 [95% CI, 55.7–68.2] versus 42.4 per 100 000 [95% CI, 36.8–48.0]; $P < 0.001$; Figure 3). Interestingly, there appeared to be a significant difference in crude incidence rates of IVA between males and females, both across age groups and over time ($P < 0.001$ for all; Figures 4 and 5A).

There was a clear increase in the documented incidence rate of VA from 2005 to 2013. The age- and sex-adjusted incidence rates in 2005 to 2007, 2008 to 2010, and 2011 to 2013 were 44.9 per 100 000 (95% CI, 38.0–51.8), 47.6 per 100 000 (95% CI, 40.8–54.5), and 62.0 per 100 000 (95% CI, 54.4–69.6), respectively, which was driven by an increase in symptomatic PVC (Figure 5B).

Idiopathic VT

Of 177 patients in this category, 97 (55%) were male and 80 (45%) were female. The average age was 59.2 ± 17.6 years. The overall age- and sex-adjusted incidence of idiopathic VT was 15.8 per 100 000 (95% CI, 13.5–18.1). The age-adjusted rate was not significantly different between sexes (19.2 per 100 000 [95% CI, 15.3–23.1] in males versus 13.3 per 100 000 [95% CI, 10.4–16.2] in females; $P = 0.11$). There was, however, an increase in incidence rate across age groups ($P < 0.001$). There was no increase in the age- and sex-adjusted incidence over time ($P = 0.30$): the age- and sex-adjusted incidence rates in 2005 to 2007, 2008 to 2010, and 2011 to 2013 were 14.9 per 100 000 (95% CI, 10.8–19.0), 13.9 per 100 000 (95% CI, 10.2–17.7), and 18.4 per 100 000 (95% CI, 14.1–22.7).

Idiopathic PVC

Of 408 patients with symptomatic PVC, 290 (71.1%) were female and 118 (28.9%) were male with an average age of 48.4 ± 15.8 years. The age- and sex-adjusted incidence rate increased throughout the study period. Specifically, the age- and sex-adjusted incidence rates between 2005 and 2007, 2008 and 2010, and 2011 and 2013 were 27.5 per 100 000 (95% CI, 22.3–32.8), 31.3 per 100 000 (95% CI, 25.8–36.8), and 40.8 per 100 000 (95% CI 34.7–46.9), respectively ($P = 0.003$). Furthermore, there was a significant increase with age ($P < 0.001$). The average PVC burden in the group was $3.8 \pm 6\%$.

IVA-Associated Cardiomyopathy

Of 29 patients with IVA-CM, 15 (51.7%) were female and 14 (48.3%) were male with an average age of 59.2 ± 19.2 years. The overall age- and sex-adjusted incidence was 2.6 per 100 000 (95% CI, 1.6–3.5). The age-adjusted incidence between sexes appeared similar (2.4 per 100 000 [95% CI, 1.2–3.7] versus 2.7 per 100 000 [95% CI, 1.3–4.2] in females and males, respectively); however, the small number of individuals precluded any formal testing. The average PVC burden in the IVA-CM group was $9.1 \pm 11\%$.

