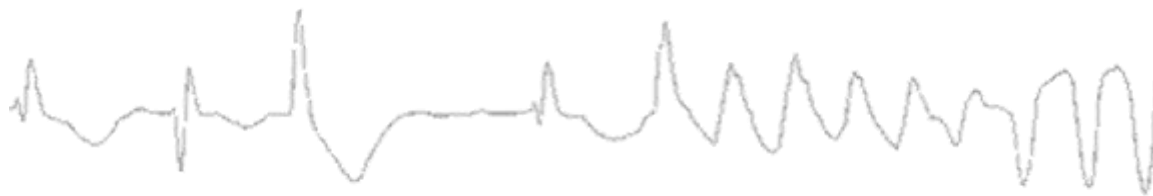




6TH EUROPEAN CONGRESS OF AEROSPACE MEDICINE
PRAGUE - SEPTEMBER 20 - 22, 2018



A 3D matrix as a help to assess the aeromedical risk : The Premature Ventricular Complex example



NATO Aviation Cardiology Working Group (RTG HFM-251)

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Disclosure information



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Olivier Manen, MD, Prof., Col

I have no financial relationships to disclose

I will not discuss off-label use and/or investigational use in my presentation



Topics in the NATO Aviation Cardiology Working Group



- Coronary artery disease
- Heart valve disease
- **Electrical abnormalities**
- Heart muscle disease
- Congenital heart disease
- Cardiac surgery

Sinus node dysfunction

Atrioventricular conduction disturbance

Bundle branch blocks

Atrial ectopy, **Ventricular ectopy**

Supraventricular tachycardia

Ventricular pre-excitation

Atrial fibrillation and flutter

Accelerated idioventricular rhythm

Ventricular tachycardia

Brugada syndrome, long QT syndrome

0.8% of ECG
in aircrew
(USAF 2015)



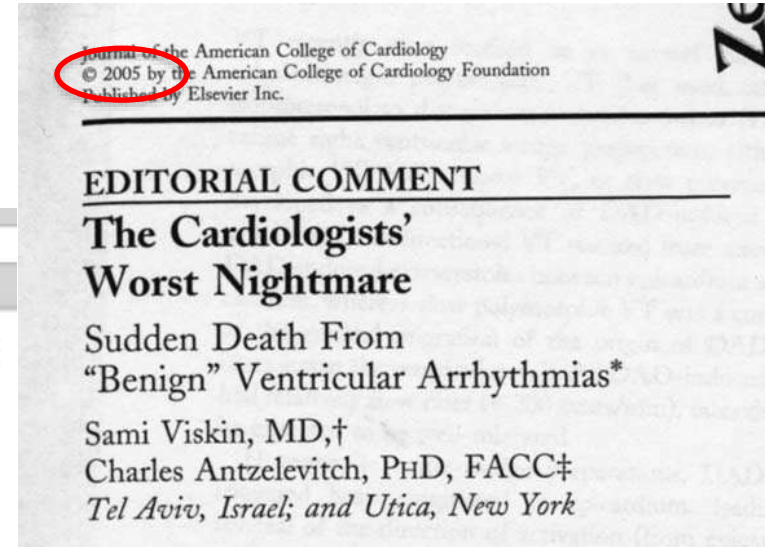
PVCs: What is the problem ?



- Most of the time...

« While we have not performed a specific follow-up study on such individuals, we are aware of hundreds who have returned to high-G cockpits with ventricular ectopy » *Pickard J.*

- Sometimes...



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US National Library of Medicine
National Institutes of Health

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Advanced

Format: Abstract +

Send to +

Int J Cardiol. 2016 Nov 1; 222:101-103. doi: 10.1016/j.ijcard.2016.06.276. Epub 2016 Jun 29.

Nightmares in cardiology: Sudden cardiac death in a patient with apparently healthy heart and "benign" outflow tract extrasystoles.

Abdin A¹, Eitel C², Thiele H², Tilz RR².



- Low risk – acceptable
- Moderate risk – aeromedical board-level discussion required
- High risk – not acceptable

