ARABKIR MEDICAL CENTRE
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ԲԺՇԿԱԿԱՆ ՀԱՄԱԼԻՐ

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Kidney Transplant Recipient with Familial Mediterranean Fever

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Case, 44 y/o female (1)

- Since 3 y/o - FMF attacks, no treatment
- Since 1998 - proteinuria, high Cr level
- Genetic testing – M694V homozygous mutation
- No native kidney biopsy
- November 2005 HD treatment
- October 2006 – KT from living donor. HLA MM: 2-2-1.
- IS: no induction, CsA, Pred, Aza
- FMF attacks within 1st week after KT, Colchicine added
- On 7th and 13th postoperative days two episodes of acute rejection. SM pulses, improvement.

Case, 44 y/o female (2)

- November 2006 - **first graft biopsy**, total necrosis (upper pole with poor vascularisation).
- May 2007 **second graft biopsy,** chronic vascular rejection. **No amyloidosis in the graft.**
- Aza switched to MMF. Proteinuria decreased , Cr 130-150 mkmol/l.
- Frequent episodes of FMF attacks. Cy A-Colchicine-MMF interactions.
- Several changes of IS due to side effects.
- June 2019 – **third graft biopsy. Amyloidosis in the graft.**
- 2020 - COVID-19 with 90% of lung involvement
- Currently she is stable, but has graft failure, eGFR (CKD-EPI) 14 mi/min

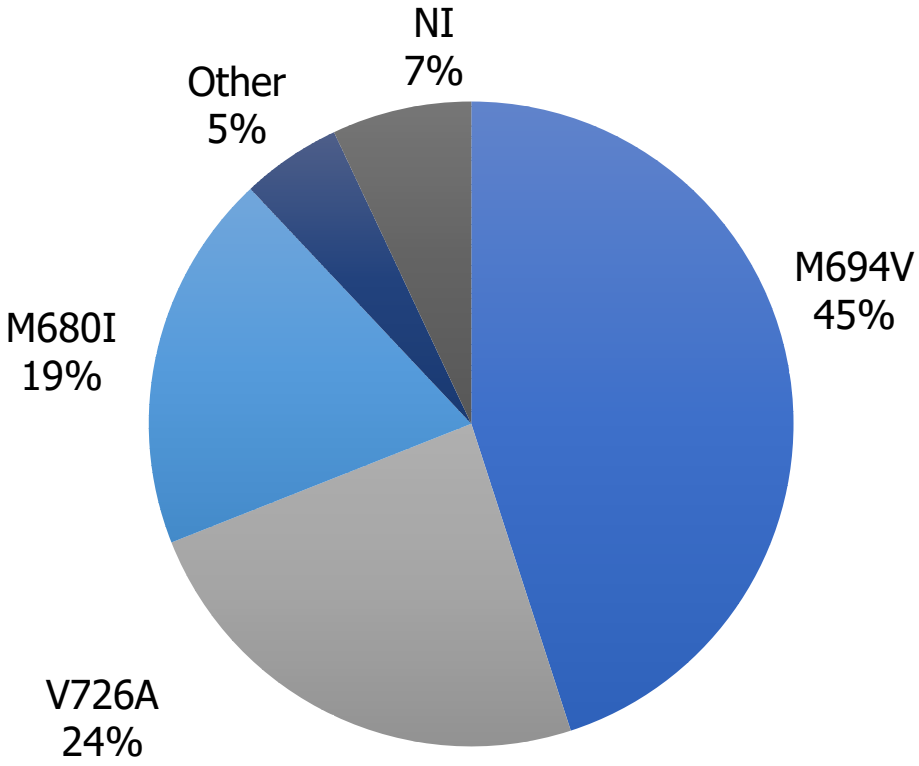
FMF: definition & clinical presentation

- Hereditary autoinflammatory disorder
- Recurrent attacks of **fever and serositis** (eg, peritonitis, pleuritis, pericarditis, synovitis) or erysipelas-like erythema.
- First attack in early childhood
- Diagnosis:
  - Clinical presentation
  - Family history
  - Genetic analysis
  - Histological examination - AA amyloidosis in most cases
- Treatment – Colchicine, IL-1 inhibitors (?)

