

La terapia della fibrillazione atriale:

Il destino dei pazienti dopo ablazione della fibrillazione atriale

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Long-term clinical outcome of patients who failed catheter ablation of atrial fibrillation

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(Under Review)

Background

- ✓ **Catheter ablation** is an effective and durable long-term therapeutic strategy for some AF patients.
- ✓ Surprisingly, a few studies have evaluated the clinical outcome and management of patients considered **non-responders to substrate ablation of refractory AF**.

Aim of the study

- ✓ The aim of this multicenter observational study was to investigate the **clinical outcome and management** of patients considered **non-responders** to substrate ablation of refractory AF.
- ✓ **Failure of AF ablation** was defined as recurrence, after the blanking period of 3 months, of one or more symptomatic ECG-documented AF episode lasting more than 30 seconds.

Inclusion criteria

- ✓ P. had failed one or more attempts at RFCA of paroxysmal or persistent recurrent AF performed at the electrophysiology centers of **Reggio Emilia**, **Mirano** and **Lavagna** (Italy) over a **10-year period** (2001-2011) for highly symptomatic AF, refractory to one or more antiarrhythmic drugs.
- ✓ had decided to **not perform further ablation** attempts (patient or physician decision).
- ✓ had a **minimum follow-up of 1 year** since the last ablation.

Ablation procedure

- ✓ The endpoint of the ablation procedure was **PV isolation**.
- ✓ Since 2007, in patients with persistent AF, in adjunct to PV isolation, empirical ablation of the atrial regions characterized by complex fractionated atrial electrograms (**CFAE**).

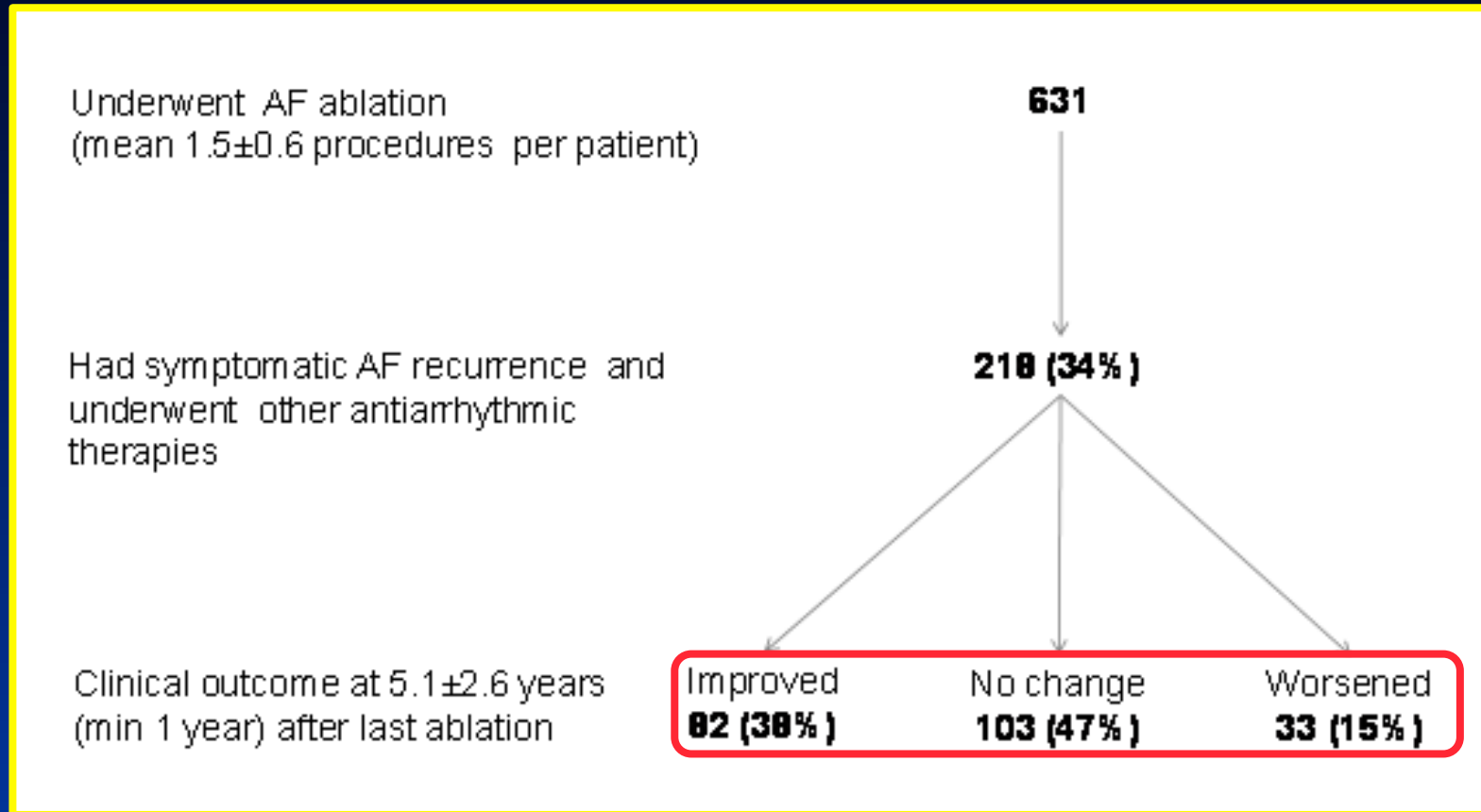
Primary endpoints

- ✓ **Quality of life** assessed by means of the definition of **Patient Global Assessment** (patients were requested to describe their current clinical status -AF symptoms and general well-being- as improved, unchanged or worse compared to the pre-ablation period).
- ✓ **Antiarrhythmic treatments** as a consequence of the failure of catheter ablation.
- ✓ **Adverse clinical events** and progression to **permanent AF**.