Assessing the aeromedical risk with the three-dimensional risk matrix

The Royal Canadian Air Force

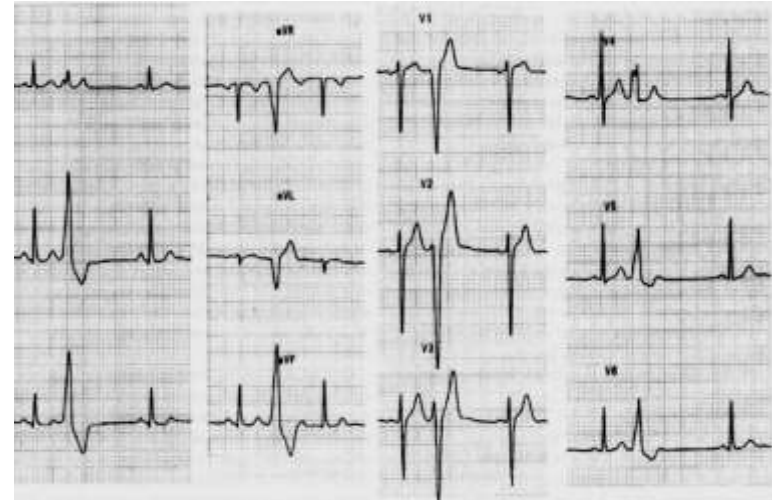


	Level 1 Medical Event	Level 2 Medical Event	Level 3 Medical Event	Level 4 Medical Event
	Minimal impact on mission	May result in a mission abort or compromised effectiveness	Likely to result in a flight safety hazard or compromise	Likely to result in a flight safety critical event
	May result in a deleterious effect on the health of the individual aircrew but minimal effect on performance	Aircrew able to continue duties with minor to moderate performance compromise.	Major decrement in performance	Total acute incapacitation (may include sudden death)
	Requires routine periodic medical follow-up	Requires medical attention	May require immediate medical attention	Requires immediate advanced medical care
PILOTS, COPILOTS				
Likely >2%/yr	Low risk	Moderate risk	High risk	High risk
Possible 1-2%/yr	Low risk	Low risk	Moderate risk	High risk
Unlikely 0.5-1%/yr	Low risk	Low risk	Low risk	Moderate risk
Highly unlikely <0.5%/yr	Low risk	Low risk	Low risk	Low risk
NAVIGATORS, FLIGHT ENGINEER, FLIGHT CONTROLLERS				
Likely >2%/yr	Low risk	Moderate risk	High risk	High risk
Possible 1-2%/yr	Low risk	Low risk	Moderate risk	Moderate risk
Unlikely 0.5-1%/yr	Low risk	Low risk	Low risk	Low risk
Highly unlikely <0.5%/yr	Low risk	Low risk	Low risk	Low risk
FLIGHT ATTENDANTS LOADMASTERS				
Likely >2%/yr	Low risk	Low risk	Moderate risk	High risk
Possible 1-2%/yr	Low risk	Low risk	Low risk	Moderate risk
Unlikely 0.5-1%/yr	Low risk	Low risk	Low risk	Low risk
Highly unlikely <0.5%/yr	Low risk	Low risk	Low risk	Low risk

Case 1



- 27-yo **flight engineer**, sportsman
- No past medical / cardiac family history
- Few palpitations
- PVCs on ECG, « **benign** » **morphology**
- Holter: **7,500** PVCs/d, monomorphic, isolated
- TTE: normal
- Exercise test: negative, disappearance of PVCs
- Late potentials: negative
- LV/RV angioscintigraphy: normal





Case 1

Assessing the risk:

- Present **palpitations** in relation to PVCs
- Risk of **VT**

Level 1 Medical Event	Level 2 Medical Event	Level 3 Medical Event	Level 4 Medical Event
Minimal impact on mission	May result in a mission abort or compromised effectiveness	Likely to result in a flight safety hazard or compromise	Likely to result in a flight safety critical event
May result in a deleterious effect on the health of the individual aircrew but minimal effect on performance	Aircrew able to continue duties with minor to moderate performance compromise.	Major decrement in performance	Total acute incapacitation (may include sudden death)
Requires routine periodic medical follow-up	Requires medical attention	May require immediate medical attention	Requires immediate advanced medical care

PILOTS, COPILOTS				
Likely >2%/yr				
Possible 1-2%/yr				
Unlikely 0.5-1%/yr				
Highly unlikely <0.5%/yr				
NAVIGATORS, FLIGHT ENGINEER, FLIGHT CONTROLLERS				
Likely >2%/yr				
Possible 1-2%/yr				
Unlikely 0.5-1%/yr				
Highly unlikely <0.5%/yr				