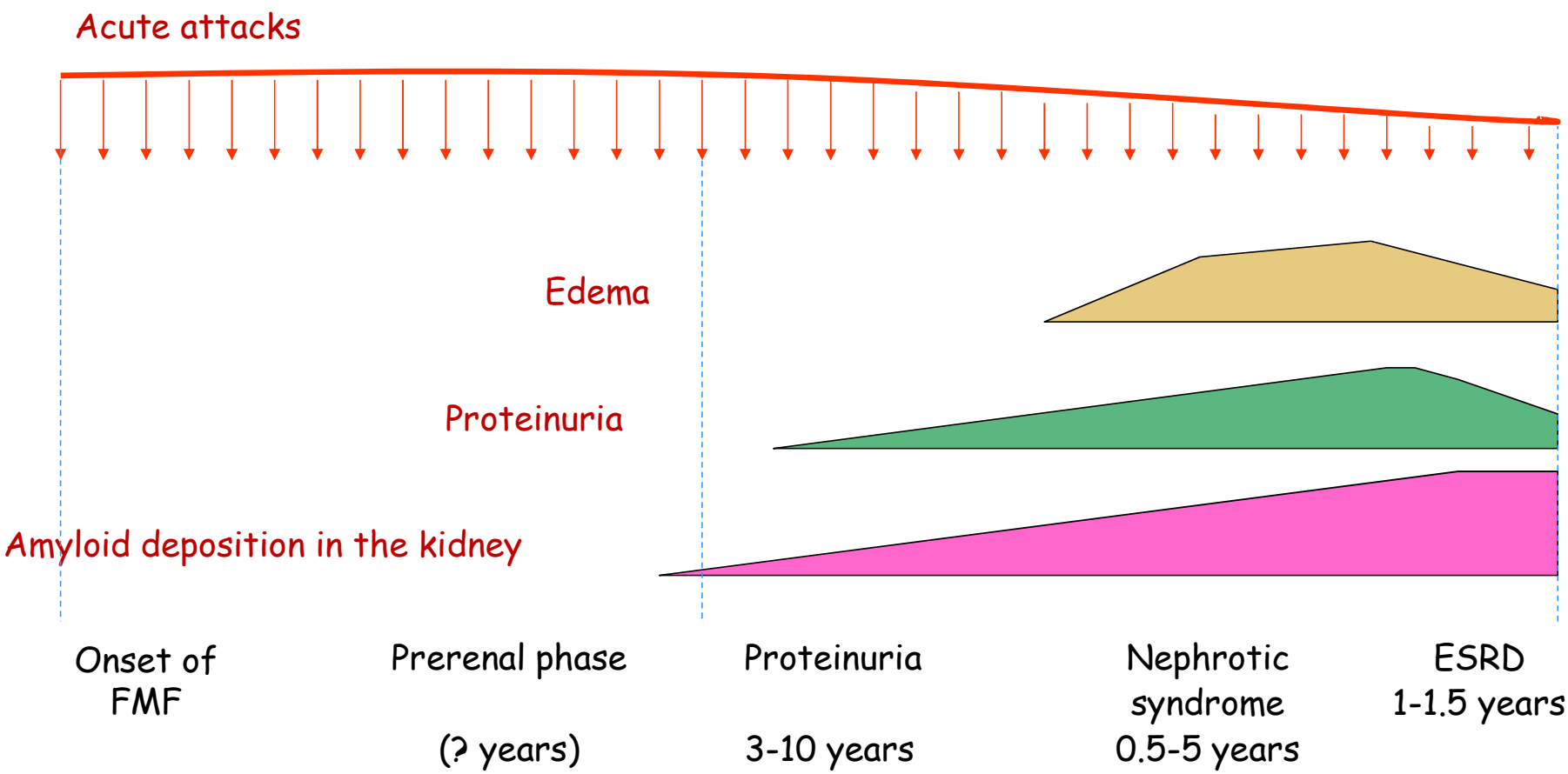
Historical milestones

- 1908 – first case report
- 1945 - described as a separate nosological entity
- 1950-1960 – detailed description and suggestion of the name - FMF
- 1972 – Colchicine for treatment
- 1992 - Mapping of the gene to the short arm of chromosome 16
- 1997 – Cloning of the gene (MEFV)