Clinical characteristics

P. undergone AF CA 2001-2011	631
P. non responders	218 (34%)
Age in years \pm SD	60 \pm 9
Male (%)	169 (77%)
AF type prior to ablation:	
Paroxysmal (%)	87 (40%)
Persistent (%)	108 (49%)
Long-lasting Persistent (%)	23 (11%)
Hypertension (%)	76 (35%)
Structural heart disease	110 (50%)
Left atrial size in mm \pm SD	48 \pm 6
Left ventricular EF \pm SD	56% \pm 12

Patients' flow chart and QOL



Antiarrhythmic treatments

Number of patients	Total n=218
No antiarrhythmic therapy	11 (5%)
Any antiarrhythmic therapy	207 (95%)
Antiarrhythmic drug therapy:	
- Rhythm control therapy (incl. amiodarone)	58 (27%)
- Rate control therapy	139 (64%)
Non-pharmacological therapy:	
- AV junction ablation & pacing	13 (6%)
- Surgical therapy	4 (2%)

Oral anticoagulant therapy was taken by 147 (67%) patients.

Adverse clinical events

Total patients	218
Adverse clinical events:	22 (10%)
- Death	5 (2,3%)
- Overt heart failure	5 (2,2%)
- Stroke	2 (0,9%)
- Transient ischemic cerebral attack	2 (0,9%)
- Severe haemorrhage	4 (1,8%)
- Pacemaker implantation (other than for AV junction ablation)	3 (1,4%)
- ICD implantation	3 (1,4%)
- Cardiac resynchronization therapy	1 (0,5%)

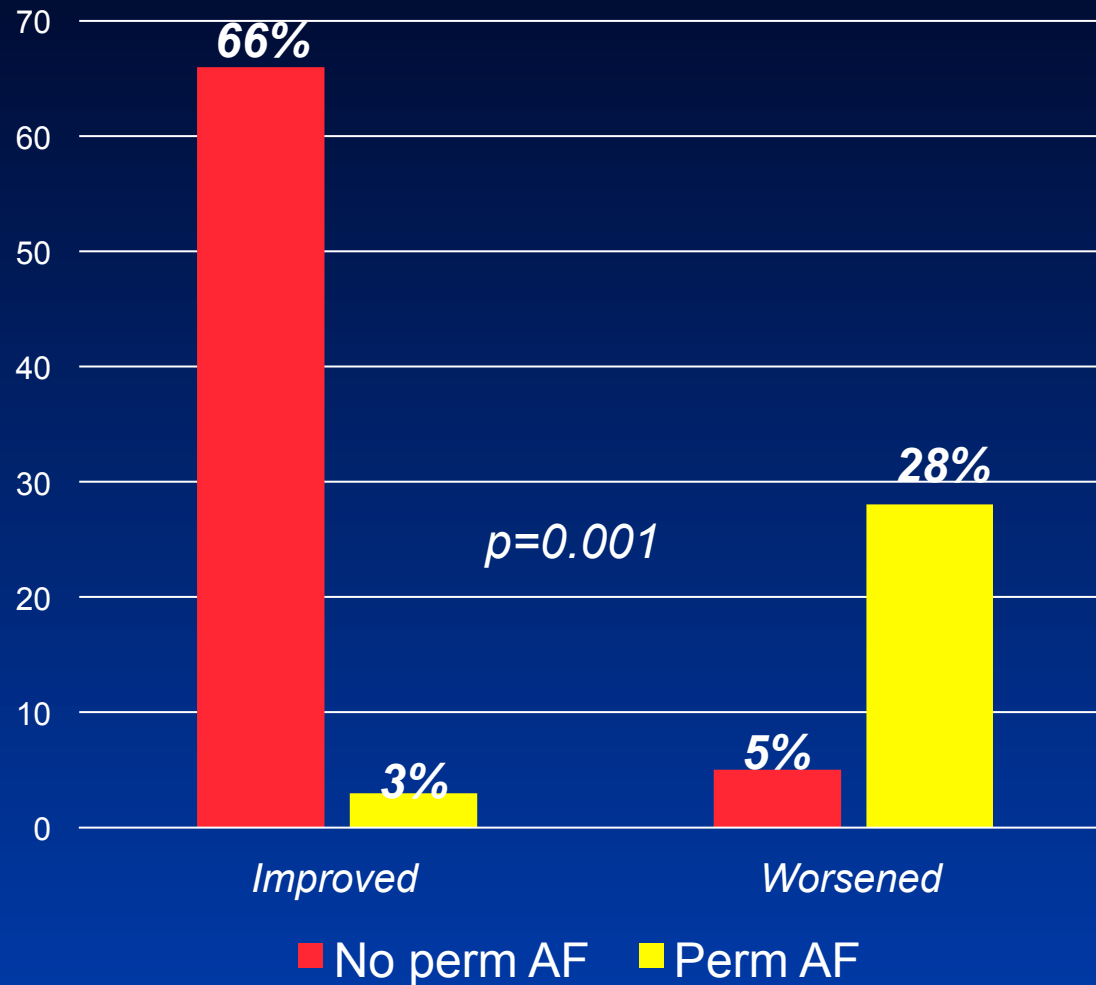
Apparent paradox: only a small minority of patients require non-pharmacological intervention.

- ❖ 38% of patients improved their PGA compared to the pre-ablation period.
- ❖ Patients learnt how to coexist with the arrhythmia, i.e., a sort of adaptation to the symptoms also observed in many other chronic illnesses.
- ❖ Resignation, i.e., the fear of adverse effects and the skepticism as regards benefits tempted these relatively young patients to refuse further invasive therapies.