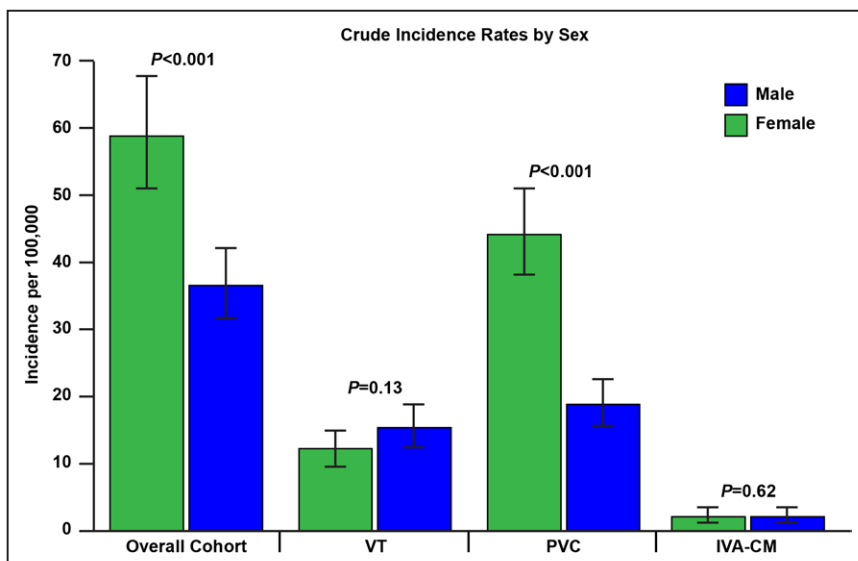


Figure 3. Crude incidence rates of idiopathic ventricular arrhythmia overall and according to subgroups according to gender. IVA-CM indicates asymptomatic premature ventricular complex-associated cardiomyopathy; PVC, premature ventricular complex; and VT, ventricular tachycardia.

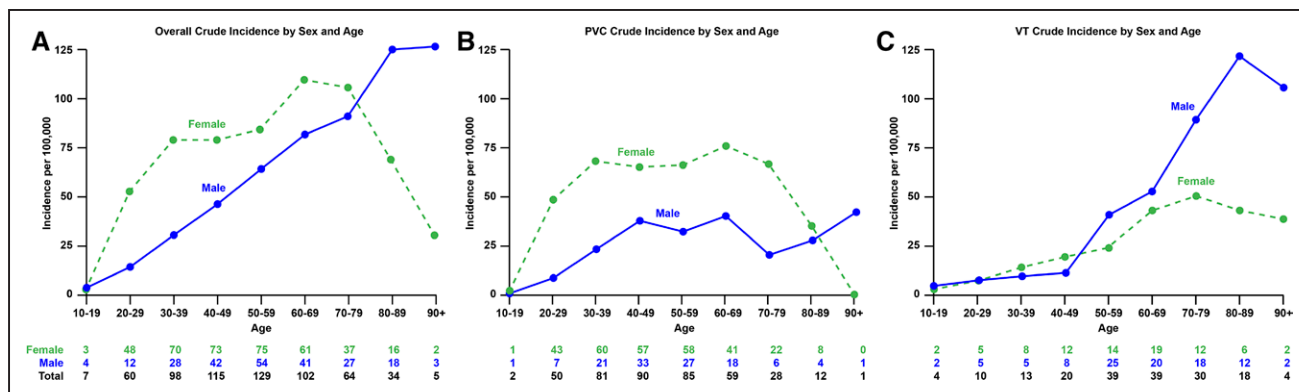


Figure 4. **A**, Crude incidence rate of idiopathic ventricular arrhythmia according to age and sex. **B**, Crude incidence rate of idiopathic PVC according to age and sex. **C**, Crude incidence rate of idiopathic VT according to age and sex. PVC indicates premature ventricular complex; and VT, ventricular tachycardia.

Ventricular Arrhythmia Burden and Development of Cardiomyopathy

The mean burden of VA (Figure in the [Data Supplement](#)) during a 24-hour period in the entire IVA cohort was $4.2 \pm 7\%$ (range 0–39). During a 24-hour period, 88 (14.3%) patients had burden $>10\%$ (Table 3). The mean EF was $46 \pm 11\%$, and the median time to low EF was 5.1 years among the IVA-CM group. The incidence of cardiomyopathy is similar among patients with $<10\%$ burden when compared with those with $>10\%$ burden (P value = 0.07) in the entire cohort.

Discussion

This population-based study of a nonreferral-based cohort of Olmsted County residents demonstrates that the overall age- and sex-adjusted incidence of idiopathic VA among individuals ≥ 18 years is 51.9 per 100,000. This is lower than the incidence of atrial fibrillation¹⁶ and other common cardiovascular disorders, including myocardial infarction,¹⁷ and heart failure.¹⁸ In addition, the incidence of IVA seems to be rising (in contrast to myocardial infarction and heart failure) and varies according to age group and sex.