Palpitations

VT

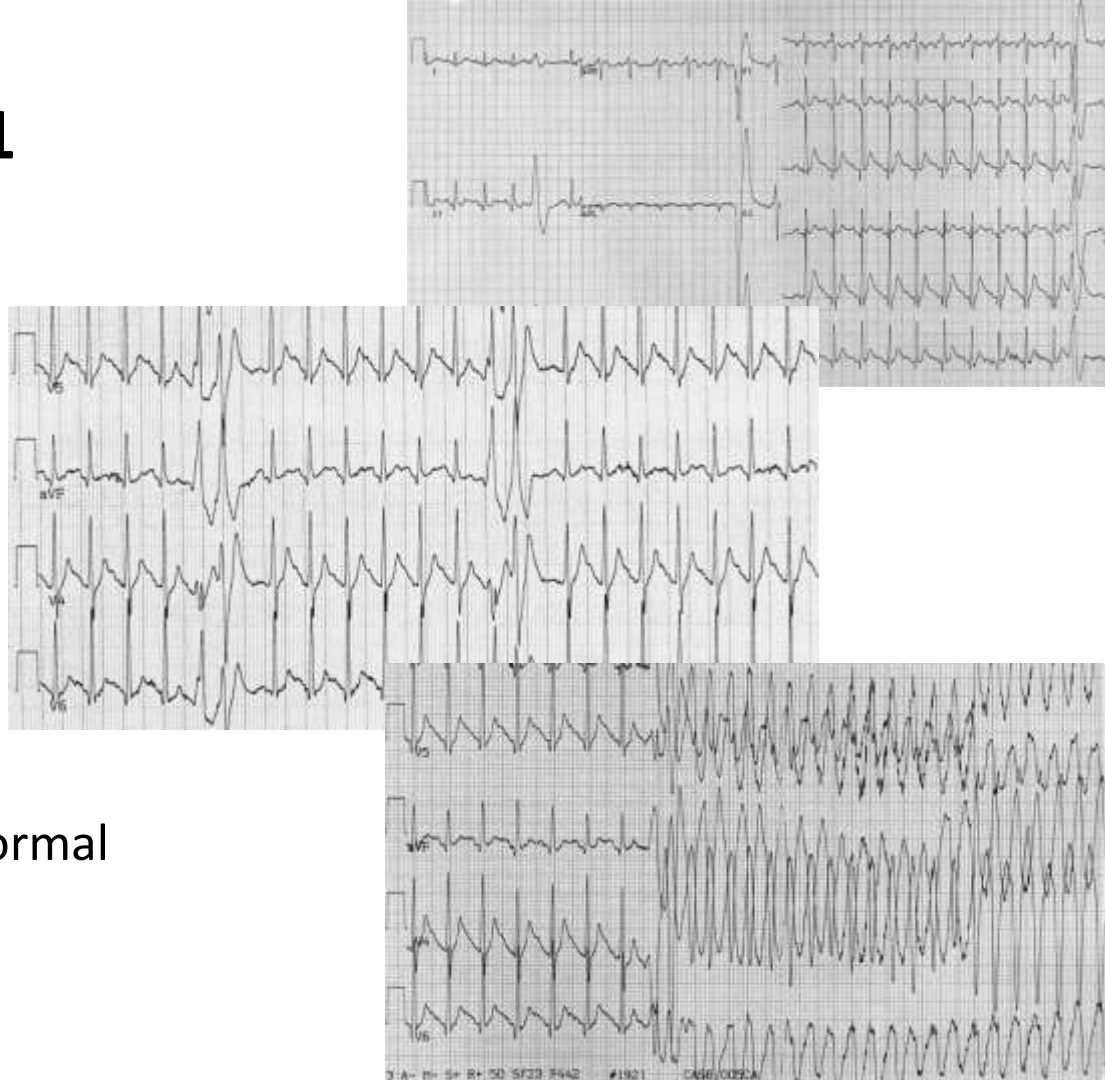
VT

VT

Case 1

2.5 years later:

- **Syncope during effort**
- Holter: 5,000 PVCs/d, monomorphic, isolated
- Late potentials: negative
- TTE: normal
- LV/RV angioscintigraphy: normal
- **Exercise test...**





Case 1

Retrospectively, risk of VT:

- For a **fighter pilot**

(exercise / +Gz)

- For a **pilot**

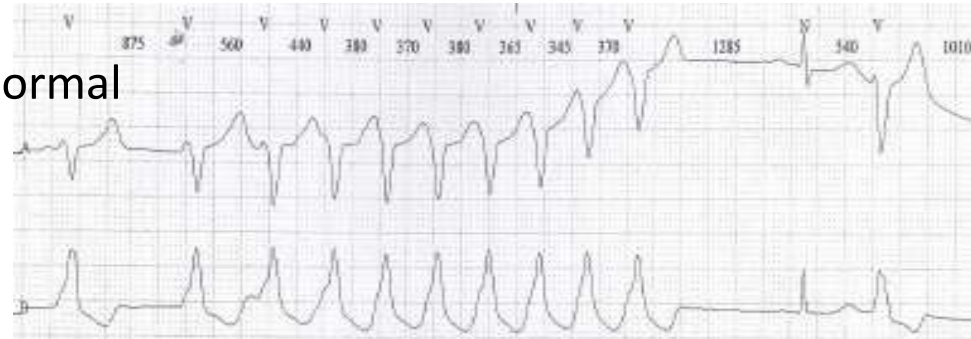
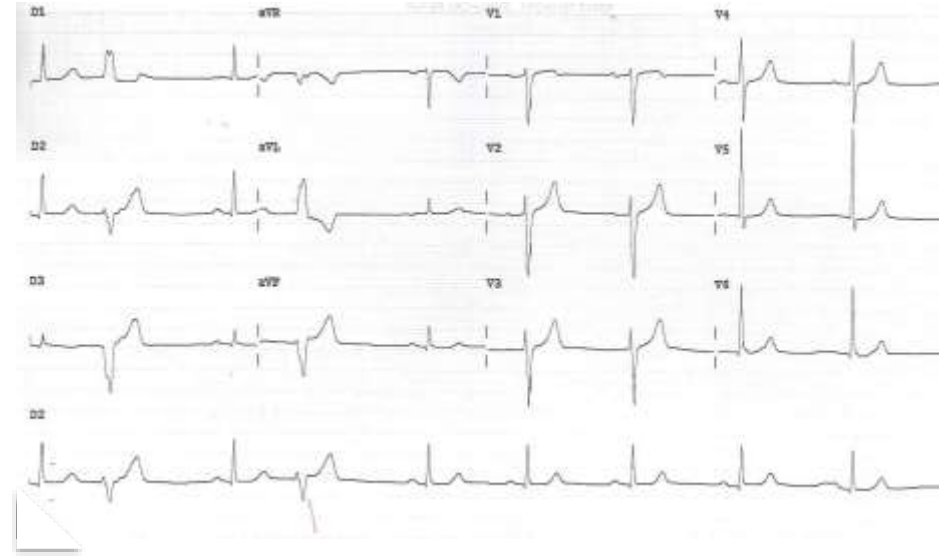
- For this **flight engineer**