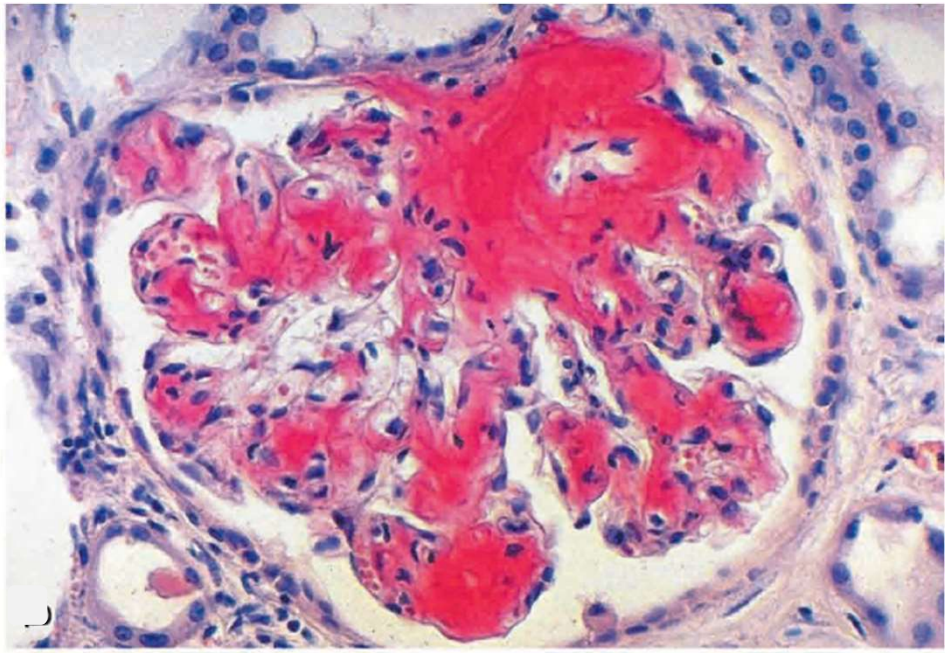
FMF – MEFV mutations



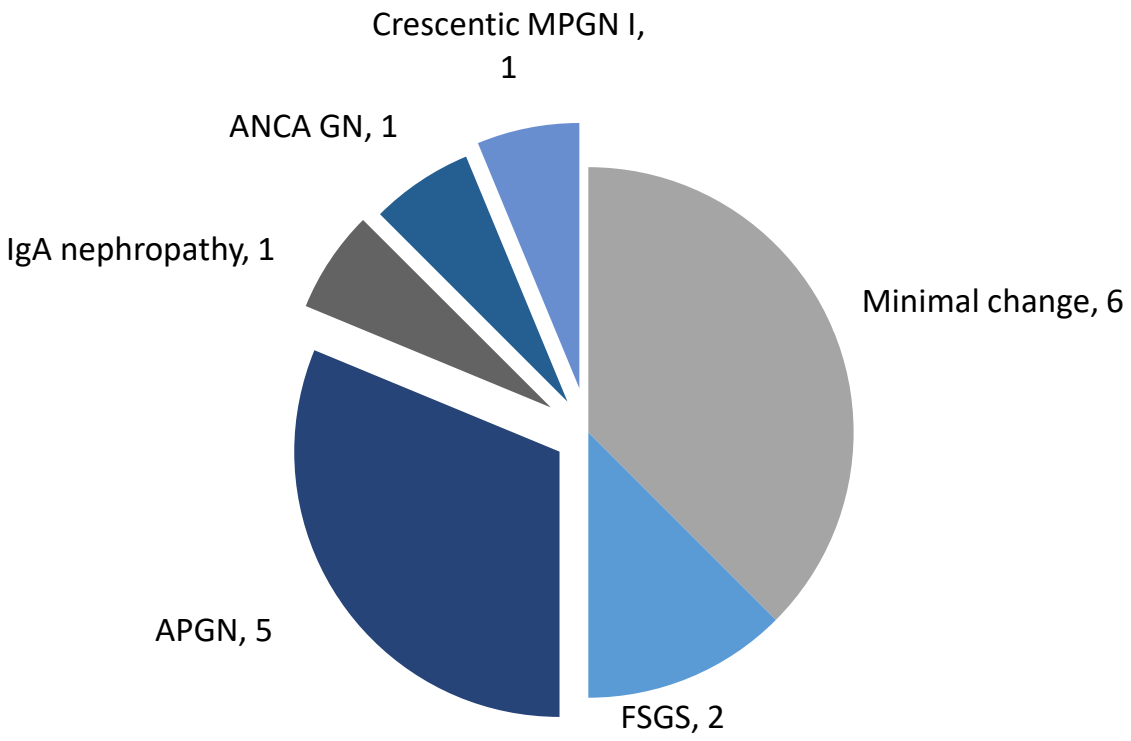
Natural course of FMF complicated by renal amyloidosis