Rising Incidence

The rising incidence of IVA is driven by an increase in idiopathic PVC incidence, which is likely because of the increasing awareness and recognition of their occurrence. For example, smart phone applications, portable single-lead ECG recorders, and an expanding menu of ambulatory recording devices more readily permit identification of arrhythmias.¹⁹ Notably, our cohort excluded patients with cardiac implantable electronic devices. Our data provide important insights by highlighting the incidence of VT and PVC by age group and sex in those typically deemed to be at low risk for cardiovascular disease, given that recent studies have associated even a low burden of PVCs with a decrease in left ventricular EF, an increase in incident heart failure, and increased mortality.^{20–22} Furthermore, the contribution of PVC burden to heart failure was comparable to conventional risk factors.²² However, it is difficult to determine whether early detection and treatment of IVA, particularly PVCs, alters the natural history

of patients. Certainly, studies assessing the impact of IVA therapy on outcomes are warranted.

Age Difference

We found an increase in incidence with age for VA—this was driven by an increase in idiopathic VT and symptomatic PVCs as patients got older. It is plausible that increased medical contact for nonspecific complaints with age leads to more testing and, thus, identification of arrhythmias that would have otherwise been unnoticed.²³ Although the emerging technology available to the public may lead to an increased detection rate in general, the low usage rate of such technology in the older population argues against this being a factor in that group.²⁴ Rather, the increased incidence in aging individuals suggests that subclinical structural changes, for example, myocardial fibrosis, may be contributing.²⁵ Therefore, the increased sensitivity of cardiac tests in the future will likely reclassify many idiopathic VA. In one study of VT patients with no structural abnormalities detected on usual cardiac investigations, cardiac magnetic resonance imaging demonstrated structural abnormalities in $\approx 5\%$ of patients with IVA of right ventricular origin and 40% of left ventricular origin.²⁶ Given the current prohibitive cost of widespread magnetic resonance imaging, in our opinion, the definition of IVA should ideally consist of the following: absence of clinically significant coronary artery and structural heart disease, EF $\geq 50\%$ (unless low EF is secondary to IVA), absence of ECG evidence of scar (eg, a fractionated QRS²⁷), and a normal signal-averaged ECG.²⁸ Certainly, the ability to detect myocardial fibrosis is important because this has been associated with an increased vulnerability for arrhythmias.^{29,30}

Sex Difference

We found that the incidence of symptomatic PVC was greater in women, while that of idiopathic VT was similar among sexes. In keeping with other studies, sex differences in arrhythmias, including idiopathic VT, have been well reported.^{31–33} Studies have suggested that the sex-related variation in the incidence of IVA may in part be secondary to hormonal difference between men and

