FAKULTNÍ NEMOCNICE® OLOMOUC

Lékařská fakulta
Univerzita Palackého v Olomouci

KOMPLEXNÍ KARDIOVASKULÁRNÍ CENTRUM
FAKULTNÍ NEMOCNICE OLOMOUC

Detection of arrhythmias in patients with cardiac amyloidosis using implantable ECG recorders

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Dedication:

Supported by Ministry of Health, Czech Republic – Conceptual development of research organization (FNOL, 00098892).

Epidemiology of Ventricular Arrhythmias in CA

- Conduction abnormalities may represent terminal events for patients with cardiac amyloidosis (CA), especially those with AL subtype.

- The prevalence of **non-sustained ventricular tachycardia** (NSVT) in AL amyloidosis ranges from 5 to 27% with routine monitoring.

- The prevalence of **VT** in the ATTR population is less often reported, but small studies suggest a prevalence of approximately 5 – 17%.

Summary of studies investigating the prevalence of VT in cardiac amyloidosis

Study summary	Number of patients	Type of cardiac amyloid	Method of monitoring	Non-sustained VT in % of patients	Other related findings
Palladini et al	51	AL	24-hour Holter monitoring	Non-sustained VT in 18% of patients.	Ventricular tachycardia was a significant prognostic determinant for survival (P = 0.04).
Sayed et al	20	AL with symptoms of pre-syncope or syncope	Implantable loop recorder	Non-sustained VT in 5% of patients	Terminal syncopal event was marked by bradycardia, not tachycardia, in every available recording.
Murtagh et al	127	AL	Electrocardiogram	Non-sustained VT in 1% of patients	Premature ventricular contractions were noted in 13% of patients.
Goldsmith et al	24	AL monitored peri autologous stem cell transplantation	Telemetry, average of 24 days	Non-sustained VT in 100% of patients	In the deceased patients (n = 3), VT/VF events were the highest of all 24 patients. There was a correlation between VT and serum BNP levels before SCT (r = 0.47, P = 0.019) and during admission for SCT (r = 0.62, P = 0.0012), serum creatinine before SCT (r = 0.62, P = 0.001), and inverse relationship with cardiac output (r = –0.72, P < 0.001)
Dubrey et al	232	AL	24-hour Holter monitoring	Non-sustained VT in 26.7% of patients	Ventricular tachycardias were not associated with increased risk of sudden cardiac death.
Hörnsten et al	30	ATTR (ATTR Val30Met trait), before liver transplant	24-hour Holter monitoring	Non-sustained VT in 16.7% of patients	–
Varr et al	31	AL 77%, ATTR 23% (V122I mutation 10%, wild type 13%)	ICD, permanent pacemaker, telemetry	VT in 74% of patients	ICD therapy was successful in most patients, with therapy in 4 of 5 (80%) patients resulting in the termination of the arrhythmia.
Kristen et al	19	AL with ICD insitu	ICD	VT/VF in 11% of patients	Ventricular extra beats (grade IVa or higher) were present more often in non-survivors than in survivors (P < 0.05).
Hamon et al	45	Familial ATTR 60%, AL 27%, senile ATTR 13%. All with ICD in situ	ICD	VT/VF in 27% of patients	Inappropriate shocks was uncommon and occurred in 2 patient (4.4%).

Pathophysiology of Ventricular Arrhythmias in CA

- There are a variety of mechanisms that form the fundamental pathogenesis for ventricular arrhythmias in CA:

1. Amyloid fibril deposition with a resultant **inflammatory response** and oxidative stress leads to a separation of myocytes resulting in remodelling and **left ventricular (LV) fibrosis**, which progressively develops arrhythmogenic potential.
2. Amyloid **fibril deposition in the conduction system** can potentiate arrhythmias.
3. **Micro- and macro- vascular myocardial ischaemia** from amyloid deposition, can be demonstrated by regional myocardial dysfunction as assessed by cardiac MRI.