Amyloidosis



Biopsy findings in non-amyloid nephropathy (n=16)



Dialysis

High morbidity and mortality

- Hypotensive episodes
- A/V fistula problems
- Infections
- Low albumin, high CRP
- Systemic amyloidosis
  - Decreased adrenal reserve (deposition in adrenal gland)
  - Anemia (deposition in bone marrow)
  - Cardiac involvement
  - Other ….

Low quality of life

Renal transplantation

- Technical complications, during the operation
- Recurrence of amyloidosis in the renal allograft
- Effects and side effects of immunosuppressive medications
- Long-term outcome (allograft , patients)
- Colchicine & IS interactions

Colchicine: side effects

- Gastrointestinal (diarrhea, nausea, vomiting, and abdominal pain)
- Hematologic (bone marrow suppression)
- Neuropathy, myopathy
- Other (alopecia, hepatic, renal…..)

Characteristics of Recipients & Donors (n=22)

Recipients:

- Mean age – 38.2 ± 11.4 y
- Age range – 20.1– 53.1 y
- Male – 13 (59.1%)
- HD duration – Me 6 mo

Donors:

- Mean age – 46.0 ± 8.5 y
- Age range– 28.6-58.9 y
- Female – 15 (68.2%)
- Relationship:
  - parents – 5
  - wife – 1
  - mother-in-low - 1
  - other - 15

Immunosuprression

- Induction with Basiliximab
- Pred + CsA + Aza

  Pred + CsA + MMF

  Pred + Tacro + MMF

- Colchicine at 1st week, 0.5 mg/d up to maximal tolerated dose

Main Complications in FMF patients (n=22)

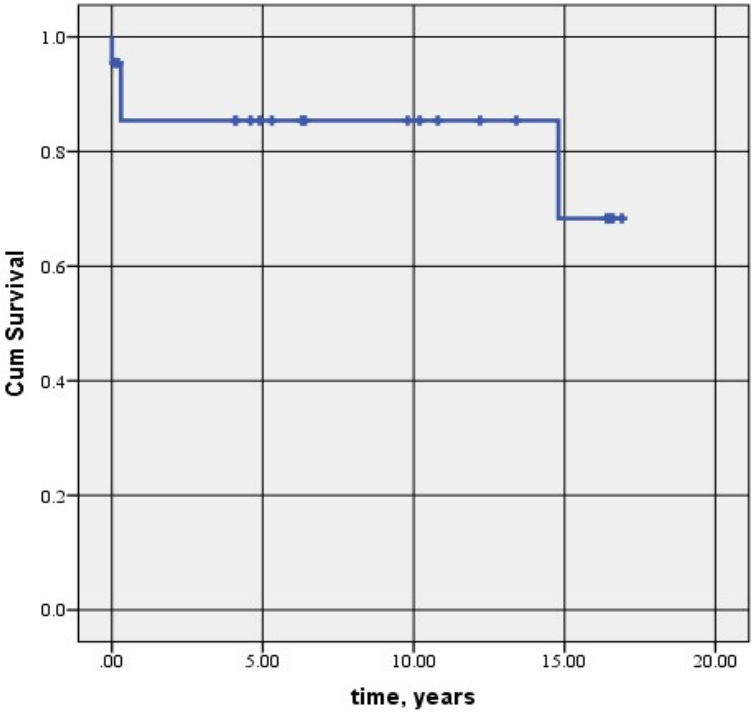
Rejection	8
Acute tubulonecrosis	2
CMV disease	1
Lung tuberculosis	1
Basalioma	1
Distal ureteral necrosis, Tx hydronephrosis	1
Urethral stricture	1
Lymphocele	2
Diabetes (transient)	1