Progression to permanent AF

Total patients	218
Progression to permanent AF	98 (45%)
- from paroxysmal	22/87 (25%)
- from persistent	63/108 (58%)
- from long-persistent	13/23 (57%)

Patient global assessment

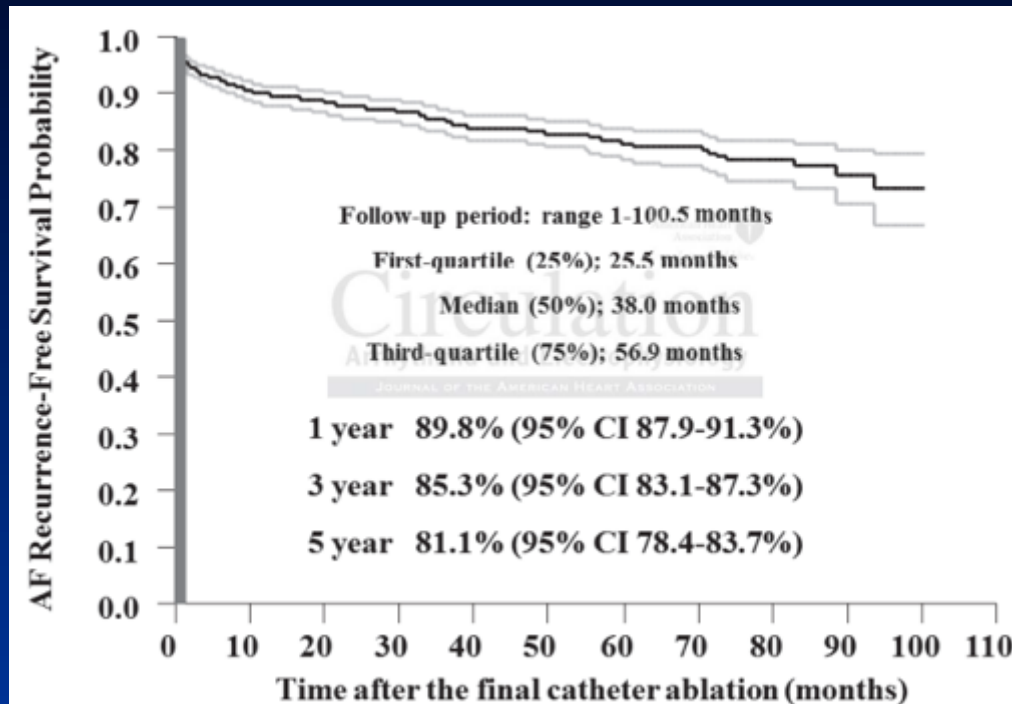


Predictors of development of permanent AF

	Total patients n=218	Perman. AF n=98	Non- permane nAF n=120	Univariable P value	Multivariable P value	Odds ratio (95 CI))
Years since last ablation procedure	5.1±2.6	5.6±2.7	3.5±2.5	0.001		
Mean age at enrolment	60±9	62±8	58±10	0.001		
Males	169 (78%)	80 (82%)	89 (74%)	0.20		
Structural heart disease	110 (50%)	61 (62%)	49 (41%)	0.02		
LV ejection fraction	58±8	57±9	59±6	0.04		
Left atrial diameter (per mm increase)	48±6	50±7	46±6	0.001	0.04	1.06 (1.0-1.1)
Persistent AF	131 (60%)	76 (78%)	55 (46%)	0.001	0.04	2.4 (1.0-5.9)
Single ablation procedure	119 (55%)	74 (76%)	45 (37%)	0.001	0.0001	7.14 (3.3-17)

Long-Term Follow-Up after Catheter Ablation of Paroxysmal Atrial Fibrillation: The Incidence of Recurrence and Progression of AF

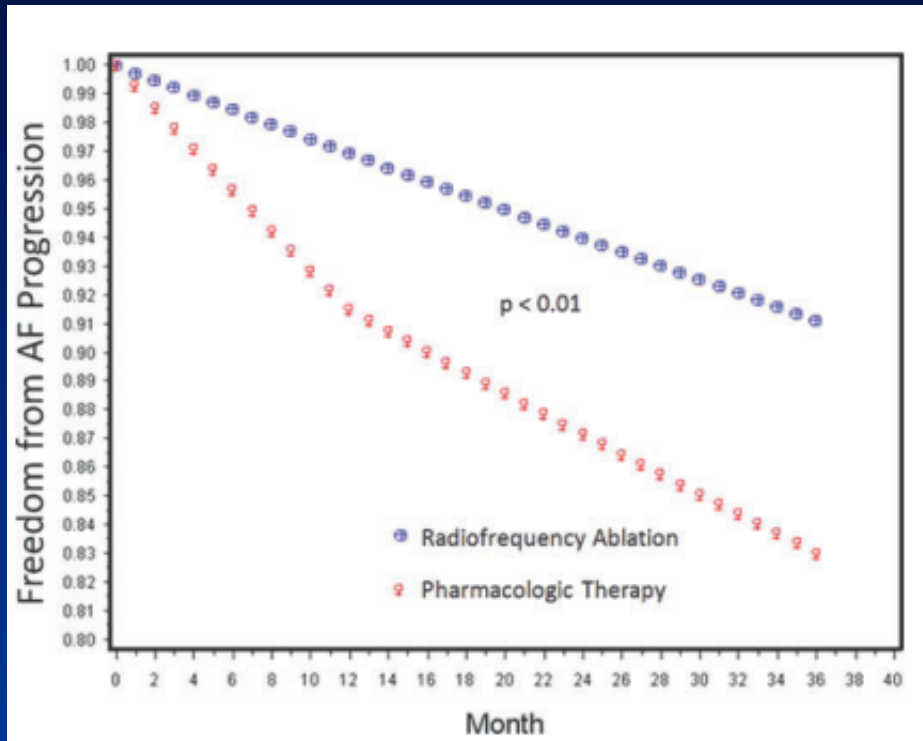
Takigawa et al. DOI: 10.1161/CIRCEP.113.000471



During a median follow-up period of 47.9 (range, 5.3–123.3) months after the initial CA, **PAF progressed to persistent AF in 15 patients (1.2% of all patients; 7.5% of those with AF-recurrence;** average AF-progression rate, 0.3%/year). Moreover, 11 of them eventually shifted to permanent AF.