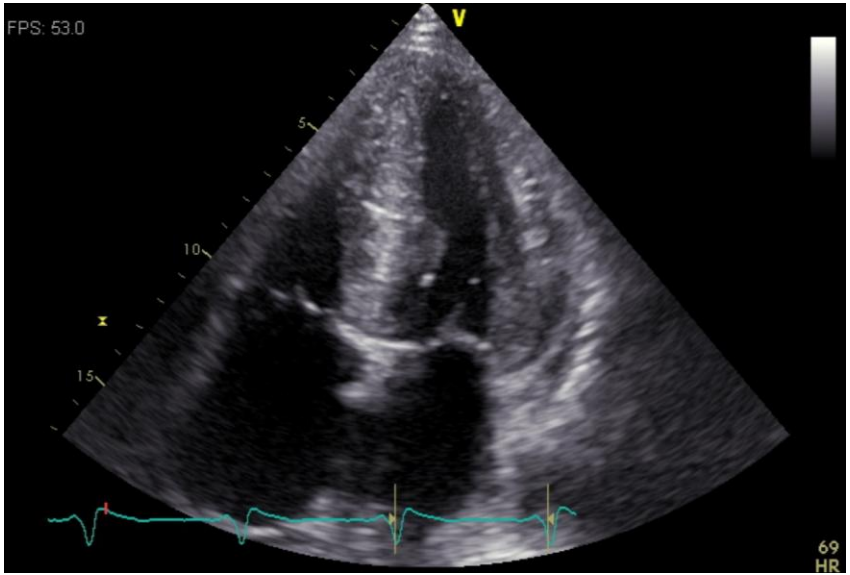
Methods

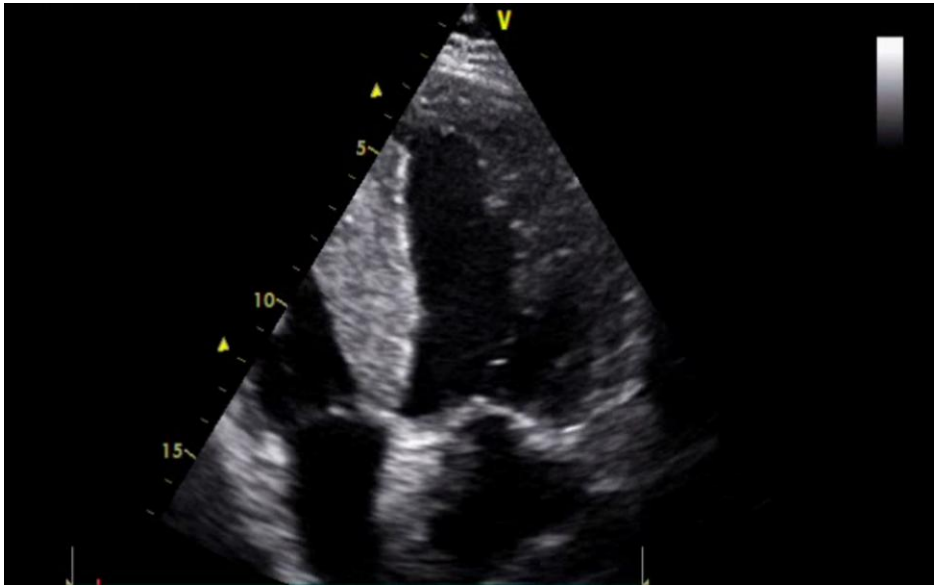
- 112 transthyretin amyloidosis (TTR) patients with completed underlying diagnosis including 99mTc-DPD scan (all pts), genetic testing (67%) and endomyocardioal biopsy (27%) without documented arrhythmias were randomized to standard clinical follow-up including arrhythmias or implantation of an ECG loop recorder (ILR).

- The classic FU took place in a heart failure clinic, and the group of patients with ILR was monitored by remote control with automatic daily report of the occurrence of arrhythmias by an independent organization.

- If an arrhythmia was detected, the patient was contacted immediately. The mean follow-up time for both groups was 17 ± 7 months.