Level 1 Medical Event	Level 2 Medical Event	Level 3 Medical Event	Level 4 Medical Event
Minimal impact on mission	May result in a mission abort or compromised effectiveness	Likely to result in a flight safety hazard or compromise	Likely to result in a flight safety critical event
May result in a deleterious effect on the health of the individual aircrew but minimal effect on performance	Aircrew able to continue duties with minor to moderate performance compromise.	Major decrement in performance	Total acute incapacitation (may include sudden death)
Requires routine periodic medical follow-up	Requires medical attention	May require immediate medical attention	Requires immediate advanced medical care

PILOTS, COPILOTS				
Likely >2%/yr				VT (+Gz) ?
Possible 1-2%/yr				VT
Unlikely 0.5-1%/yr				
Highly unlikely <0.5%/yr				
NAVIGATORS, FLIGHT ENGINEER, FLIGHT CONTROLLERS				
Likely >2%/yr				
Possible 1-2%/yr				VT
Unlikely 0.5-1%/yr				
Highly unlikely <0.5%/yr				

Case 2

- 64-yo retired airline pilot, FI
- Lymphoma 2002 (chemotherapy)
- Asymptomatic, PVCs with **left axis**
- Holter: 350 PVCs/d, monomorphic, 5 couplets and a **non-sustained VT**
- Exercise test: negative
- TTE, coronary angiography, CMR: normal
- With β -blocker: 420 PVCs/d
7 couplets





Case 2

Assessing the risk:

- Risk of **sustained VT** or clinical event if idiopathic NSVT
- (Side-effects of β -blocker)

Level 1 Medical Event	Level 2 Medical Event	Level 3 Medical Event	Level 4 Medical Event
Minimal impact on mission	May result in a mission abort or compromised effectiveness	Likely to result in a flight safety hazard or compromise	Likely to result in a flight safety critical event
May result in a deleterious effect on the health of the individual aircrew but minimal effect on performance	Aircrew able to continue duties with minor to moderate performance compromise.	Major decrement in performance	Total acute incapacitation (may include sudden death)
Requires routine periodic medical follow-up	Requires medical attention	May require immediate medical attention	Requires immediate advanced medical care
PILOTS, COPILOTS			
Likely >2%/yr			
Possible 1-2%/yr			
Unlikely 0.5-1%/yr			
Highly unlikely <0.5%/yr	VT	VT	VT

GARDNER RA, KRUYER WB, PICKARD JS, CELIO PV. *Nonsustained ventricular tachycardia in 193 U.S. military aviators: long-term follow-up.* Aviat Space Environ Med 2000; 71:783-90.

Conclusions: Nonsustained VT did not predict future documented sustained VT. Cofactors failed to predict a subgroup at increased risk for events. Idiopathic nonsustained VT appeared to be a low risk population for whom expanded waiver criteria are proposed with suggested limits on duration and number of episodes of VT.



Case 3

- 33-yo military helicopter monopilot
- No past medical / cardiac family history
- Asymptomatic
- PVCs with « benign » morphology
- Holter: **30,000 - 40,000** PVCs/d, monomorphic, isolated
- Exercise test: negative, disappearance of PVCs
- Late potentials: negative
- TTE and CMR: normal (no LV dilation, LVEF > 50%)





Case 3

Assessing the risk:

- NSVT / SVT
- **PVC-induced cardiomyopathy**

(with LV dysfunction)

PILOTS, COPILOTS				
Likely >2%/yr		CM (> 5 y)	CM (> 5 y) / +Gz	
Possible 1-2%/yr		CM (3-5 y)	CM (3-5 y) / +Gz	
Unlikely 0.5-1%/yr		CM (< 3 y)	CM (< 3 y) / +Gz	
Highly unlikely <0.5%/yr		VT	VT	VT

- Possible if PVC burden > 10%, usually when PVCs > 20,000/d
- Higher impact of a lower LVEF in fighter pilots

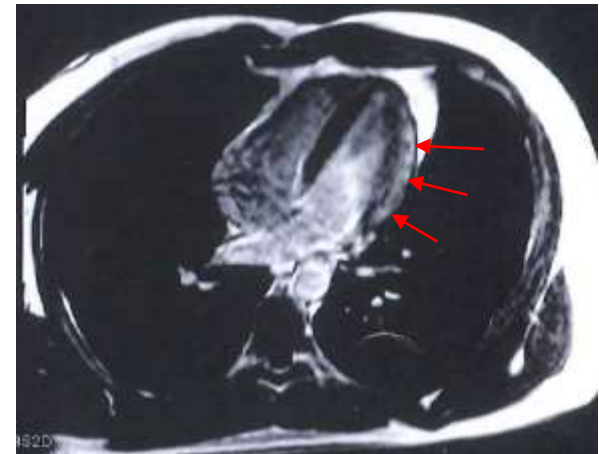
Delise P. Am J Cardiol 2013; 112(9): 1396-402

