

# TONSILLECTOMY IN A PAN-EUROPEAN COHORT OF 1147 PATIENTS WITH IgA NEPHROPATHY


Roberta Camilla, Rosanna Coppo, Shubha Bellur, Daniel Cattran, Terence Cook, John Feehally, Stephan Troyanov, Ian Roberts, Luca Vergano and Laura Morando.

on behalf of the collaborative multicenter study **VALIGA** validation of the Oxford classification of **IgA** Nephropathy in Europe (**VALIGA**)

## List of the Center of the VALIGA study

**Participating Centers**

- CROATIA:**
  - Opatovac-Ljubanovic ZAGREB
- CZECH REPUBLIC:**
  - Teatr-Hospova-Babstova PRAHA
- ESTONIA:**
  - Rosenberg-Rispara TARTU
- GERMANY:**
  - Floege-Dreese-Eiber AACHEN/HEIDELBERG
- GREECE:**
  - Goumenos PATRA
  - Stamopoulos-Bambas IOANNINA
  - Maropoli THESSALONIKI
- ITALY:**
  - Belfrate-Mazzuoli-Quarrelli-Rollino TURIN
  - Berga-Mazzuoli-Cravero BIELLA
  - Bona-Mazzuoli TURIN
  - Canciarini-Ravera BRESCIA
  - Cirami-Balvador FLORENCE
  - Coppo-Mazzuoli-Amore TURIN
  - Cusinato-Mazzuoli-Bezzoli BORDOMANERO
  - Del Canton-Spavolo-Migotto PAVIA
  - Di Giulio-Olannakakis ROME
  - D'Amico-Ferrario COMO
  - Enna-Olannakakis ROME
  - Ferretti-Olannakakis-Pisoli VITERBO
  - Furini-Magistroni MODENA
  - Galliani-Olannakakis ROME
  - Gessardo-Di Palma FOGGIA
  - Giannini-Mazzuoli TREVISO
  - Locatelli-Del Vecchio LECCO
  - Lupo-Bernich VERONA
  - Maggio-Ferrario LODI
  - Martina-Messueri-Mazzuoli CHIVASSO
  - Mena-Olannakakis ROME
  - Moggi-Mazzuoli-Furlanetto CUNEO
  - Morales-Olannakakis ROME
  - Pani-Santi-Angeli-Piras CAGLIARI
  - Pozzi-Ferrario CINISELLO B.
- POLAND:**
  - Durki-Perkowska Plasziska WARSAW
  - Wiecek-Karkoszka KATOWICE
  - Mizerska Wasiak-Majczyk WARSAW
- PORTUGAL:**
  - Carvalho-Ferreira LISBON
- SWEDEN:**
  - Berg-Soderberg HUDONDE
  - Falstrom-Smerus-Sundin UPPSALA
  - Lundberg-Sundelin STOCKHOLM
- SPAIN:**
  - Ballerin-Aro Terroba BARCELONA
  - Egido-Camells Orta-Catalina MADRID
  - Gimeno-Fuertes Olvera BARCELONA
  - Praga-Oublerre MADRID
- THE NETHERLANDS:**
  - van Kooten-Rabelink LEIDEN
  - Wetzels NIMEGEM
- TURKEY:**
  - Caltiskan-Ozlu ISTANBUL
  - Topaloglu-Orhan ANKARA
- UNITED KINGDOM:**
  - Fearnley-Barratt LEICESTER
  - Geddes-Kippen OLSBOW



## INTRODUCTION AND AIMS

The beneficial effect of tonsillectomy in patients with IgA nephropathy (IgAN) is controversial. Tonsillectomy has been proposed with the aim of removing a source of pathogens and reducing Gut Associated Lymphoid Tissue (GALT) and decreasing polymeric IgA synthesis.

In Asia, particularly Japan, benefits of tonsillectomy have been claimed from uncontrolled studies and from recent RCTs, mostly in association with steroids. In Europe small single center uncontrolled studies failed to show any benefit of tonsillectomy in IgAN.

There is a lack of a European multicenter study on tonsillectomy in IgAN.



Tonsils and mucosal immunity



The 1147 patients with IgAN enrolled in the European validation study of the Oxford Classification of IgAN (VALIGA), from 55 Centers of 13 European Countries, has offered a unique opportunity to investigate the effect of tonsillectomy in IgAN patients very well characterized both histologically and clinically. Retrospective data were obtained over a mean follow-up >5 years.

## PATIENTS AND METHODS

Data on tonsillectomy were available in 1049 patients: tonsillectomy was performed in 62 patients (5.9%), 10 children and 52 adults; 95% were Caucasian and 77% males.

Mean values in the 62 tonsillectomized patients versus 987 non-tonsillectomized are reported in table 1 and 2.

Estimated-GFR (eGFR) was calculated using the MDRD formula in adults and Schwartz formula in children. The slope of e-GFR was calculated from serial measurements over the follow-up. The end-points were end stage renal disease (ESRD) and 50% loss of eGFR.

