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FAKULTNÍ NEMOCNICE U SV. ANNY V BRNĚ

Léčba arytmogenní kardiomyopatie

Treatment of arrhythmogenic cardiomyopathy

Jan Krejčí

I. interní kardioangiologická klinika FNUSA v Brně

Treatment of arrhythmogenic cardiomyopathy

Treatment of arrhythmogenic right ventricular cardiomyopathy/dysplasia: an international task force consensus statement

Domenico Corrado[1*], Thomas Wichter[2], Mark S. Link[3], Richard Hauer[4], Frank Marchlinski[5], Aris Anastasakis[6], Barbara Bauce[1], Cristina Basso[1], Corinna Brunckhorst[7], Adalena Tsatsopoulou[8], Harikrishna Tandri[9], Matthias Paul[10], Christian Schmied[7], Antonio Pelliccia[11], Firat Duru[7], Nikos Protonotarios[8], NA Mark Estes III[3], William J. McKenna[12], Gaetano Thiene[1], Frank I. Marcus[13], and Hugh Calkins[9]

Most important goals of the therapy

- Reduction of mortality (SCD and HF related)
- Prevention of disease progression
- Improvement of symptoms (increase in QoL)
- Reducing HF symptoms

European Heart Journal (2015) **36**, 3227–3237

Treatment of arrhythmogenic cardiomyopathy

- **Life-style changes**
- **Pharmacological therapy**
- **Catheter ablation**
- **ICD implantation**
- **Heart transplantation**

European Heart Journal (2015) **36**, 3227–3237

Risk stratification

- **Annual mortality rate < 1%**
- **Risc factors**
  - **History of VT/VF**
  - **Unexplained syncope**
  - **RV, LV (or both) dysfunction**
  - **Positive EP study**
  - **Male gender**
  - **Young age at diagnosis**
  - **nsVT at Holter monitoring**
  - **Electroanatomic scars with ECG fragmentation…**

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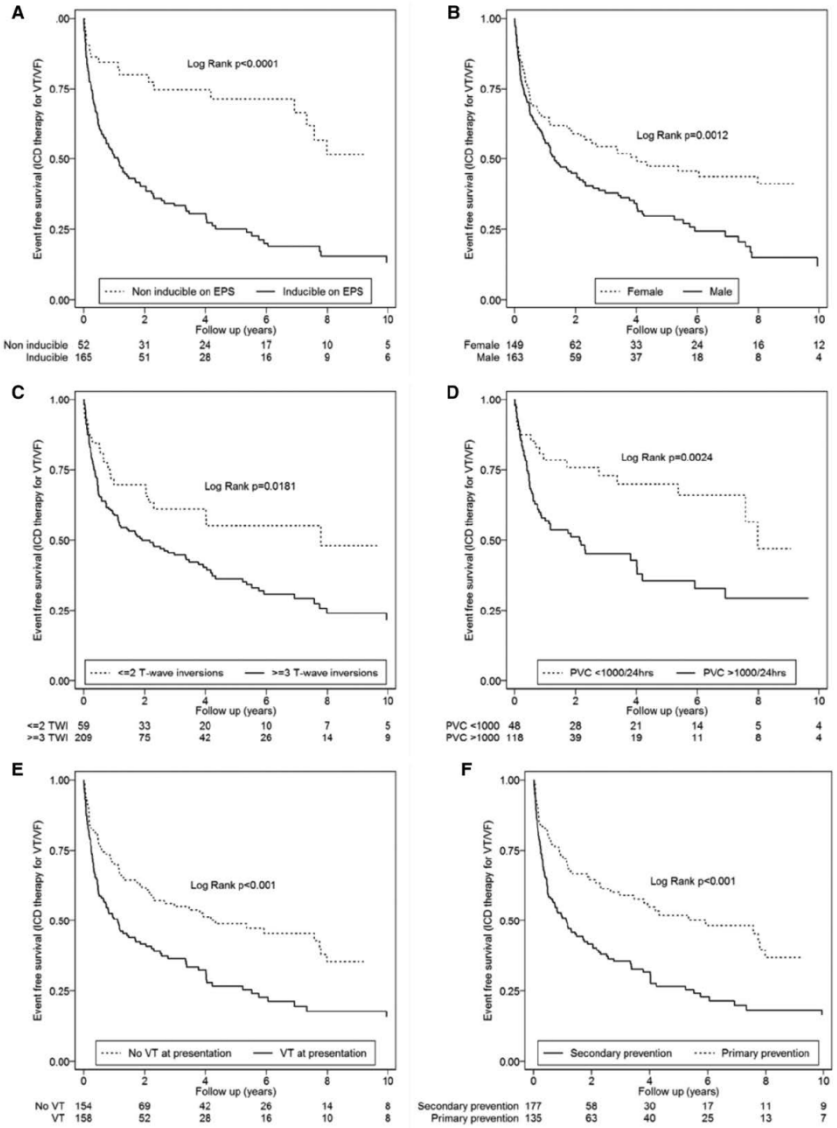
Risk stratification