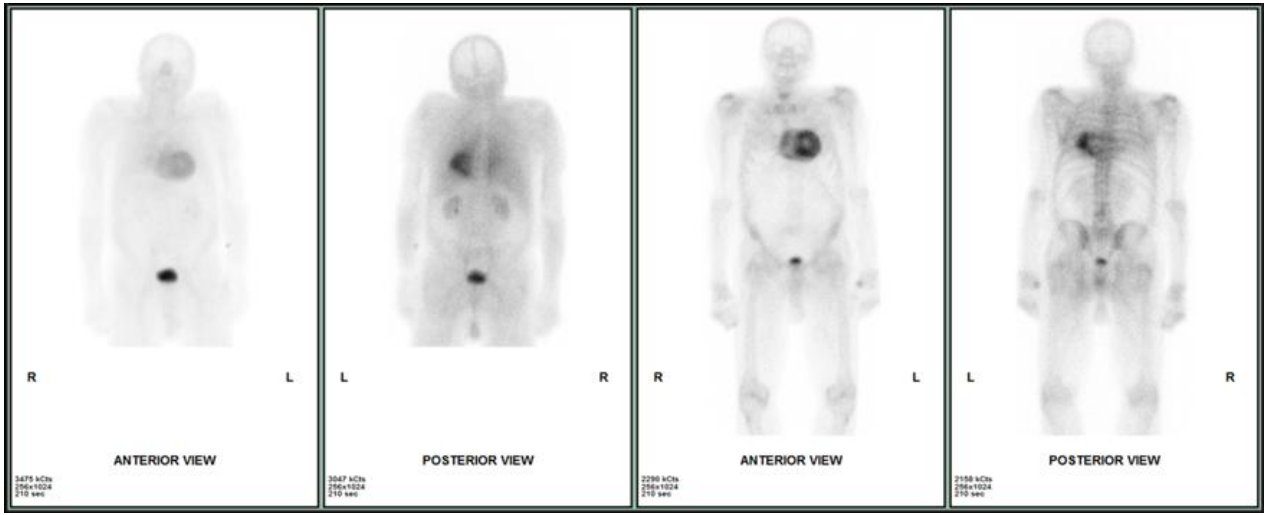
A combination of imaging methods is essential for predicting arrhythmogenicity in patients with TTR





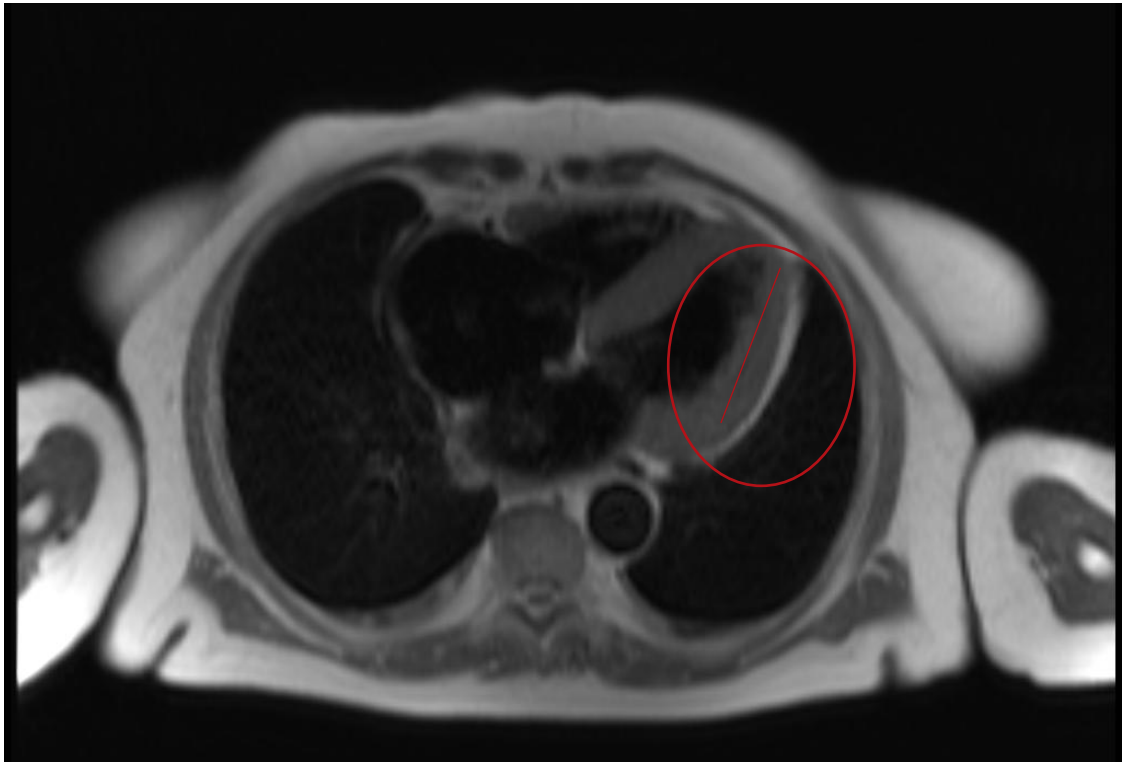
Source: Dr. Renáta Aiglová

DPD Scan confirms diagnosis



Source: prof. Milan Kamínek

MR-LGE and its evaluation is an essential predictor of the occurrence of ventricular arrhythmias in patients with TTR