Baman TS. Heart Rhythm 2010; 7(7): 865-9

Niwano S. Heart 2009; 95(15): 1230-7

Case 4

- 35-yo airline pilot
- No past medical / cardiac family history
- Asymptomatic
- PVCs of **right ventricular presumed origin**
- Holter: 5,700 PVCs/d, 10 couplets
- TTE: normal
- Exercise test: negative, disappearance of PVCs
- Late potentials: negative
- CMR: **subepicardial late gadolinium enhancement** in the inferolateral segments (LVEF 55%): sequela of myocarditis





Case 4

Assessing the risk:

- **Additional risk of VT**
- How long ? (critical period of

6 months after acute
myocarditis)

- Relation between the number of segments involved and the risk of VT
- What about if PVCs with RV presumed origin ?

Level 1 Medical Event	Level 2 Medical Event	Level 3 Medical Event	Level 4 Medical Event
Minimal impact on mission	May result in a mission abort or compromised effectiveness	Likely to result in a flight safety hazard or compromise	Likely to result in a flight safety critical event
May result in a deleterious effect on the health of the individual aircrew but minimal effect on performance	Aircrew able to continue duties with minor to moderate performance compromise.	Major decrement in performance	Total acute incapacitation (may include sudden death)
Requires routine periodic medical follow-up	Requires medical attention	May require immediate medical attention	Requires immediate advanced medical care

PILOTS, COPILOTS				
Likely >2%/yr				VT / SCD ?
Possible 1-2%/yr			VT ?	
Unlikely 0.5-1%/yr		VT ?		
Highly unlikely <0.5%/yr				

Medicine (Baltimore). 2017 May;96(18):e6633. doi: 10.1097/MD.00000000000006633.

Increased risk of ventricular tachycardia and cardiovascular death in patients with myocarditis during the long-term follow-up: A national representative cohort from the National Health Insurance Research Database.

Je ALD¹, Wu TC, Lin YJ, Chen YY, Chung FP, Chang SL, Lo LW, Hu YF, Tuan TC, Chao TE, Liao JN, Chien KL, Lin CY, Chang YT, Chen SA.

No subgroups

Outcomes	Variables	Total numbers	Event, %	Incidence rate (per 100,000 PY)	Models	Hazard ratio (95% CI)	P [*]
VT	No myocarditis	13,250	62 (0.47)	43	–	1 (Reference)	–
	With myocarditis	13,250	716 (5.41)	519	0	12.1 (9.30–15.6)	<.001
					1	12.1 (9.35–15.7)	<.001
					2	12.1 (9.35–15.7)	<.001
					3	16.1 (12.37–20.9)	<.001
CV death	No myocarditis	13,250	421 (3.18)	293	–	1 (Reference)	–
	With myocarditis	13,250	864 (6.52)	613	0	2.12 (1.88–2.38)	<.001
					1	2.10 (1.87–2.36)	<.001
					2	2.10 (1.87–2.36)	<.001
					3	2.42 (2.14–2.73)	<.001
All-cause mortality	No myocarditis	13,250	2497 (18.90)	1737	–	1 (Reference)	–
	With myocarditis	13,250	3243 (24.50)	2301	0	1.33 (1.26–1.40)	<.001
					1	1.30 (1.24–1.37)	<.001
					2	1.30 (1.24–1.37)	<.001
					3	1.41 (1.33–1.49)	<.001
ICD implantation	No myocarditis	13,250	2 (0.02)	1	–	1 (Reference)	–
	With myocarditis	13,250	17 (0.13)	12	0	2.98 (0.93–9.50)	.07
					1	8.68 (2.00–37.6)	.01
					2	8.64 (2.00–37.4)	.01
					3	12.1 (2.74–53.1)	<.001

Model 0: crude effect size; Model 1: age and sex; Model 2: Model 1 + underlying comorbidities: hypertension, diabetes mellitus, chronic obstructive pulmonary disease, chronic kidney disease, hyperlipidemia, and thyroid disease; Model 3: Model 2 + medications: ACEI, ARB, and BB. ACEI = angiotensin-converting enzyme inhibitor, ARB = angiotensin II receptor blocker, BB = beta-blocker, CV = cardiovascular, ICD = implantable cardiac defibrillator, VT = ventricular tachycardia.

^{*} P values <.05 were considered to indicate statistical significance.



Prognostic Value of Cardiac Magnetic Resonance Tissue Characterization in Risk Stratifying Patients With Suspected Myocarditis.

Gräni C, et al. J Am Coll Cardiol. 2017.

Authors

Gräni C¹, Eichhorn C¹, Bière L¹, Murthy VL², Agarwal V³, Kaneko K¹, Cuddy S¹, Aghayev A³, Steigner M³, Blankstein R⁴, Jerosch-Herold M³, Kwong RY⁵.