Effect of Catheter Ablation on Progression of Paroxysmal Atrial Fibrillation

Jongnarangsin K, JCE 2012



Among the 504 patients in this study, **AF progressed to persistent** in 7 patients (**1.5%**) after RFA. Progression to persistent AF occurred in 7 of the 56 patients (**13%**) in whom **RFA was not effective** in eliminating paroxysmal AF ($P < 0.001$).

The incidence of AF progression after RFA was 0.6% per year.

Progression from paroxysmal to persistent AF

RFA

- ❖ **Takigawa** et al: **1,2%** during a median follow-up period of 5 years
- ❖ **Jongnarangsin** et al: **1,5%** during a median follow-up period of 2 years
- ❖ **Bottoni** et al: **5,7%** (22/388) during a median follow-up period of 5 years

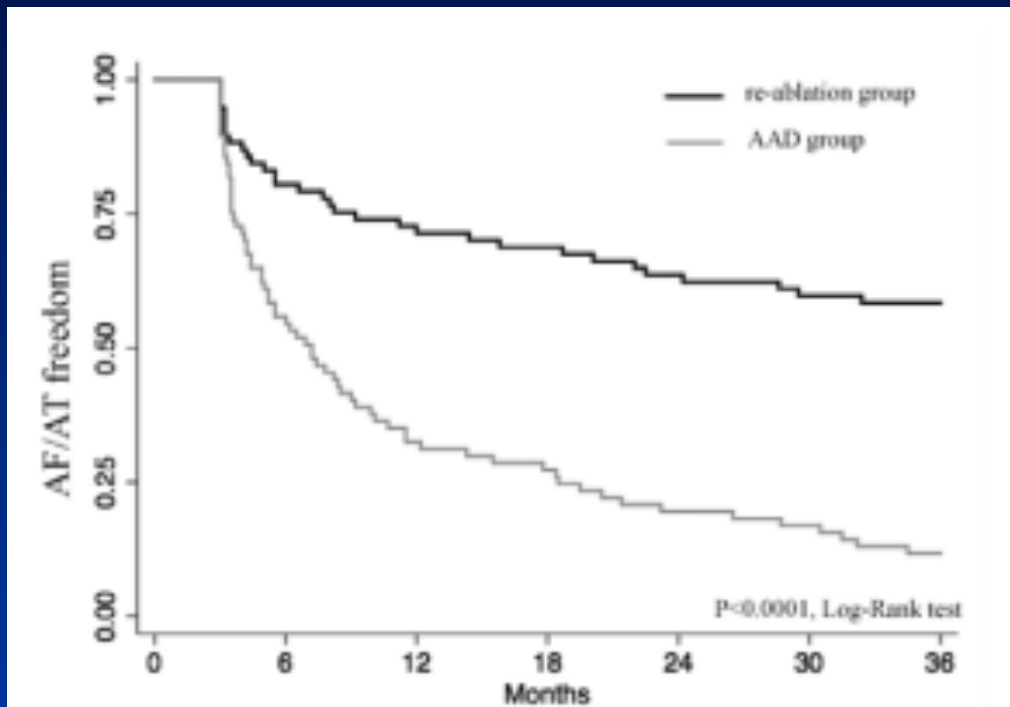
AAD

- ❖ **Kerr** et al (CARAF): **25%** during a median follow-up period of 5 years

RFA may substantially reduce the rate of progression of AF in comparison to pharmacological therapy

Progression of Atrial Fibrillation After a Failed Initial Ablation Procedure in Patients With Paroxysmal Atrial Fibrillation

Pokushalov E, Circ Arrhythm Electrophysiol 2013



On multivariate logistic regression analysis, only **reablation** strategy (OR=0.13; 95% CI, 0.04–0.47; $P < 0.01$) and **diabetes** mellitus (OR=3.5; 95% CI, 1.1–11.3; $P = 0.04$) were **independent predictors** of progression to persistent AF (4% RFA vs 23% AAD).