Colchicine & Immunosupressants (n=22)

- FMF attacks – 10
- Colchicine & Cs A – myalgia, neuropathy (3)
- Colchicine & MMF – diarrhea (9)
- Colchicine & Tacrolimus - FMF attacks (2)

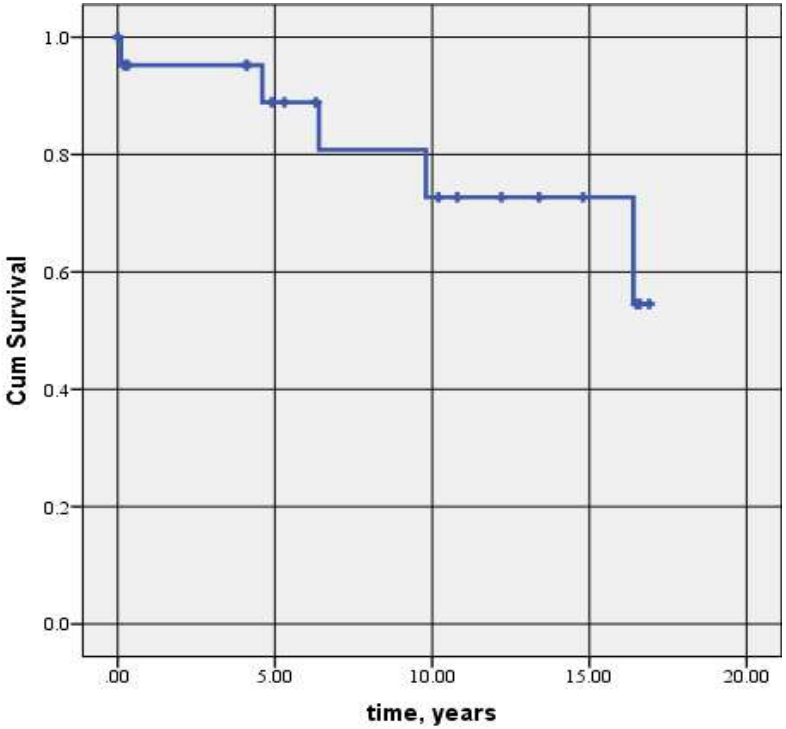
Graft & pts' survival

1-year - 95.5%
5-year - 85.4%
10-year - 85.4%



Graft survival

1-year - 95.2%
5-year - 88.9%
10-year – 72.7%



Pts' survival

Causes of graft failure (n=4)