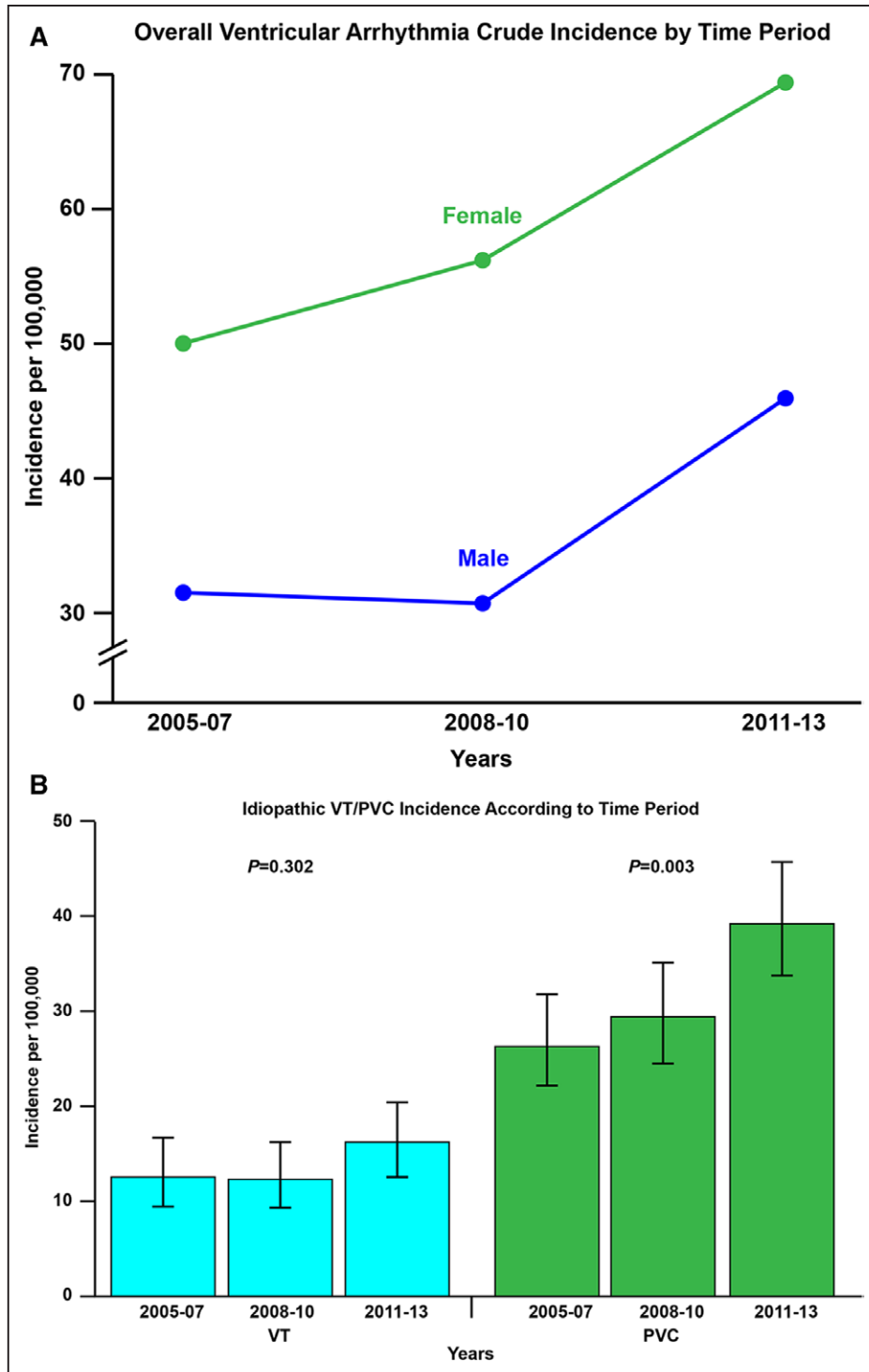


Figure 5. A, Incidence rate of idiopathic ventricular arrhythmia according to specific study time periods. **B,** Incidence rate of idiopathic ventricular tachycardia (VT) and premature ventricular complex (PVC) according to specific study time periods.

women.¹² Additionally, sex steroids may alter K^+ channel activity, thus, altering the action potential duration and susceptibility to reentrant VA.³⁴ However, although action potential duration may be longer in women, they have less transmural dispersion of refractoriness, which may actually protect against reentrant arrhythmias.³² Of course, the variability in the incidence of IVA may be related to difference in symptom perception and tendency to seek medical

attention.³⁵ For example, in addition to hormonal differences, women may be more sensitive to PVCs such that they seek medical attention sooner, while males wait for more severe symptoms, which might explain our observed lack of difference with idiopathic VT. This is supported by studies demonstrating that males are more likely to develop IVA-CM.⁴ However, it is not possible to determine this from our study.

Table 3. Arrhythmia Burden Among Patients With Idiopathic VA

PVC Burden*	Total n (%)	Idiopathic VT (N=177)	Symptomatic PVC (N=408)	IVA-CM
<10%	382 (81.3)	110 (70.9)	254 (88.2)	18 (66.7%)
11%–20%	55 (11.7)	26 (16.8)	26 (9.0)	3 (11.1%)
21%–30%	22 (4.7)	13 (8.4)	5 (1.7)	4 (14.8%)
31%–40%	10 (2.1)	5 (3.2)	3 (1.0)	2 (7.4%)
>41%	1 (0.2)	1 (0.6)	0	0

IVA-CM indicates idiopathic ventricular arrhythmia–associated cardiomyopathy; PVC, premature ventricular complex; VA, ventricular arrhythmias; and VT, ventricular tachycardia.

*PVC burden=PVC count/total number of beats over a 24-h period expressed as percent. PVC burden reported here are at the time of diagnosis.