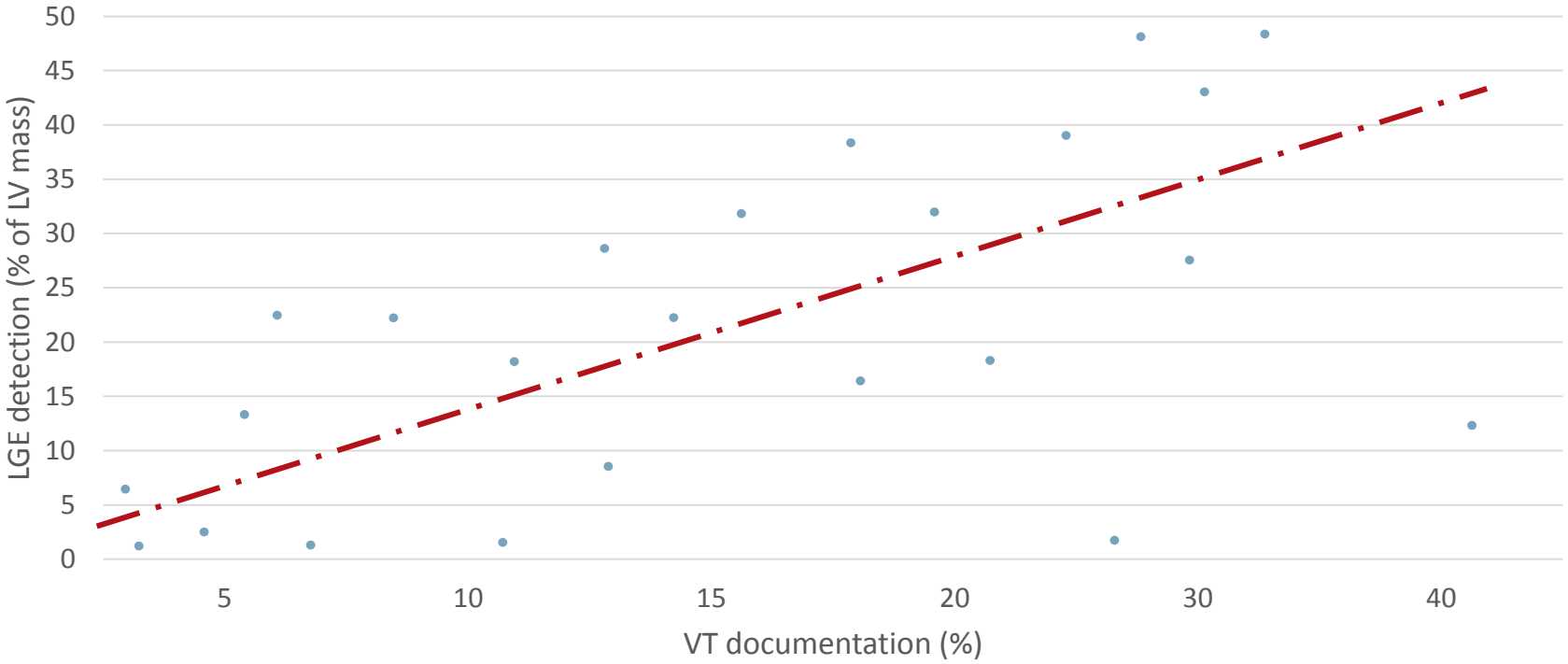


Source: Dr. Z.Tűdos

CMR is useful as a diagnostic and prognostic marker for patients with CA

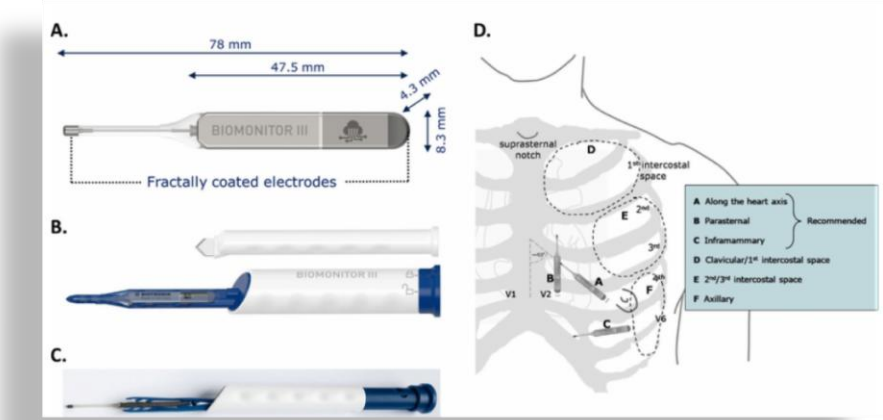
- There is a growing role for cardiac MRI-LGE in the assessment of CA, which **typically occurs in a global subendocardial pattern**.
- This is important as LGE is increasingly being recognised as a marker of amyloidogenesis and fibrosis and a predicts arrhythmogenic potential.
- This substrate has been associated with increased risk LGE-predicted death.