Risk Stratification in Arrhythmogenic Right Ventricular Cardiomyopathy

Hugh Calkins, MD
Domenico Corrado, MD, PhD
Frank Marcus, MD

Circulation. 2017;136:2068–2082.



Risk stratification

- **Risc of arrhythmic SCD**
- **Risc of heart failure progression**

Natural History and Risk Stratification of Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy

Jean-Sébastien Hulot, MD; Xavier Jouven, MD, PhD; Jean-Philippe Empana, MD; Robert Frank, MD; Guy Fontaine, MD, PhD

- **130 pts from the years 1977-2000**
- **Annual mortality rate 2.3%**
- **21 CV deaths – 14 HF, 7 SCD**

Circ. 2004;110(14):1879-84

Treatment of arrhythmogenic cardiomyopathy

- **Life-style changes**
- Pharmacological therapy
- Catheter ablation
- ICD implantation
- Heart transplantation

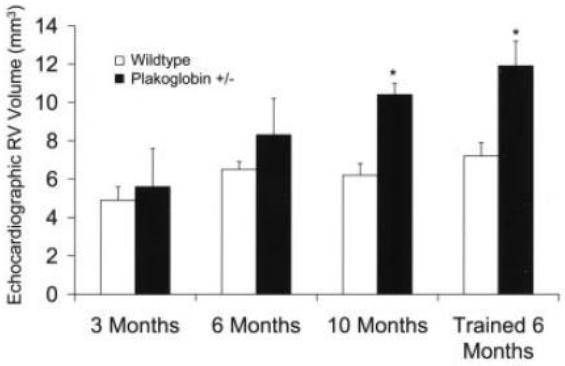
European Heart Journal (2015) **36**, 3227–3237

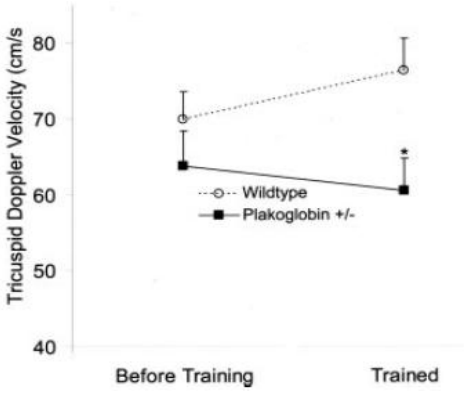
Treatment of arrhythmogenic cardiomyopathy

Life-style changes

Age- and Training-Dependent Development of Arrhythmogenic Right Ventricular Cardiomyopathy in Heterozygous Plakoglobin-Deficient Mice