No subgroup with PVCs

FIGURE 3 Annualized Event Rates Between LGE Presence and LGE Absence in Patients With Suspected Myocarditis

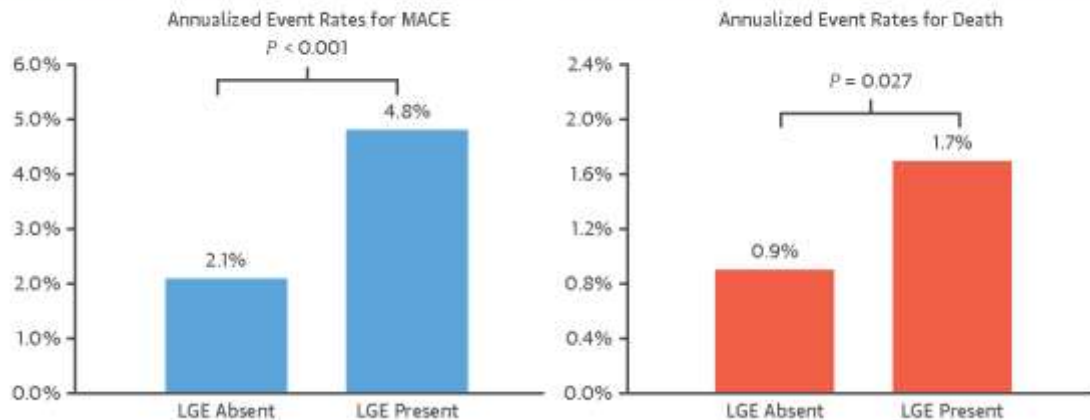


TABLE 1 Baseline Characteristics

	All Patients (n = 810)	LGE Present (n = 294)	LGE Absent (n = 516)	p Value
Baseline				
Age, yrs	47.8 ± 16.0	49.2 ± 16.4	46.8 ± 15.5	0.062
Female	278 (34)	90 (31)	188 (36)	<0.001
Body mass index, kg/m ²	27.8 ± 6.3	27.7 ± 5.9	27.8 ± 6.2	0.893
Acute-onset presentation				
Acute chest pain syndrome (<2 weeks)	350 (52)	189 (53)	161 (48)	<0.001
Subacute presentation (≥2 weeks) with dyspnea or left ventricular dysfunction	261 (32)	95 (31)	166 (32)	
Subacute presentation (≥2 weeks) with ventricular arrhythmias, syncope, or abnormal ECG	119 (15)	54 (18)	65 (12)	
Cardiovascular history				
Hypertension	181 (22)	78 (27)	103 (20)	0.093
Tobacco	76 (9)	38 (13)	38 (7)	0.304
Diabetes	80 (10)	22 (8)	58 (11)	0.495
Dyslipidemia	138 (17)	66 (23)	72 (14)	0.036
Medications				
Aspirin	186 (23)	94 (32)	92 (18)	0.035
ACE inhibitors	229 (28)	118 (40)	111 (21)	0.009
Beta-blockers	266 (33)	142 (48)	124 (24)	<0.001
Diuretics	135 (17)	78 (27)	57 (11)	<0.001
Statins	142 (18)	74 (25)	68 (13)	0.020
Other	23 (3)	7 (2)	16 (3)	0.032
ECG				
Left bundle branch block	57 (7)	27 (9)	30 (6)	0.579
Right bundle branch block	43 (5)	20 (7)	23 (4)	0.799
PR duration, ms	195 (24–126)	188 (24–128)	158 (24–124)	0.067
PR prolongation (>200 ms)	36 (5)	17 (6)	19 (4)	0.604
QRS duration, ms	99.7 ± 23.3	100.5 ± 23.9	99.3 ± 22.9	0.670
QRS prolongation (>120 ms)	89 (11)	40 (14)	49 (10)	0.901
QTc duration, ms	444.5 ± 40.6	449.5 ± 42.3	440.5 ± 39.2	0.005
QTc prolongation (>470 ms female, >450 ms male)	241 (30)	118 (40)	123 (24)	0.206
Significant Q-wave	74 (9)	38 (13)	36 (7)	0.245
ST-segment elevation	32 (4)	19 (6)	13 (3)	0.267
ST-depression	26 (3)	13 (4)	13 (3)	0.576
T-wave inversion	170 (21)	83 (28)	87 (17)	0.195
Low voltage	46 (6)	30 (10)	16 (3)	0.003
Abnormal ECG	278 (34)	139 (47)	139 (27)	0.206
Laboratory testing				
Troponin abnormal	170 (21)	104 (35)	66 (13)	<0.001
Troponin peak, ng/mL	0.08 (0.0–0.48)	0.34 (0.0–0.8)	0.02 (0.0–0.3)	0.002
Creatine kinase abnormal	70 (9)	40 (14)	30 (6)	0.580
Creatine kinase peak, U/L	0.99 ± 0.33	1.07 ± 0.36	0.91 ± 0.27	<0.001
White blood cell count abnormal	105 (13)	61 (21)	44 (9)	0.121
White blood cell count (10 ³ /L)	8.3 (6.5–11.4)	8.7 (6.7–11.4)	7.9 (6.4–10.0)	0.317