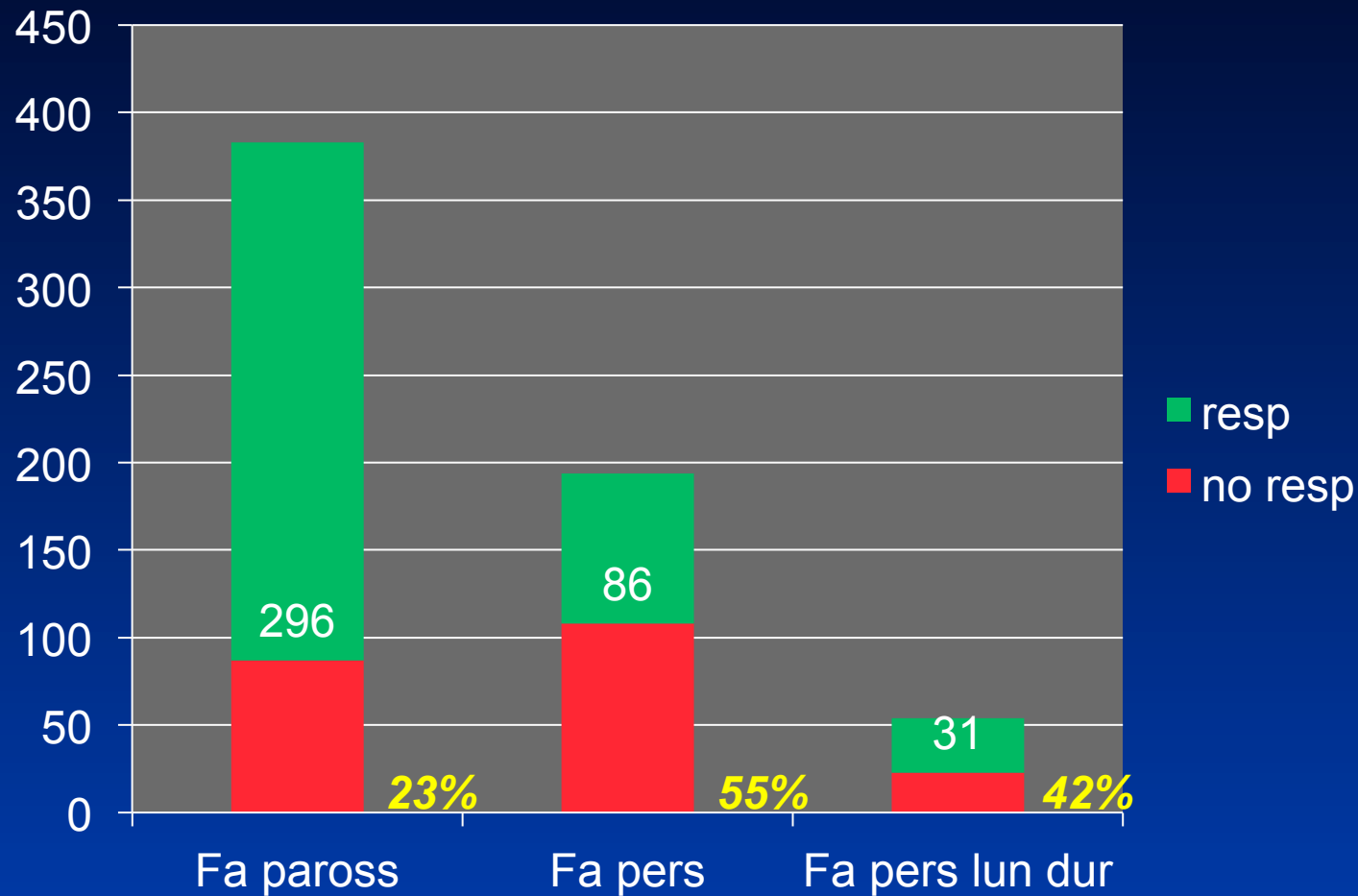
Conclusions

- ❖ More than 5 years after a failed strategy of AF ablation, a small minority of patients had their quality of life so impaired as to require non-pharmacological interventions.
- ❖ Almost half had developed permanent AF, which impaired their quality of life.
- ❖ Permanent AF was more common in patients who had performed a single ablation procedure and in those who had left atrial enlargement or a history of persistent AF.
- ❖ A low stroke risk was observed in the long-term follow-up.

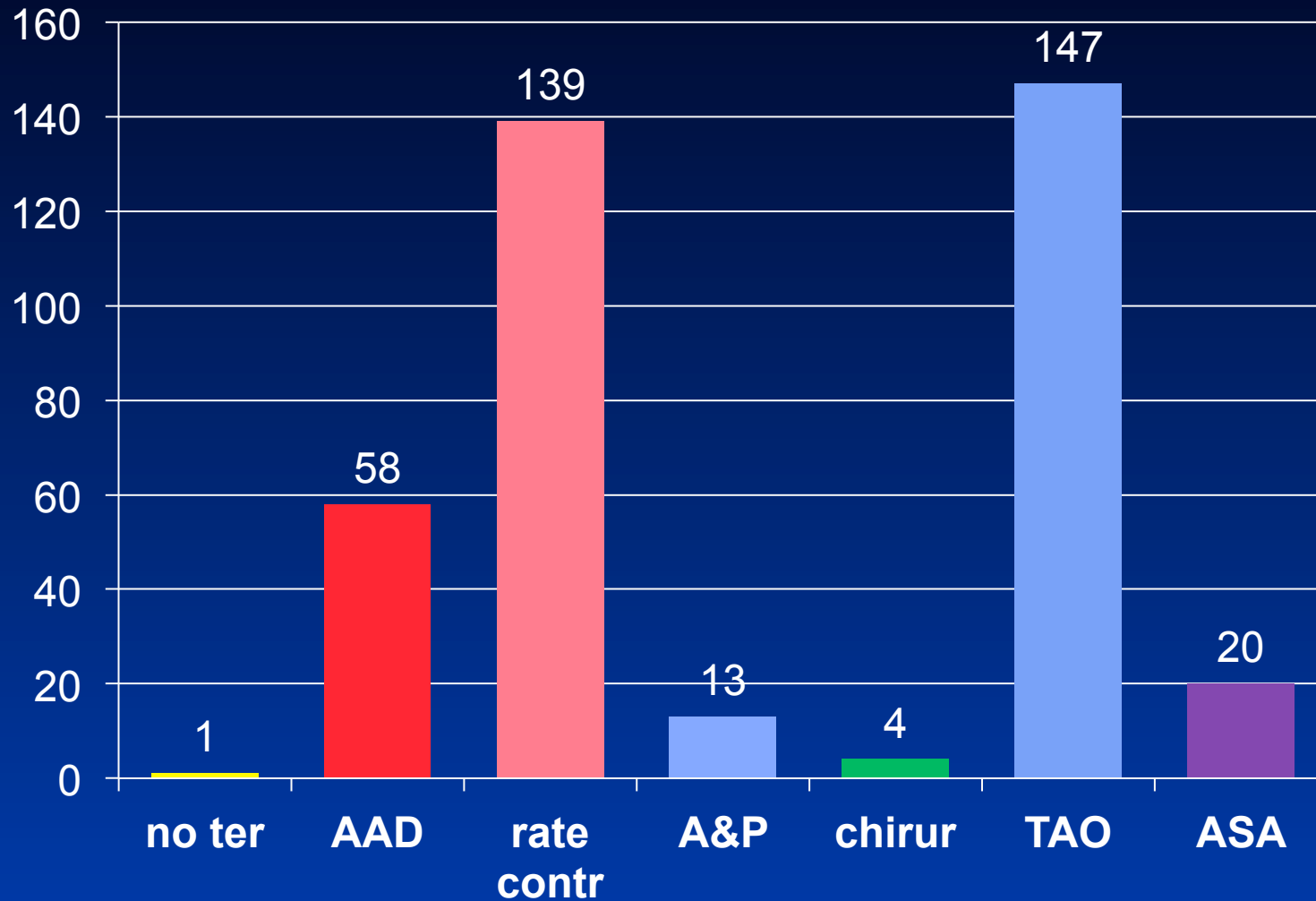
Pazienti no responder

- P. **no responder I** (*dopo 1 proc.*): **119**
- P. **no responder II** (*dopo 2 o più proc; 2,1 proc/pz*): **99**