Limitations

An incorrect estimation of the true incidence of idiopathic ventricular arrhythmia by this study may have occurred. The standard definition for idiopathic VT may miss individuals with subclinical CAD or scar; more sensitive imaging techniques may detect these abnormalities and, thus, reclassify these patients, lowering true incidence rates. Current evidence suggests that IVA-CM is seen in patients with >10% burden. It is possible that some of the patients with burden <10% had nonischemic cardiomyopathy, and PVCs were secondary to underlying disease processes. Sensitive imaging tests to detect myocardial scar and longitudinal population studies evaluating the relationship are needed to clarify the relationship between PVC burden and development of cardiomyopathy. Further, not every resident of Olmsted County had some form of ECG recorded during the study period; thus, our incidence rate may be an underestimate. Thus, the trends may reflect ascertainment bias with time. Given that the majority of residents in Olmsted County are from a homogeneous ethnic group (Caucasians), incidence estimates may not be applicable to other ethnicities. Treatment rates with medical therapy are low in our cohort. It is plausible that incidence rates of IVA may be lower with higher rates of medical therapy. Small number of patients in the IVA-CM group precluded meaningful descriptive or discriminative analysis. Finally, location or type of IVA is not reported; further data detailing this may provide important insights.

Conclusion

The incidence of IVA seems to be increasing and is mainly driven by increasing PVC incidence rates. The overall incidence of VA increases with age, and women have a higher incidence of symptomatic PVC. The relationship between PVC burden and development of cardiomyopathy is less clear in our population-based study; however, the rate of IVA-CM seems to be extremely low in the general population.

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Disclosures

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References

- Brooks R, Burgess JH. Idiopathic ventricular tachycardia. A review. *Medicine (Baltimore)*. 1988;67:271–294.
- Viskin S, Rosso R, Rogowski O, Belhassen B. The “short-coupled” variant of right ventricular outflow ventricular tachycardia: a not-so-benign form of benign ventricular tachycardia? *J Cardiovasc Electrophysiol*. 2005;16:912–916. doi: 10.1111/j.1540-8167.2005.50040.x.
- Brugada P, Gijssels S, Brugada J, Andries E. Investigation of palpitations. *Lancet*. 1993;341:1254–1258.
- Latchamsetty R, Bogun F. Premature ventricular complexes and premature ventricular complex induced cardiomyopathy. *Curr Probl Cardiol*. 2015;40:379–422. doi: 10.1016/j.cpcardiol.2015.03.002.
- Singh SM, Kadmon E, Suszko A, Chauhan VS. Syncope triggered by a premature ventricular complex: a case of atrial fibrillation and paroxysmal atrioventricular block. *Heart Rhythm*. 2012;9:1650–1651. doi: 10.1016/j.hrthm.2011.09.061.