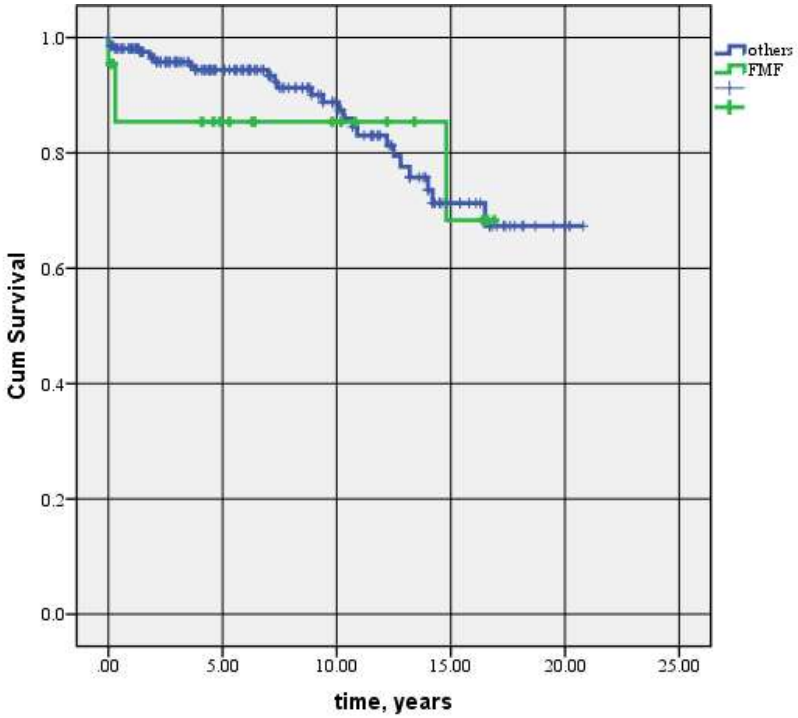
- Rejection 2
- Non-compliance 1
- CTN 1

Causes of death with functioning graft (n=5)

- Cardio-vascular complication 1
- Systemic amyloidosis 1
- Polyorgan insufficiency 1
- Compartment syndrome after cholecystectomy 2