Paulus Kirchhof, MD; Larissa Fabritz, MD; Melanie Zwiener, VetD; Henning Witt, PhD; Michael Schäfers, MD; Stephan Zellerhoff, MD; Matthias Paul, MD; Timur Athai, BS; Karl-Heinz Hiller, PhD; Hideo A. Baba, MD; Günter Breithardt, MD; Patricia Ruiz, PhD; Thomas Wichter, MD; Bodo Levkau, MD





- Plakoglobin deficient mouse had RV dilatation and reduced systolic function
- Endurance training accelerated the changes

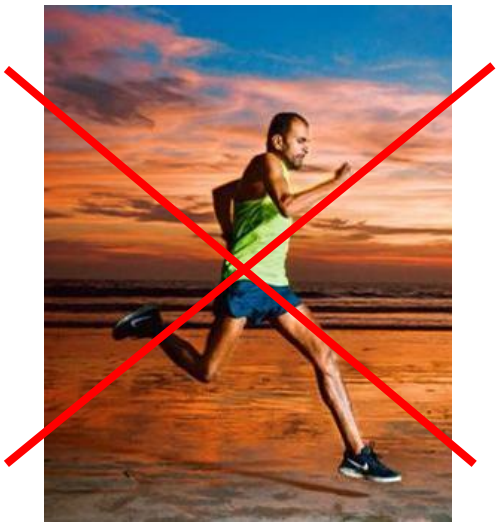
[*Circulation*. 2006;114:1799-1806.]

Treatment of arrhythmogenic cardiomyopathy

Life-style changes

Recommendations

- It is recommended that patients with a definite diagnosis of ARVD/C not participate in competitive and/or endurance sports (Class I).
- Patients with a definite diagnosis of ARVD/C should be restricted from participation in athletic activities, with the possible exception of recreational low-intensity sports (Class IIa).
- Restriction from competitive sports activity may be considered in ARVC/D family members with a negative phenotype, either healthy gene carriers (class IIa) or with unknown genotype (class IIb).



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Treatment of arrhythmogenic cardiomyopathy

- **Pharmacological therapy**
  - **Antiarrhythmic drugs**
  - **Heart failure therapy**

European Heart Journal (2015) **36**, 3227–3237

Treatment of arrhythmogenic cardiomyopathy

Pharmacological therapy

- **Antiarrhythmic drugs**

AADs are effective in reduction of arrhythmias (and ICD therapies)

Prevention of SCD was not proved

Recommendations

- AADs are recommended as an adjunct therapy to ICD in ARVC/D patients with frequent appropriate device discharges (class I).
- The use of AADs should be considered to improve symptoms in patients with frequent premature ventricular beats and/or non-sustained VT (class IIa).
- AADs may be considered as an adjunct therapy to catheter ablation without a back-up ICD in selected ARVC/D patients with recurrent, haemodynamically stable VT (class IIb).
- AAD treatment of asymptomatic ARVC/D patients without documented ventricular arrhythmias and healthy gene carriers is not recommended (class III).

European Heart Journal (2015) **36**, 3227–3237

Treatment of arrhythmogenic cardiomyopathy

Pharmacological therapy

- **Betablockers**

Prevention of effort-induced ventricular arrhythmias

Slow progression of the disease by reducing RV wall stress

Recommendations

- Beta-blocker therapy is recommended in ARVC/D patients with recurrent VT, appropriate ICD therapies, or inappropriate ICD interventions resulting from sinus tachycardia, supraventricular tachycardia, or atrial fibrillation/flutter with high-ventricular rate (class I).
- Beta-blocker therapy should be considered in all patients with ARVD/C irrespective of arrhythmias (class IIa).
- The prophylactic use of beta-blockers in healthy gene carriers is not recommended (class III).