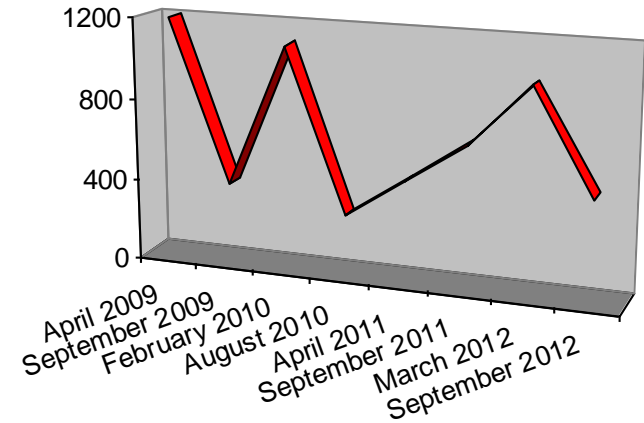
Values are mean ± SD, n (%), or median (interquartile range). The following numbers were available for laboratory testing: troponin n = 368 (45 missing), creatine kinase n = 170 (639 missing), white blood cell count n = 302 (508 missing). Frequency data were represented as number of cases (percent of corresponding group, excluding missing data). ACE = angiotensin-converting enzyme; ECG = electrocardiogram; LGE = late gadolinium enhancement.



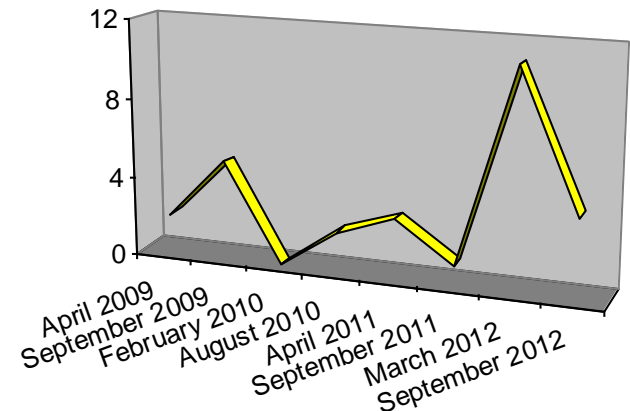
Case 5

- 48-yo fighter pilot
- No past medical history
- Asymptomatic
- PVCs of **LBBB morphology** from 2009 to 2013
- During repetitive investigations:
 - TTE: normal
 - Exercise test: negative, disappearance of PVCs
 - Late potentials: negative

Total PVBs / 24h

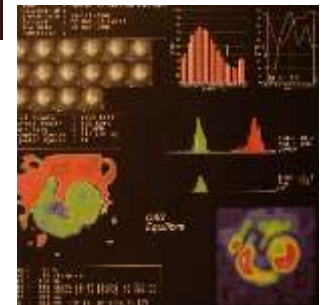
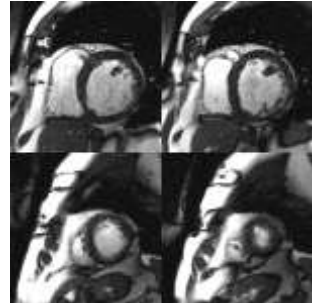


Couplets / 24h



Case 5

- Holter in 2013:
 - 3,300 multiform PVCs
 - 37 couplets, 1 triplet, **1 NSVT**
- CMR and isotopic ventriculography:
 - RV regional **akinesia**, RVEF **35%**
- Genetic test: 2 typical **mutations** identified



Final diagnosis: **Arrhythmogenic Ventricular Cardiomyopathy**

(> 2 major criteria)



Case 5

Assessing the risk:

- **Before:** low risk of VT (as for Case 1)
- **Now:** very high risk of VT and sudden cardiac death (SCD) (3.7 - 10.6 %/yr)

Level 1 Medical Event	Level 2 Medical Event	Level 3 Medical Event	Level 4 Medical Event
Minimal impact on mission	May result in a mission abort or compromised effectiveness	Likely to result in a flight safety hazard or compromise	Likely to result in a flight safety critical event
May result in a deleterious effect on the health of the individual aircrew but minimal effect on performance	Aircrew able to continue duties with minor to moderate performance compromise.	Major decrement in performance	Total acute incapacitation (may include sudden death)
Requires routine periodic medical follow-up	Requires medical attention	May require immediate medical attention	Requires immediate advanced medical care

PILOTS, COPILOTS				
Likely >2%/yr		VT	VT	VT / SCD
Possible 1-2%/yr				
Unlikely 0.5-1%/yr				
Highly unlikely <0.5%/yr		VT	VT	VT

- But **when** exactly did this risk significantly increase from 2009 to 2013 ? **How long** was the initial risk assessment available ?

[Heart Rhythm](#), 2018 Feb 3. pii: S1547-5271(18)30095-X. doi: 10.1016/j.hrthm.2018.01.031. [Epub ahead of print]

Predicting arrhythmic risk in arrhythmogenic right ventricular cardiomyopathy: A systematic review and meta-analysis.

Bosman LP¹, Sammani A², James CA³, Cadrin-Tourigny J⁴, Calkins H⁵, van Tintelen JP⁶, Hauer RNW⁷, Asselbergs FW⁸, teRiele ASJM⁹.



Advantages of a 3D matrix



- Attractive modelling
- Consideration for the likelihood of event, the type of event, the type of aircrew
- Expected to be objective and reproducible
- Can be presented to the aircrew
- Simple to use



Limits of a 3D matrix



- Correct level (1 - 4) for a same event (PVCs, VT) difficult to estimate

The more frequent or the more critical level ?