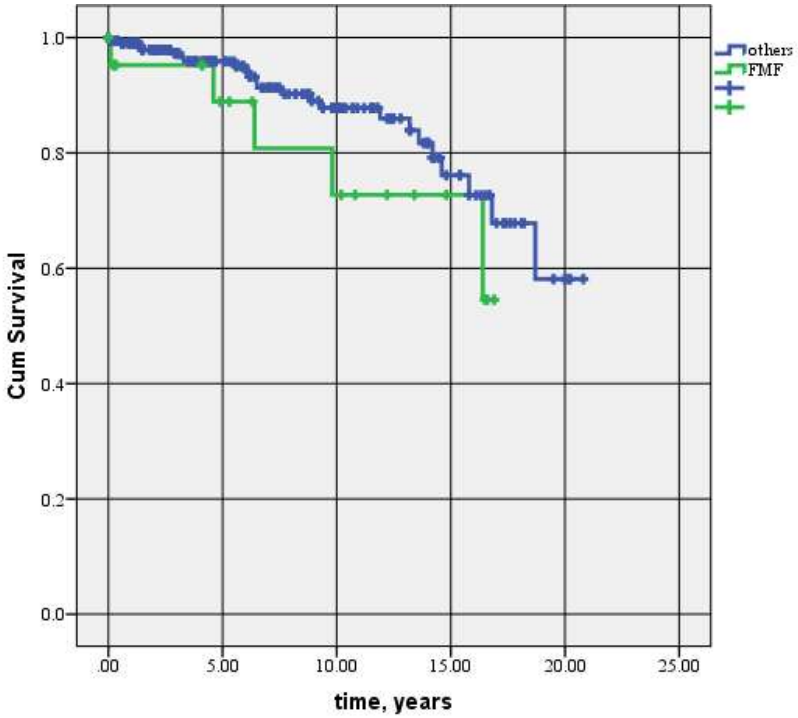
Survival comparison: FMF vs others

Graft survival



Log rank p=0,679

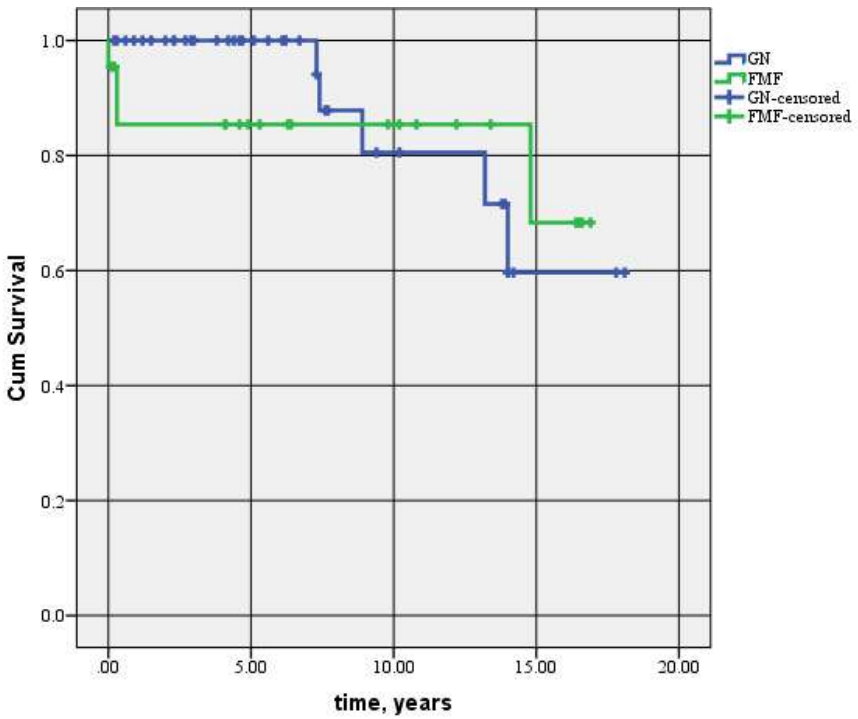
Pts survival



Log rank p=0,217

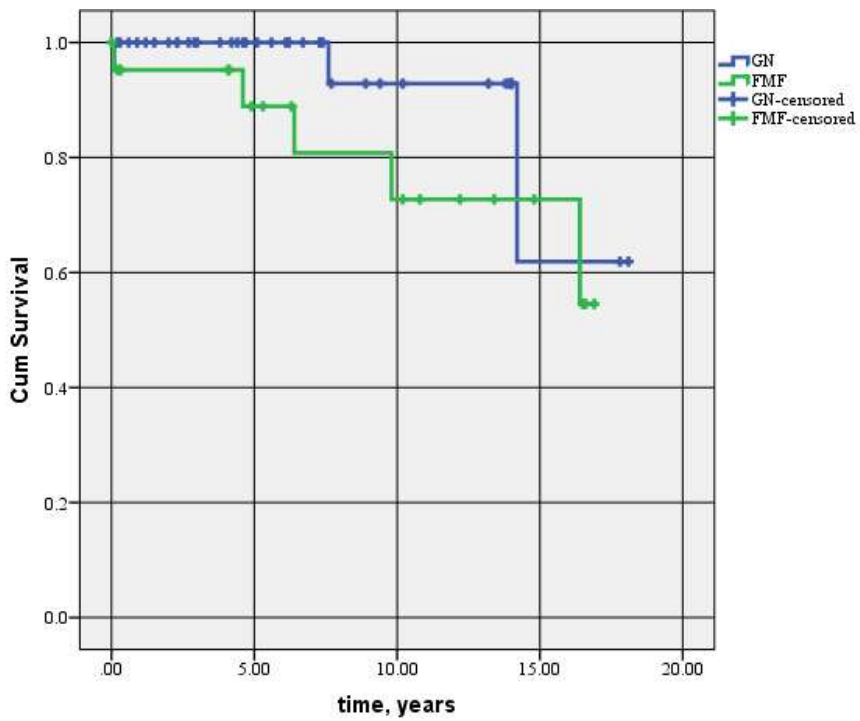
Survival comparison: FMF vs GN

Graft survival



Log rank p=0,892

Pts' survival



Log rank p=0,187

Conclusion

- FMF is a serious health problem in some regions (Mediterranean)
- Systemic amyloidosis is a preventable but often fatal complication of FMF, even under RRT
- Colchicine is a medication effective in ameliorating acute attacks and in preventing of amyloidosis in most cases
- Renal transplantation is an effective mode of treatment in patients with renal amyloidosis of FMF

Thank you!