European Heart Journal (2015) **36**, 3227–3237

Treatment of arrhythmogenic cardiomyopathy

Pharmacological therapy

- **Heart failure therapy**

Recommendations

- For ARVC/D patients who developed right- and/or left-sided heart failure standard pharmacological treatment with angiotensin-converting-enzyme inhibitors, angiotensin II receptor blockers, beta-blockers, and diuretics is recommended (class I).
- Long-term oral anticoagulation is generally indicated for secondary prevention in patients with documented intracavitary thrombosis or venous/systemic thromboembolism (class I).
- For ARVC/D patients with asymptomatic RV and/or LV dysfunction treatment with angiotensin-converting-enzyme inhibitors or angiotensin II receptor blockers may be considered (class IIb).

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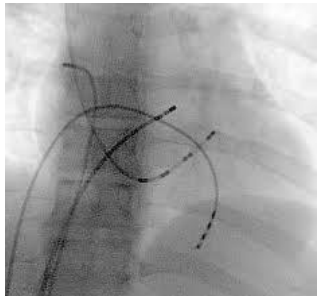
Treatment of arrhythmogenic cardiomyopathy

Catheter ablation



Good acute results, risk of VT recurrence due to disease progression

Not proved to prevent SCD

Recommendations

- Catheter ablation of VT is recommended in ARVC/D patients with incessant VT or frequent appropriate ICD interventions on VT despite maximal pharmacological therapy, including amiodarone (class I).
- An epicardial approach to VT ablation is recommended in patients who fail one or more attempts of endocardial VT ablation (class I).
- Catheter ablation of VT should be considered in ARVC/D patients with incessant VT or frequent appropriate ICD interventions on VT who have failed pharmacological therapy other than amiodarone (class IIa).
- Catheter ablation is not recommended as an alternative to ICD for prevention of SCD in ARVC/D (class III).

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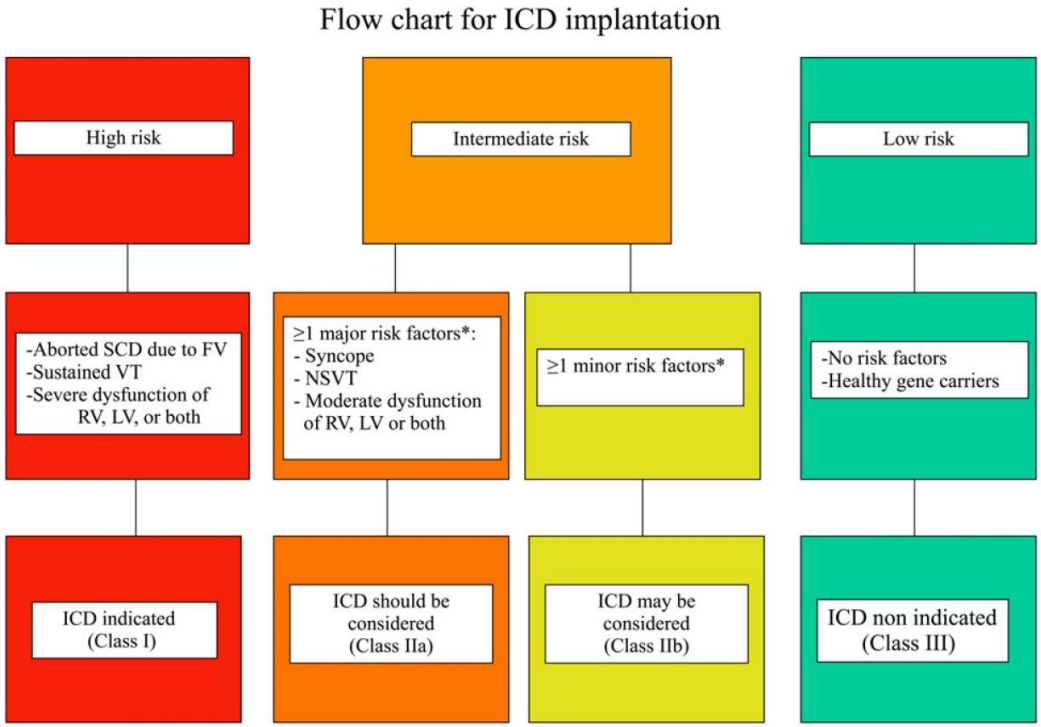
Treatment of arrhythmogenic cardiomyopathy