- **T2 imaging for assessment of myocardial oedema** is a surrogate of active inflammation, and has been intrinsically linked to arrhythmogenic potential.

Correlation between the finding of LGE in the LV and the occurrence of ventricular arrhythmias

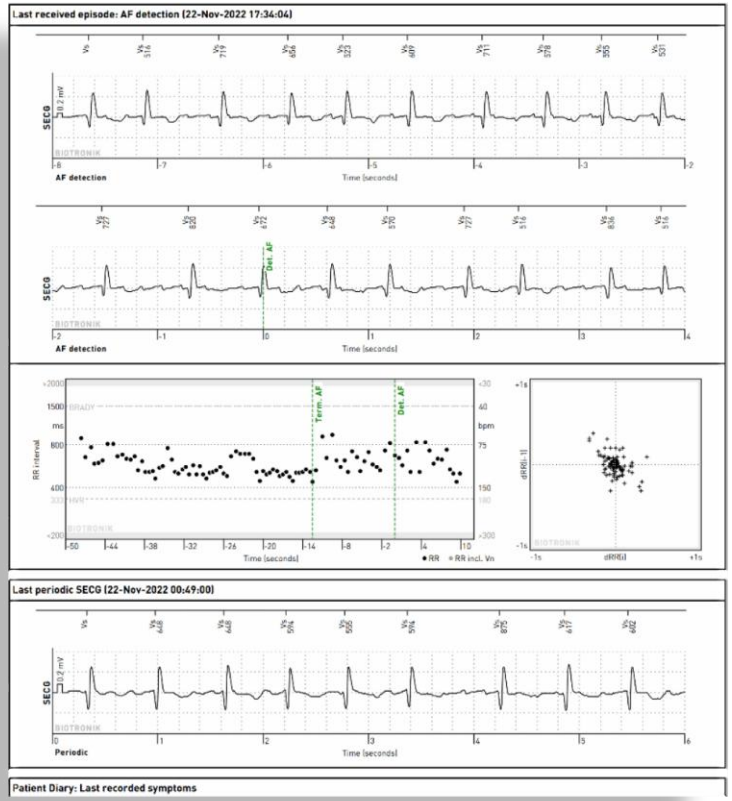


ECG monitor implantation strategy:

- Immediately after the complete finalization of TTR diagnostics
- Outpatient performance
- The patient is educated and equipped with a patient unit, an activator and a smartphone application (if able)
- It is continuously monitored by NTMC UH Olomouc
- In case of detection of arrhythmias, he is immediately contacted by phone