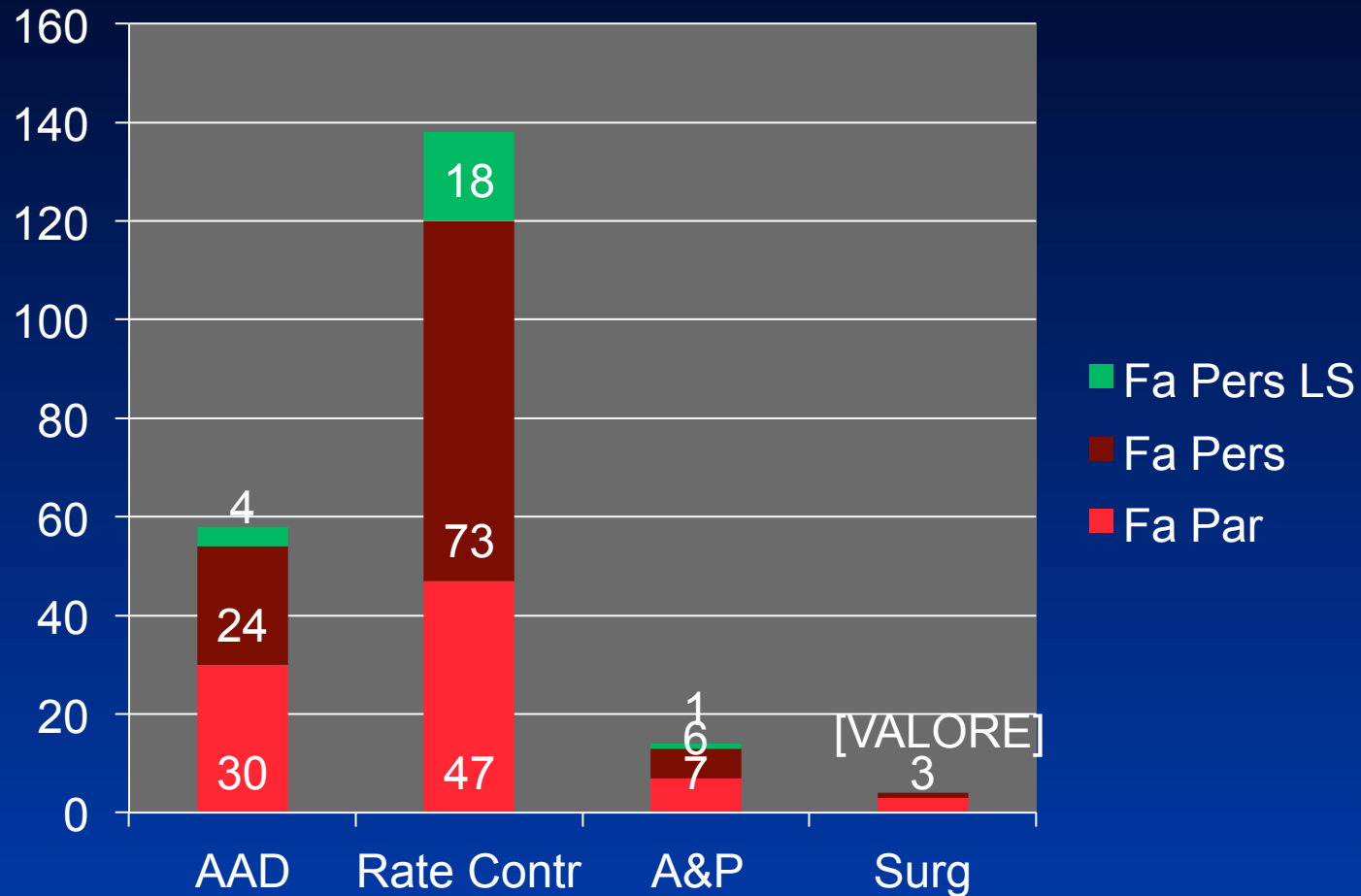
Resp./no-Resp. in base tipo Fa



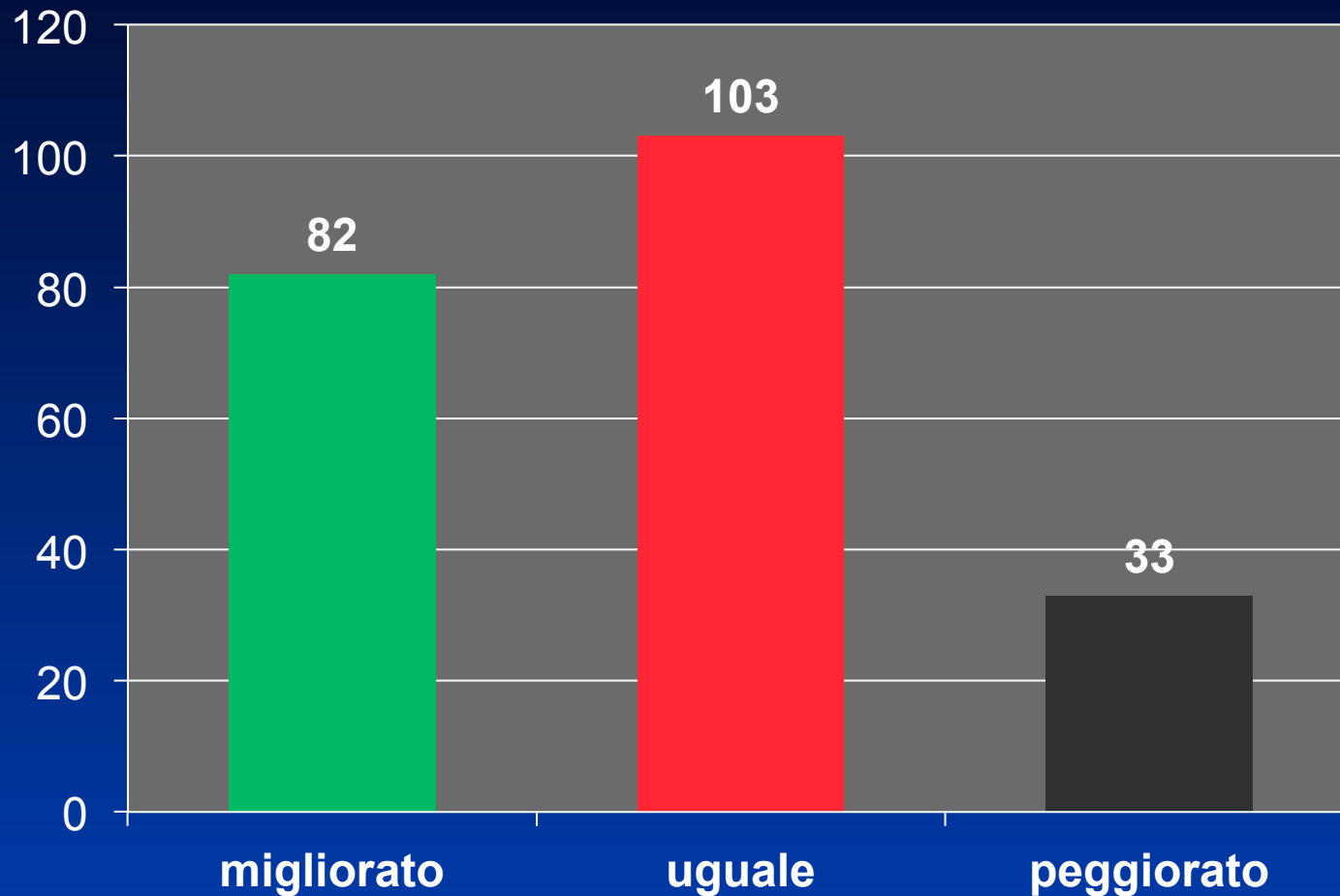
Terapia no responder



Terapia no responder



Patient global assessment



A&P (#13)

M: 1

U: 6

P: 6

(->FA perm: 5)

T. Chir (#4)

M: 0

U: 4

P: 0

(->FA perm: 1)