ICD implantation

Most important and logical therapeutic approach

No prospective studies

Proven prognostic benefit



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Treatment of arrhythmogenic cardiomyopathy

Risk Stratification in Arrhythmogenic Right Ventricular Cardiomyopathy

Hugh Calkins, MD
Domenico Corrado, MD, PhD
Frank Marcus, MD

- 439 pts
- Initial presentation: 11% cardiac arrest, 50% VT
- Mean age at presentation 36y, age at cardiac arrest 25y
- sVT during follow-up in 72%, HF developed in 13%
- SCD incidence in 16% without ICD vs 0.6% with ICD ($p<0.001$)
- 94% alive at last follow-up (5y)

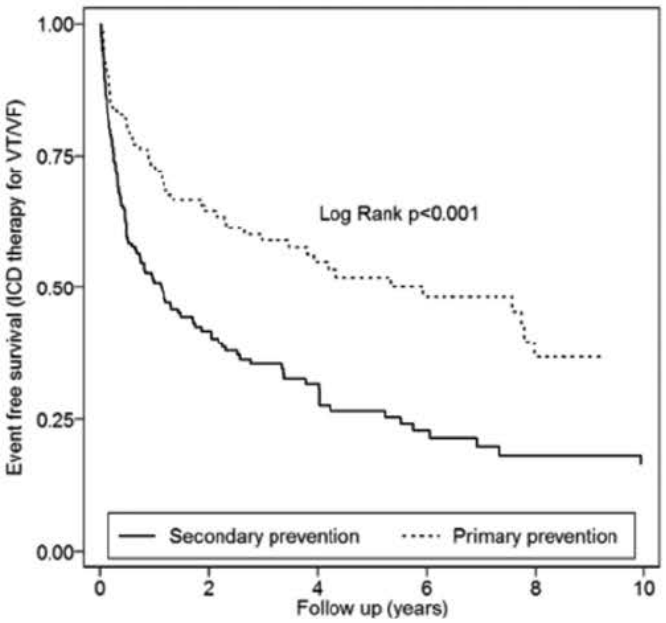
Circulation. 2017;136:2068–2082.

Treatment of arrhythmogenic cardiomyopathy

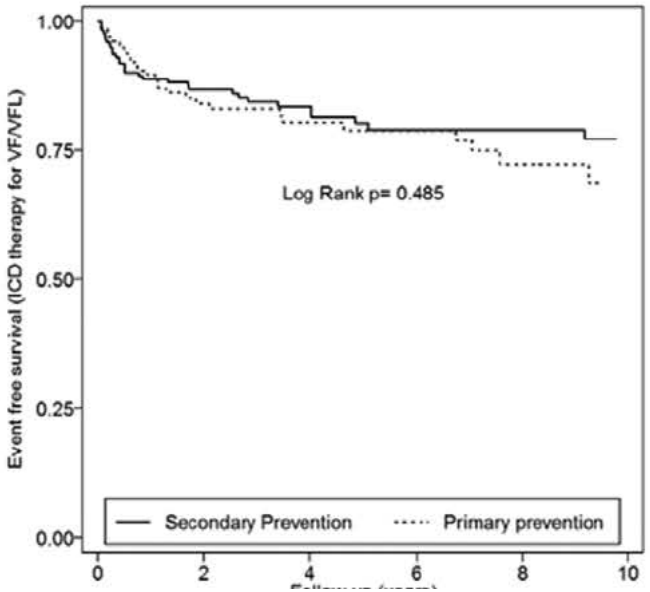
Primary vs secondary prevention

Risk Stratification in Arrhythmogenic Right Ventricular Cardiomyopathy

1st ICD intervention



Cumulative event-free survival



Circulation. 2017;136:2068–2082.