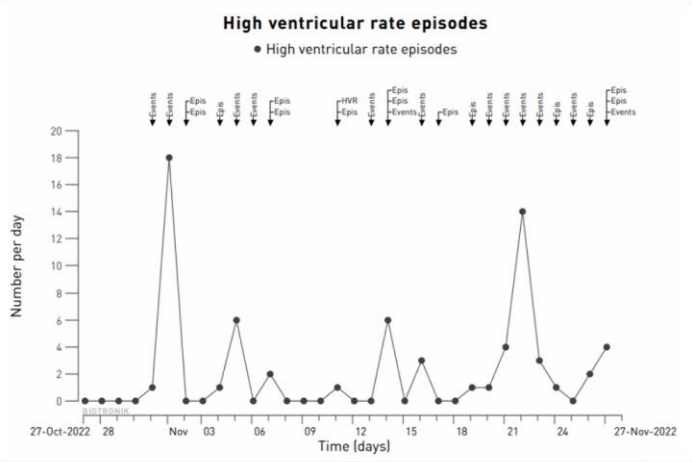


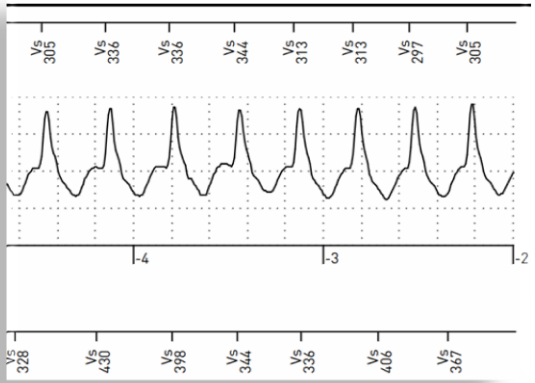
New onset of AF



Source: Home Monitoring Service Center

Detection of tachycardias with a wide QRS complex





VZP does not accept treatment reducing the mortality of patients with TTR ...

Rozhodnutí

Všeobecná zdravotní pojišťovna České republiky se sídlem v Praze 3, Orlická 4/2020, PSČ 130 00, IČ 41197518, Regionální pobočka Ostrava, pobočka pro Moravskoslezský, Olomoucký a Zlínský kraj, Odbor zdravotní péče, Oddělení kontroly a revize zdravotní péče, dále jen VZP ČR, příslušná k rozhodování dle § 67 zákona č. 500/2004, správní řád, ve znění

podané prostřednictvím poskytovatele zdravotních služeb: Fakultní nemocnice Olomouc, MUDr. Renáta Aiglová, kardiologická ambulance, se sídlem I. P. Pavlova 185/6, 779 00 Olomouc, dále jen „PZS“, o úhradě zdravotních služeb z prostředků veřejného zdravotního pojištění

takto

Žádost pojištěnce podaná ve smyslu ust. § 16 zákona č. 48/1997 Sb., o veřejném zdravotním pojištění a o změně a doplnění některých souvisejících zákonů, ve znění pozdějších předpisů, dále jen „ZVZP“, se z a m í t á.

Dle dokumentace byla transthyretinová srdeční amyloidóza u pojištěnce potvrzena scintigraficky a nikoliv biopticky (chybí údaj o potvrzení amyloidových depozit v endomyokardiální či extrakardiální biopsii).

U pojištěnce nebyla splněna zařazovací kritéria pro studii ATTR-AC. Pro jeho klinickou situaci není doložena účinnost a bezpečnost tafamidisu ve smyslu EBM (evidence based medicine).

Source: VZP, Local Office, Ostrava

Comparison of standard FU and intensive monitoring of arrhythmias using ILR in patients with CA

	Standard FU (n=56)	Intensive FU (ILR) (n=55)	p
AF	11 (19,6%)	19 (49%)	<0.05
AV block	6 (10.7%)	11 (20%)	<0.05
non sust. VT	8 (14.2%)	27 (49%)	<0.05
sust. VT	0	6 (10.9%)	<0.05
VF	0	1 (1.81%)	<0.05
AT	1 (1.8%)	4 (7.3%)	<0.05

Conclusions

- There is no consensus on the absolute benefit that ICDs in patients with cardiac amyloidosis.
- When non-sustained VT and syncope are captured and documented, ICD implantation for prevention of SCD in CA is most likely a reasonable approach.
- However, intensive monitoring of arrhythmias in patients with CA using ILR can lead to accurate and early detection of ventricular arrhythmias in particular and early initiation of ICD treatment as a prevention of SCD.
- Documentation of ventricular arrhythmias in CA patients was significantly higher by ILR ($p < 0.005$) and was a clear predictor of patient survival (HR 2.51).
- The standard assessment of the occurrence of LGE can undoubtedly be an interesting predictor of the occurrence of ventricular tachycardia in patients with TTR, however, it will certainly require further studies and intensive interdisciplinary cooperation.

Thanks for your attention

University Hospital Olomouc

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