Using a logistic regression model, a predicted probability (propensity score) to have tonsillectomy was given to each patient. Features measured for the propensity score at renal biopsy and therapies influencing the outcome included: gender, age, MEST score, MAP, prior immunosuppression, RAS blockade, initial eGFR and proteinuria. These variables were selected on the basis of a maximum 0.05 difference in propensity score. Cox proportional hazard survival analysis was used to detect if the risk of renal outcome was different in patients with or without tonsillectomy.

Variables associated with risk of renal outcomes were tested by univariate analysis, then interaction was tested.

## RESULTS

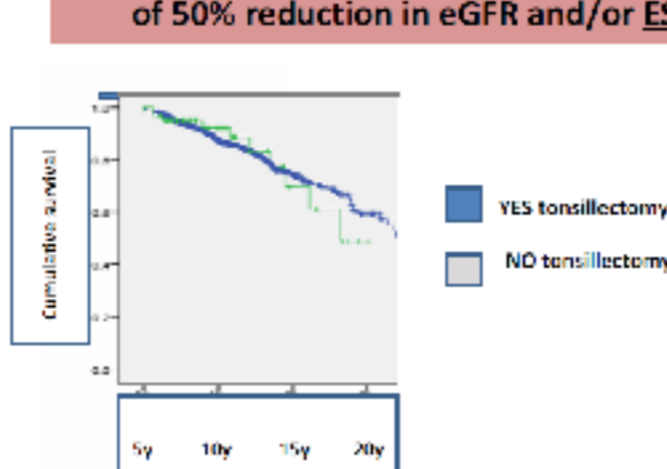
### Mean values in the 62 tonsillectomized patients versus 987 non-tonsillectomized patients with IgAN (table 1)

	NO tonsillectomy	YES tonsillectomy	P value
Age at renal biopsy (years)	35.8 ± 16.5	37.4 ± 16.2	ns
Follow-up (years)	5.71 ± 4.48	5.62 ± 4.12	ns
eGFR at renal biopsy (ml/min/1.73 m2)	76.7 ± 34.6	73.4 ± 31.76	ns
Proteinuria at renal biopsy (g/day/1.73 m2)	1.20 (0.52-2.56)	1.35 (0.59-2.83)	ns
Mean proteinuria over follow-up (g/day/1.73 m2)	0.78 (0.40-1.62)	0.73 (0.37-1.68)	ns

### Mean values in the 62 tonsillectomized patients versus 987 non-tonsillectomized patients with IgAN (table 2)

	NO tonsillectomy	YES tonsillectomy	P value
Loss of eGFR during follow-up (ml/min/1.73 m2/year)	-2.08 ± 8.08	-1.01 ± 7.75	ns
ESRD	112/987 (11.3%)	9/62 (14.5%)	ns
50% loss of initial GFR	137/987 (13.9%)	9/62 (14.5%)	ns
combined end-point (ESRD or 50% loss of initial GFR)	156/987 (15.8%)	10/62 (16.1%)	ns

Survival from the combined end-point of 50% reduction in eGFR and/or ESRD



PATIENTS SELECTED FOR PROPENSITY SCORE		Yes tonsillectomy	No tonsillectomy	P value
N° of patients		41	41	
Gender		21M / 20F	21M / 20F	ns
Ethnicity		All caucasian	All caucasian	ns
At renal biopsy	Age (years)	34.9 ± 16.0	36.1 ± 17.9	ns
	Prior ACE or ARB treatment	39%	46%	ns
	Prior immunosuppression	17%	27%	ns
	eGFR (ml/min/1.73m2)	82.2 ± 37.3	77.0 ± 36.7	ns
	MAP (mmHg)	100.0 ± 13.4	98.6 ± 11.5	ns
During follow-up	Proteinuria (g/day/1.73m2)	2.0 ± 2.0	2.2 ± 2.0	ns
	TA-MAP (mmHg)	97.0 ± 9.6	96.5 ± 9.6	ns
	TA-Proteinuria (g/day/1.73m2)	1.0 ± 0.9	1.3 ± 0.9	ns
	eGFR slope (ml/min/1.73m2)	-1.9 ± 7.7	-0.5 ± 8.7	ns
	50% decrease of eGFR or ESRD	3 patients	8 patients	ns
MEST score	Mesangial proliferation	22.0%	24.4%	ns
	Endocapillary proliferation	14.6%	14.6%	ns
	Focal segmental sclerosis	63.4%	73.2%	ns
	Tubular atrophy/Interstitial fibrosis	7.3%	12.2%	ns

PROPENSITY SCORE RESULTS	Yes tonsillectomy	No tonsillectomy	P value
eGFR slope (ml/min/1.73m2)	-1.9 ± 7.7	-0.5 ± 8.7	ns
50% decrease of initial eGFR or ESRD	3 patients	8 patients	ns

## CONCLUSIONS:

The VALIGA retrospective study of a large cohort of European subjects with IgAN did not demonstrate a significant correlation between tonsillectomy and survival from the end point of ESRD or 50% loss of e-GFR.