- Tanaka Y, Tada H, Ito S, Naito S, Higuchi K, Kumagai K, Hachiya H, Hirao K, Oshima S, Taniguchi K, Aonuma K, Isobe M. Gender and age differences in candidates for radiofrequency catheter ablation of idiopathic ventricular arrhythmias. *Circ J*. 2011;75:1585–1591.
- Rocca WA, Yawn BP, St Sauver JL, Grossardt BR, Melton LJ 3rd. History of the Rochester Epidemiology Project: half a century of medical records linkage in a US population. *Mayo Clin Proc*. 2012;87:1202–1213. doi: 10.1016/j.mayocp.2012.08.012.
- St Sauver JL, Grossardt BR, Yawn BP, Melton LJ 3rd, Pankratz JJ, Brue SM, Rocca WA. Data resource profile: the Rochester Epidemiology Project (REP) medical records-linkage system. *Int J Epidemiol*. 2012;41:1614–1624. doi: 10.1093/ije/dys195.
- St Sauver JL, Grossardt BR, Leibson CL, Yawn BP, Melton LJ 3rd, Rocca WA. Generalizability of epidemiological findings and public health decisions: an illustration from the Rochester Epidemiology Project. *Mayo Clin Proc*. 2012;87:151–160. doi: 10.1016/j.mayocp.2011.11.009.
- St Sauver JL, Grossardt BR, Yawn BP, Melton LJ 3rd, Rocca WA. Use of a medical records linkage system to enumerate a dynamic population over time: the Rochester epidemiology project. *Am J Epidemiol*. 2011;173:1059–1068. doi: 10.1093/aje/kwq482.
- Hoffmayer KS, Gerstenfeld EP. Diagnosis and management of idiopathic ventricular tachycardia. *Curr Probl Cardiol*. 2013;38:131–158. doi: 10.1016/j.cpcardiol.2013.02.002.
- Marchlinski FE, Deely MP, Zado ES. Sex-specific triggers for right ventricular outflow tract tachycardia. *Am Heart J*. 2000;139:1009–1013. doi: 10.1067/mhj.2000.106164.
- Pedersen CT, Kay GN, Kalman J, Borggrefe M, Della-Bella P, Dickfeld T, Dorian P, Huikuri H, Kim YH, Knight B, Marchlinski F, Ross D, Sacher F, Sapp J, Shivkumar K, Soejima K, Tada H, Alexander ME, Triedman JK, Yamada T, Kirchhof P, Lip GY, Kuck KH, Mont L, Haines D, Indik J, Dimarco J, Exner D, Iesaka Y, Savelieva I; EP-Europe/UK. EHRA/HRS/APHRS expert consensus on ventricular arrhythmias. *Heart Rhythm*. 2014;11:e166–e196. doi: 10.1016/j.hrthm.2014.07.024.
- Wellens HJ. Electrophysiology: Ventricular tachycardia: diagnosis of broad QRS complex tachycardia. *Heart*. 2001;86:579–585.
- Zipes DP, Camm AJ, Borggrefe M, Buxton AE, Chaitman B, Fromer M, Gregoratos G, Klein G, Moss AJ, Myerburg RJ, Priori SG, Quinones MA, Roden DM, Silka MJ, Tracy C, Smith SC Jr, Jacobs AK, Adams CD, Antman EM, Anderson JL, Hunt SA, Halperin JL, Nishimura R, Ornato JP, Page RL, Riegel B, Blanc JJ, Budaj A, Dean V, Deckers JW, Despres C, Dickstein K, Lekakis J, McGregor K, Metra M, Morais J, Osterspey A, Tamargo JL, Zamorano JL; American College of Cardiology/American Heart Association Task Force; European Society of Cardiology Committee for Practice Guidelines; European Heart Rhythm Association; Heart Rhythm Society. ACC/AHA/ESC 2006 Guidelines for Management of Patients With Ventricular Arrhythmias and the

