Beyond catheter ablation for VT

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Therapeutics options

- Radiotherapy
- Autonomics
- Gene therapy
- Renal denervation
Radiotherapy

Cyberknife

• Challenges:
  – Fiducial placement and tracking
  – Treatment planning time
Radiotherapy

- 5 pts with refractory VT
- Substrate identification
- VT origin mapped non-invasively
- Dose planned with fluoroscopic registration

Cuculich et al NEJM 2018
Radiotherapy

- Ablation time 11-18 mins
- FU 6 week blanking followed by 46 pt months
- One unrelated death

Cuculich et al NEJM 2018
Radiotherapy

- Early lung abnormalities with complete resolution at 12 months
- One AF stroke related death (83 year old)
  - Fibrosis of myocardium
  - Ectactic vessels at borderzone
  - Endothelium unaffected

Cuculich et al NEJM 2018
Autonomic modulation
Stellate ganglion block

• Local anaesthetic injected under US or Fluoroscopic guidance
Autonomic modulation
Stellate ganglion block

- Bupivacaine longest duration (6 hours-1 week)
Autonomic modulation
Cardiac sympathetic denervation

- International shared data base
- Left videoscopic CSD performed in all
- Bilateral according to investigator preference
- Lower 1/3 of stellate ganglion, thoracic ganglia T2-4 and nerve of Kuntz
- Histology performed
Autonomic modulation
Cardiac sympathetic denervation

- 121 pts, 5 centres, mean FU 1.5±1.4 years
- Ischaemic 27%
- Amiodarone 99%, betablocker 92%
- 4% mild Horners syndrom
- 17% VT ablation after CSD
Autonomic modulation
Cardiac sympathetic denervation

VT/shocks

Death/transplant

Vaseghi et al JACC 2017
Autonomic modulation
Cardiac sympathetic denervation

Left vs bilateral

Survival

VT/ICD Shock-Free Transplant-Free

Follow-Up (Months)

No. at Risk

0.0 0.2 0.4 0.6 0.8 1.0
0 2 4 6 8 10 12

P = 0.014

Left CSD Bilateral CSD

No. at Risk

98 66 58 50 48 42 37
23 13 9 7 7 7 7

Vaseghi et al JACC 2017
Renal denervation

- Vasospastic angina resulting in VT
- Refractory to ISMN, amiodarone, metoprolol, verapamil
- Arrhythmia free for >12 months post renal denervation
Renal denervation

- 10 pts refractory VT
- failed meds and catheter ablation
- excl renal artery anatomy, hypotension
Gene therapy

- Only viable in arrhythmia with well defined single gene aetiology
- CPVT
- CASQ2 knockout mice
- newborn and 3 month old
- Infected with Adeno associated viral vector (AAV9) -CASQ2 or empty virus
- Histology, electrophysiology

Denegri et al Circulation 2014
Gene therapy

• Penetration of virus to cells

Phase contrast + Green Fluorescent protein = Merge 50% infection rate

Denegri et al Circulation 2014
Gene therapy

- Response to adrenaline

**WT**

Epinephrine (2 mg/Kg)

200 ms

**R33Q**

Epinephrine (2 mg/Kg)

200 ms

**R33Q-INF**

Epinephrine (2 mg/Kg)

200 ms

**R33Q-GFP**

Epinephrine (2 mg/Kg)

200 ms

control - SR

untreated affected mouse bidirectional VT

treated affected mouse - SR

empty virus affected mouse bidirectional VT

Denegri et al Circulation 2014
Conclusions

• A number of innovative non-ablation options are showing promise
• Radiotherapy probably the most promising of these but best suited to localised anatomically derived mechanisms
• Stellate ganglion block probably the one that under used