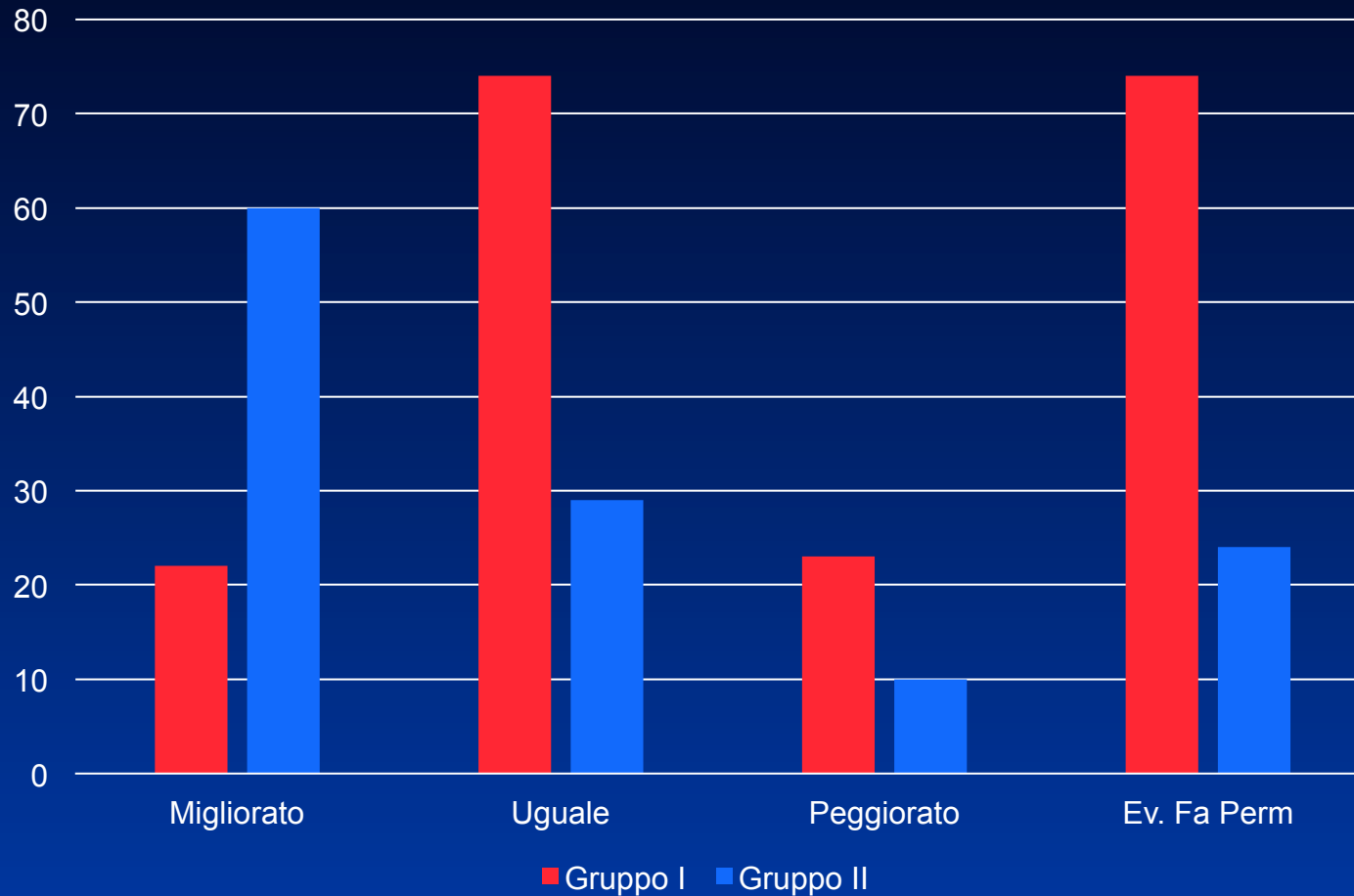
Pazienti no responder: I

- **119** pz (90 m)
- età media: **62 ± 8** anni
- **cardiopatìa**: **65 pz** (FE media 56% ±12)
- **atrio** SN: diametro medio **48 ± 6** mm
- Fa **parossistica**: **44**
- Fa **persistente**: **63**
- Fa **persistente di lunga durata/permanente**: **13**

Pazienti no responder: II

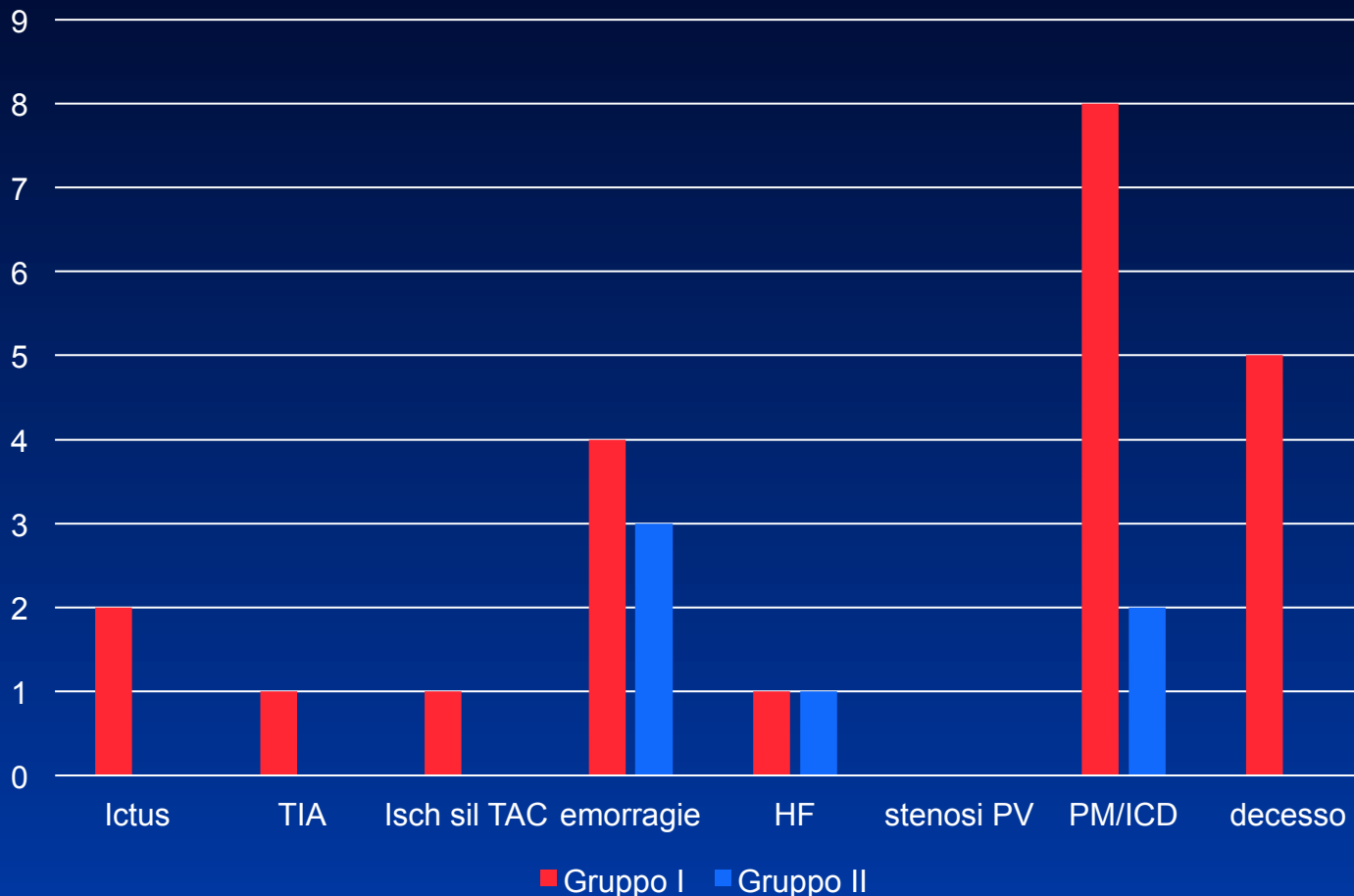
- **99** pz (79 m)
- **età** media: **57 ± 9** anni
- **cardiopatìa**: **45 pz** (FE media 56% ±12)
- **atrio** SN: diametro medio **47 ± 7** mm
- Fa **parossistica**: **43**
- Fa **persistente**: **45**
- Fa **persistente di lunga durata/permanente**: **10**

Patient global assessment



Eventi avversi nel F-UP

In totale **22 p.** (10%)



Evoluzione Fa permanente

In totale **20** p./88 (22%);

RE-LA
(2/42 par
4.7%)

In totale 78 p./130 (60%);

Mirano
(20/45 par
44.4%)