- Prevention of Sudden Cardiac Death: a report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (writing committee to develop Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death): developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. *Circulation*. 2006;114:e385–e484. doi: 10.1161/CIRCULATIONAHA.106.178233.
16. Miyasaka Y, Barnes ME, Gersh BJ, Cha SS, Bailey KR, Abhayaratna WP, Seward JB, Tsang TS. Secular trends in incidence of atrial fibrillation in Olmsted County, Minnesota, 1980 to 2000, and implications on the projections for future prevalence. *Circulation*. 2006;114:119–125. doi: 10.1161/CIRCULATIONAHA.105.595140.
 17. Roger VL, Jacobsen SJ, Weston SA, Goraya TY, Killian J, Reeder GS, Kottke TE, Yawn BP, Frye RL. Trends in the incidence and survival of patients with hospitalized myocardial infarction, Olmsted County, Minnesota, 1979 to 1994. *Ann Intern Med*. 2002;136:341–348.
 18. Gerber Y, Weston SA, Redfield MM, Chamberlain AM, Manemann SM, Jiang R, Killian JM, Roger VL. A contemporary appraisal of the heart failure epidemic in Olmsted County, Minnesota, 2000 to 2010. *JAMA Intern Med*. 2015;175:996–1004. doi: 10.1001/jamainternmed.2015.0924.
 19. Walsh JA 3rd, Topol EJ, Steinhubl SR. Novel wireless devices for cardiac monitoring. *Circulation*. 2014;130:573–581. doi: 10.1161/CIRCULATIONAHA.114.009024.
 20. Bikkina M, Larson MG, Levy D. Prognostic implications of asymptomatic ventricular arrhythmias: the Framingham Heart Study. *Ann Intern Med*. 1992;117:990–996.
 21. Agarwal SK, Simpson RJ Jr, Rautaharju P, Alonso A, Shahar E, Massing M, Saba S, Heiss G. Relation of ventricular premature complexes to heart failure (from the Atherosclerosis Risk In Communities [ARIC] Study). *Am J Cardiol*. 2012;109:105–109. doi: 10.1016/j.amjcard.2011.08.009.
 22. Dukes JW, Dewland TA, Vittinghoff E, Mandyam MC, Heckbert SR, Siscovick DS, Stein PK, Psaty BM, Sotoodehnia N, Gottdiener JS, Marcus GM. Ventricular ectopy as a predictor of heart failure and death. *J Am Coll Cardiol*. 2015;66:101–109. doi: 10.1016/j.jacc.2015.04.062.
 23. Perissinotto CM, Ritchie C. Atypical presentations of illness in older adults. In: Williams B.A., Chang A., Ahalt C., Chen H., Conant R., Landefeld C.S., Ritchie C., Yukawa M., eds. *Current Diagnosis & Treatment: Geriatrics*, 2nd ed. New York, NY: McGraw-Hill Education; 2014.
 24. Fox CS, Hwang SJ, Nieto K, Valentino M, Mutalik K, Massaro JM, Benjamin EJ, Murabito JM. Digital Connectedness in the Framingham Heart Study. *J Am Heart Assoc*. 2016;5:e003193. doi: 10.1161/JAHA.116.003193.
 25. Nogami A. Gender differences in idiopathic ventricular arrhythmias. *Circ J*. 2011;75:1569–1570.
 26. Nucifora G, Muser D, Masci PG, Barison A, Rebellato L, Piccoli G, Daleffe E, Toniolo M, Zanuttini D, Facchin D, Lombardi M, Proclemer A. Prevalence and prognostic value of concealed structural abnormalities in patients with apparently idiopathic ventricular arrhythmias of left versus right ventricular origin: a magnetic resonance imaging study. *Circ Arrhythm Electrophysiol*. 2014;7:456–462. doi: 10.1161/CIRCEP.113.001172.
 27. Das MK, Khan B, Jacob S, Kumar A, Mahenthiran J. Significance of a fragmented QRS complex versus a Q wave in patients with coronary artery disease. *Circulation*. 2006;113:2495–2501. doi: 10.1161/CIRCULATIONAHA.105.595892.
 28. Gomes JA, Cain ME, Buxton AE, Josephson ME, Lee KL, Hafley GE. Prediction of long-term outcomes by signal-averaged electrocardiography in patients with unsustained ventricular tachycardia, coronary artery disease, and left ventricular dysfunction. *Circulation*. 2001;104:436–441.
 29. de Jong S, van Veen TA, van Rijen HV, de Bakker JM. Fibrosis and cardiac arrhythmias. *J Cardiovasc Pharmacol*. 2011;57:630–638. doi: 10.1097/FJC.0b013e318207a35f.
 30. Aljaroudi WA, Flamm SD, Saliba W, Wilkoff BL, Kwon D. Role of CMR imaging in risk stratification for sudden cardiac death. *JACC Cardiovasc Imaging*. 2013;6:392–406. doi: 10.1016/j.jcmg.2012.11.011.
 31. Nakagawa M, Takahashi N, Nobe S, Ichinose M, Ooie T, Yufu F, Shigematsu S, Hara M, Yonemochi H, Saikawa T. Gender differences in various types of idiopathic ventricular tachycardia. *J Cardiovasc Electrophysiol*. 2002;13:633–638.
 32. Nakagawa M, Takahashi N, Watanabe M, Ichinose M, Nobe S, Yonemochi H, Ito M, Saikawa T. Gender differences in ventricular repolarization: terminal T wave interval was shorter in women than in men. *Pacing Clin Electrophysiol*. 2003;26(1 pt 1):59–64.
 33. Yamada T, Maddox WR, McElderry HT, Doppalapudi H, Plumb VJ, Kay GN. Radiofrequency catheter ablation of idiopathic ventricular arrhythmias originating from intramural foci in the left ventricular outflow tract: efficacy of sequential versus simultaneous unipolar catheter ablation. *Circ Arrhythm Electrophysiol*. 2015;8:344–352. doi: 10.1161/CIRCEP.114.002259.
 34. Pham TV, Sosunov EA, Gainullin RZ, Danilo P Jr, Rosen MR. Impact of sex and gonadal steroids on prolongation of ventricular repolarization and arrhythmias induced by I(K)-blocking drugs. *Circulation*. 2001;103:2207–2212.
 35. Humphries KH, Kerr CR, Connolly SJ, Klein G, Boone JA, Green M, Sheldon R, Talajic M, Dorian P, Newman D. New-onset atrial fibrillation: sex differences in presentation, treatment, and outcome. *Circulation*. 2001;103:2365–2370.