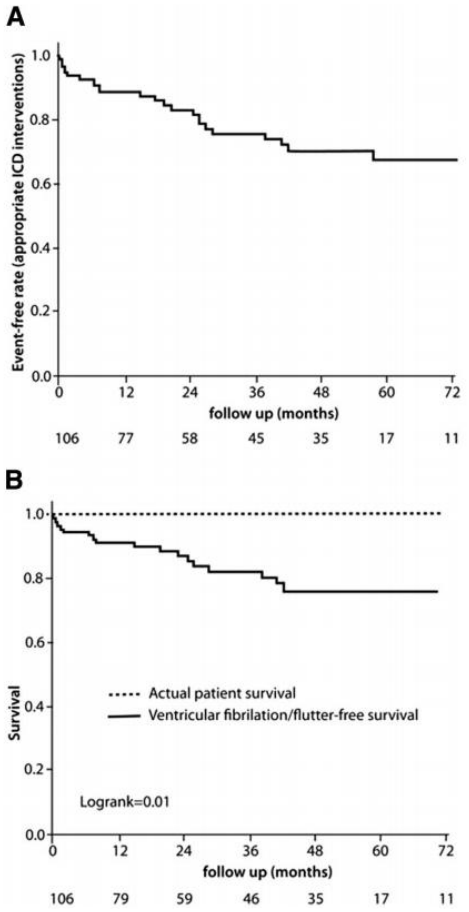
Treatment of arrhythmogenic cardiomyopathy

ICD implantation

Prophylactic Implantable Defibrillator in Patients With Arrhythmogenic Right Ventricular Cardiomyopathy/ Dysplasia and No Prior Ventricular Fibrillation or Sustained Ventricular Tachycardia

Domenico Corrado, MD, PhD; Hugh Calkins, MD; Mark S. Link, MD; Loira Leoni, MD, PhD; Stefano Favale, MD; Michela Bevilacqua, MD; Cristina Basso, MD, PhD; Deirdre Ward, MD; Giuseppe Boriani, MD; Renato Ricci, MD; Jonathan P. Piccini, MD; Darshan Dalal, MD, MPH; Massimo Santini, MD; Gianfranco Buja, MD; Sabino Iliceto, MD; N.A. Mark Estes III, MD; Thomas Wichter, MD; William J. McKenna, MD; Gaetano Thiene, MD; Frank I. Marcus, MD

- 106 pts (62 men; 35.6 ± 18 y)
- ≥ 1 risk factor (syncope, nsVT, SCD in family, posit. EPS)
- appropriate ICD th in 24% (16% for VF) in 58-month F-U x inappr. ICD th in 19%
- Survival 100%, VF-free survival 77%



Circulation 2010;122:1144-1152.

Treatment of arrhythmogenic cardiomyopathy

ICD implantation

Implantable Cardioverter-Defibrillator Therapy in Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy: Predictors of Appropriate Therapy, Outcomes, and Complications

Gabriela M. Orgeron, MD; Cynthia A. James, ScM, PhD, CGC; Anneline Te Riele, MD, PhD; Crystal Tichnell, MGC; Brittney Murray, MS; Aditya Bhonsale, MD; Ihab R. Kamel, MD, PhD; Stephan L. Zimmerman, MD; Daniel P. Judge, MD; Jane Crosson, MD; Harikrishna Tandri, MD; Hugh Calkins, MD

- 312 pts, follow-up 8.8 ± 7.3 y, 186 pts (60%) appropriate ICD th, 58 pts (19% VF); 64 pts (21%) inappropriate ICD th
- Overall mortality 2%, HTx in 4%
- independent predictor for appropriate ICD th was positive EP-study (HR 2.28)
- independent predictor for VF were younger age at presentation (HR 3.14), high number of ventricular arrhytmias (HR 4.43)

J Am Heart Assoc. 2017;6:e006242. DOI: 10.1161/JAHA.117.006242.