- Likelylihood of event (%) difficult to determine

Data of the literature with specific subgroups may not exist all the time !

- Colors for aircrew categories may be subjective

1-2% Risk of SCD in a (solo) flight engineer: yellow ?



Limits of a 3D matrix

- Pilots are considered as a unique homogeneous group. True ?
 - Rafale / 10-h war mission
 - Alphajet / Patrouille de France
 - Alphajet / FI
 - A330 / Presidential transport
 - A400M / overseas operational missions
 - Caracal / Combat rescue
 - ...



Limits of a 3D matrix

- Risk (%) based on literature studies carried out on the ground

The likelihood of occurrence may be higher in pilots flying in high-performance aircraft



COURCEL'S TRIANGLE OF ARRHYTHMOGENESIS

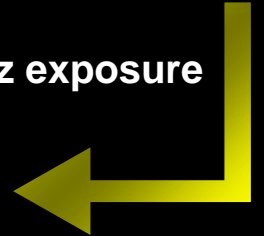
Anatomic or electrophysiological substrate



Trigger factor (PVCs)

Modulation factors
(Autonomic nervous system ++)

+Gz exposure





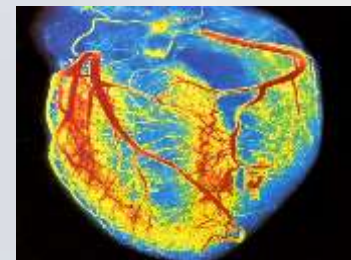
Conclusion



- 3D matrix: a valuable tool that requires thought to use even for a « simple » situation as PVCs
- Its limits highlight the complexity and potential evolution of this arrhythmia and the risk assessment
- To think / argue / discuss, not being prisoner of one box



Any questions ?





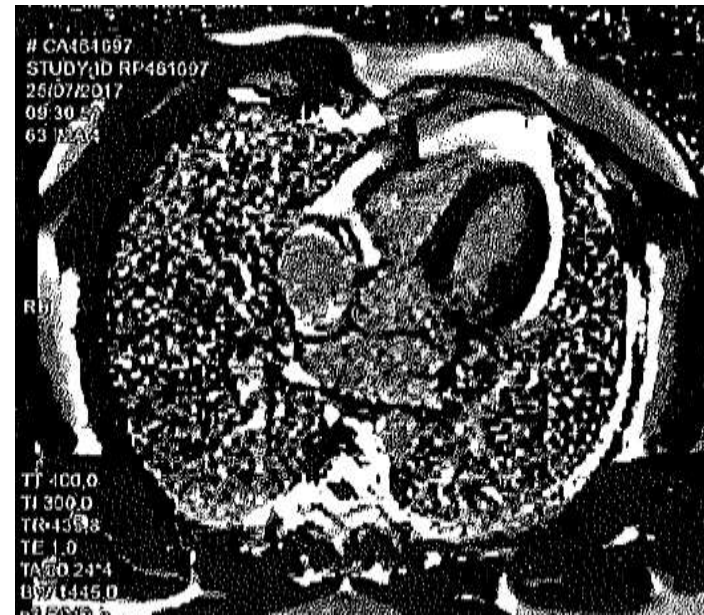
Case 6



- 50-yo military transport pilot (not operational)
- No past medical / cardiac family history
- **Palpitations** during sport
- PVCs of « benign » morphology
- Holter: **16,000** PVCs/d, > **300** repetitive forms (2, 3 and 4-complexes)
- Exercise test: negative but aborted because of repetitive PVCs
- TTE: normal
- Coronary angiography: normal
- CMR: **non diagnostic** (artefacts)

Case 6

- β -blocker then Sotalol with no efficiency
 - Many persistent repetitive forms
 - Symptomatic patient
- **Radiofrequency ablation** after RV cartography
 - 2 PVC-seats treated (antero-septal/postero-septal)
 - Initial success, asymptomatic
 - Holter: 200 PVCs/d
- New CMR after procedure: normal LV and RV but **intra-myocardial septal late gadolinium enhancement** (with normal thickness)





Case 6

Assessing the risk:

- **Before RF treatment:** very symptomatic
- **After RF treatment:** residual risk of recurrence

PILOTS, COPILOTS				
Likely >2%/yr		Palpitations	Palpitations	
Possible 1-2%/yr		VT ?	VT ?	VT ?
Unlikely 0.5-1%/yr	PVCs			
Highly unlikely <0.5%/yr				

- Significance of **imaging findings**:
 - Anatomic substrate (cardiopathy) ?
 - Consequence of RF procedure (fibrosis) ?
 - In both situations: **additional risk** of residual VT ?

Level 1 Medical Event	Level 2 Medical Event	Level 3 Medical Event	Level 4 Medical Event
Minimal impact on mission	May result in a mission abort or compromised effectiveness	Likely to result in a flight safety hazard or compromise	Likely to result in a flight safety critical event
May result in a deleterious effect on the health of the individual aircrew but minimal effect on performance	Aircrew able to continue duties with minor to moderate performance compromise.	Major decrement in performance	Total acute incapacitation (may include sudden death)
Requires routine periodic medical follow-up	Requires medical attention	May require immediate medical attention	Requires immediate advanced medical care