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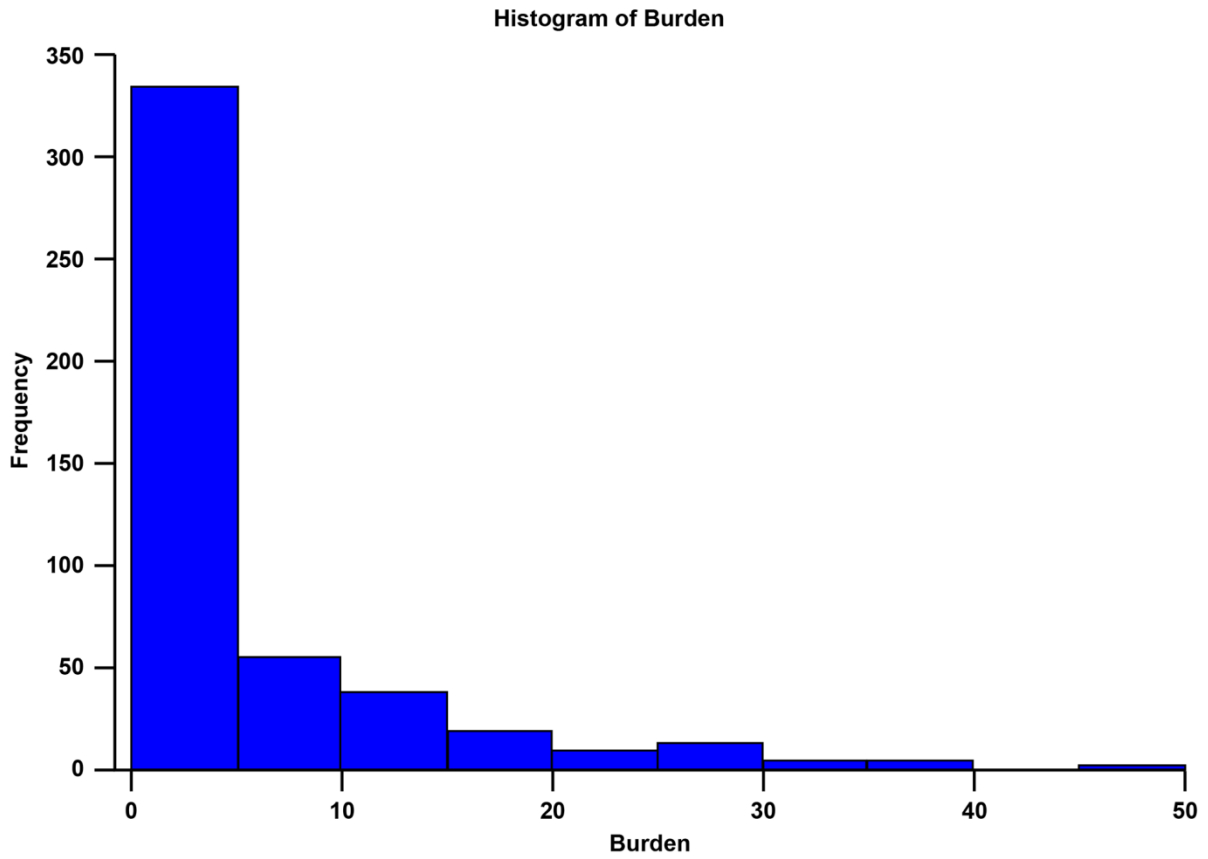
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SUPPLEMENTAL MATERIAL



Supplemental Figure: Histogram of PVC burden among the idiopathic VA cohort. Majority of the patients had fairly low arrhythmia burden.