Treatment of arrhythmogenic cardiomyopathy

Recommendations

- Implantation of an ICD is recommended in ARVC/D patients who have experienced ≥1 episodes of haemodynamically unstable, sustained VT or VF (class I).
- Implantation of an ICD is recommended in ARVC/D patients with severe systolic dysfunction of the RV, LV, or both, irrespective of arrhythmias (class I).
- Implantation of an ICD should be considered in ARVC/D patients who have experienced ≥1 episodes of haemodynamically stable, sustained VT (class IIa).
- Implantation of an ICD should be considered in patients who have 'major' risk factors such as unexplained syncope, moderate ventricular dysfunction, or NSVT (class IIa).
- Implantation of an ICD may be considered in patients with 'minor' risk factors after a careful discussion of the long-term risks and benefits of ICD implantation (class IIb).
- Prophylactic ICD implantation is not recommended in asymptomatic ARVC/D patients with no risk factors or healthy gene carriers (class III).

European Heart Journal (2015) **36**, 3227–3237

Treatment of arrhythmogenic cardiomyopathy

Heart transplantation

Arrhythmogenic ventricular cardiomyopathy: A paradigm shift from right to biventricular disease

Ardan M Saguner, Corinna Brunckhorst, Firat Duru

- LV involvement as a sign of disease progression
- Better diagnostic methods
- Specific fenotype of the disease (Left dominant forms)

World J Cardiol 2014 April 26; 6(4): 154-174

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Treatment of arrhythmogenic cardiomyopathy

Heart transplantation

Cardiac Transplantation in Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy

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Cynthia James, PhD
Daniel P. Judge, MD
Crystal Tichnell, MS
Brittney Murray, MS
Aditya Bhonsale, MBBS, MD
Binu Philips, MD
Theodore Abraham, MD
Darshan Dalal, MD
Marc K. Halushka, MD, PhD
Harikrishna Tandri, MD
Hugh Calkins, MD
Stuart D. Russell, MD

- 21 pts (1 died before HTx)
- Initial symptoms HF in 28%, arrhythmic sy in 28%
- HF symptoms in 90%, VT in 20% at HTx
- LVD in 61% at HTx
- 1-year post-HTx survival 94%
- 88% of pts were alive 6.2 ± 4.8 years postHTx (med 4.5y)

JACC Vol. 59, No. 3, 2012
January 17, 2012:289–93

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Treatment of arrhythmogenic cardiomyopathy

Heart transplantation

Heart transplantation in arrhythmogenic right ventricular cardiomyopathy — Experience from the Nordic ARVC Registry

Thomas Gilljam [a], Kristina H. Haugaa [b,c], Henrik K. Jensen [d], Anneli Svensson [e], Henning Bundgaard [f], Jim Hansen [g], Göran Dellgren [h], Finn Gustafsson [i], Hans Eiskjær [d], Arne K. Andreassen [j], Johan Sjögren [k], Thor Edvardsen [b,c], Anders G. Holst [i], Jesper Hastrup Svendsen [i], Pyotr G. Platonov [l,*]

- 31 pts, HF symptoms in 91% (biventricular HF 58%, RVF 28%, LVF 3%) at HTx
- VT present in 50%, single reason for HTx in 10%
- HTx more often in patient diagnosed in age < 35 (OR 7.59, p <0,001)
- 5-year post-HTx survival 91%, 88% of pts were alive 6.2 ± 4.8 years post-HTx (med 4.5y)

International Journal of Cardiology 250 (2018) 201–206

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Conclusions

- Risk stratification is fundamental for any therapeutic decision
- Therapy is still only palliative
- Pharmacological therapy improves QoL but not mortality
- The key decision is whether and when to implant ICD with dramatic prognostic improvement
- HTx can be performed in selected candidates for end-stage disease with excellent results

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Děkuji za pozornost!