

Early and intermediate changes in eGFR and proteinuria to predict progression to kidney failure in C3G and IC-MPGN using UK RaDaR data

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INTRODUCTION

- C3G and IC-MPGN are ultra-rare treatment resistant kidney disorders characterised by C3 deposition
- Kidney failure is common over the long-term
- Clinical trials in these ultra rare disorders are limited by short duration & difficulty in demonstrating efficacy for late outcomes such as progression to kidney failure
- Longstanding issue within nephrology, promoting the search for surrogate markers

AIMS

- Describe the demographics, clinical characteristics and outcomes of patients with C3G and IC-MPGN within RaDaR
- Explore if early changes in urine PCR & eGFR (irrespective of how this occurs) can predict progression to kidney failure

METHODS

Cohort- Adult & paediatric patients with biopsy proven C3G & IC-MPGN diagnosed 1989-2020 without co-existing paraprotein within RaDaR. Central histology review for 118 patients.

RaDaR- recruits from 108 centres in UK with automated collection of retrospective and prospective laboratory and clinical data

Variables & Outcome- Diagnosis date = biopsy date. eGFR was calculated using CKD-EPI and Schwartz. Absolute and % change in time averaged & urine protein creatinine ratio (UPCR) between 0 & 12 months investigated (Adjusted for eGFR). Kidney failure = initiation renal replacement therapy or eGFR <15ml/min/1.73m² (≥ 4wks).

Analyses- Kidney survival was assessed using Kaplan–Meier and Cox regression. eGFR slope was estimated using linear mixed models

RESULTS

Table 1. Baseline characteristics and clinical outcomes

	C3G		IC-MPGN	
	N	%	N	%
Age at diagnosis (years)	135	100	152	100
Median (IQR)	14 (9 - 34)		23 (9 - 55)	
Pediatric	82	61	71	47
Sex	135	100	152	100
Female	70	52	73	48
UPCR at diagnosis, n (%)	62	46	59	39
mg/mmol Median (IQR)	412 (126 - 700)		466 (167 - 820)	
eGFR at diagnosis, n (%)	38	28	42	28
Median (IQR), mL/min/1.73 m ²	70 (30 - 92)		58 (40 - 110)	
Kidney Failure event, n (%)	135	100	152	100
Yes	50	37	45	30
No	85	63	107	70
eGFR slope, n (%)	80	60	91	60
Mean (95% CI), mL/min/1.73 m ² /year	-4.9 (-7.0, -2.9)		-3.3 (-4.6, -2.1)	

Figure 1. Time to kidney failure C3G and IC-MPGN

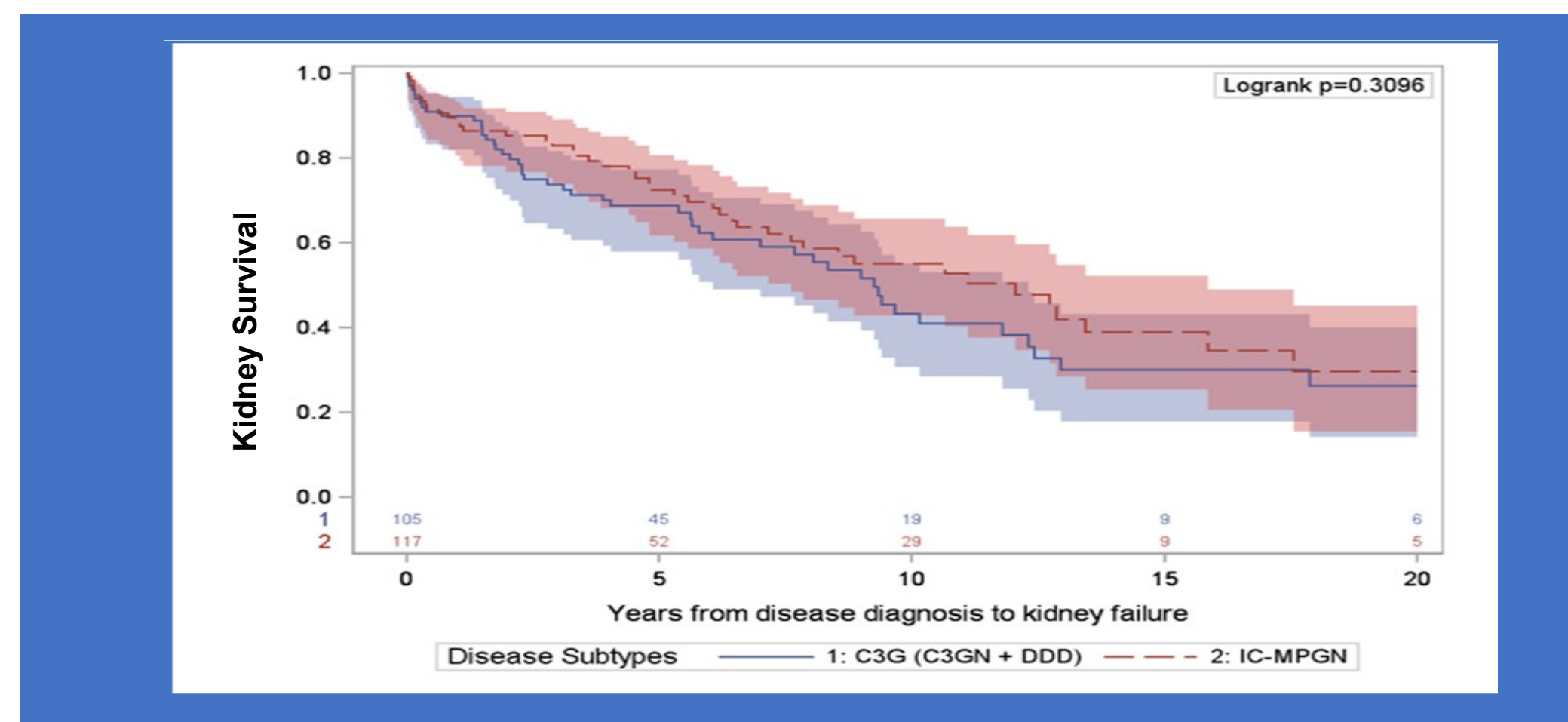


Figure 2. Forest plot GFR slope in 1st 2yrs & kidney failure

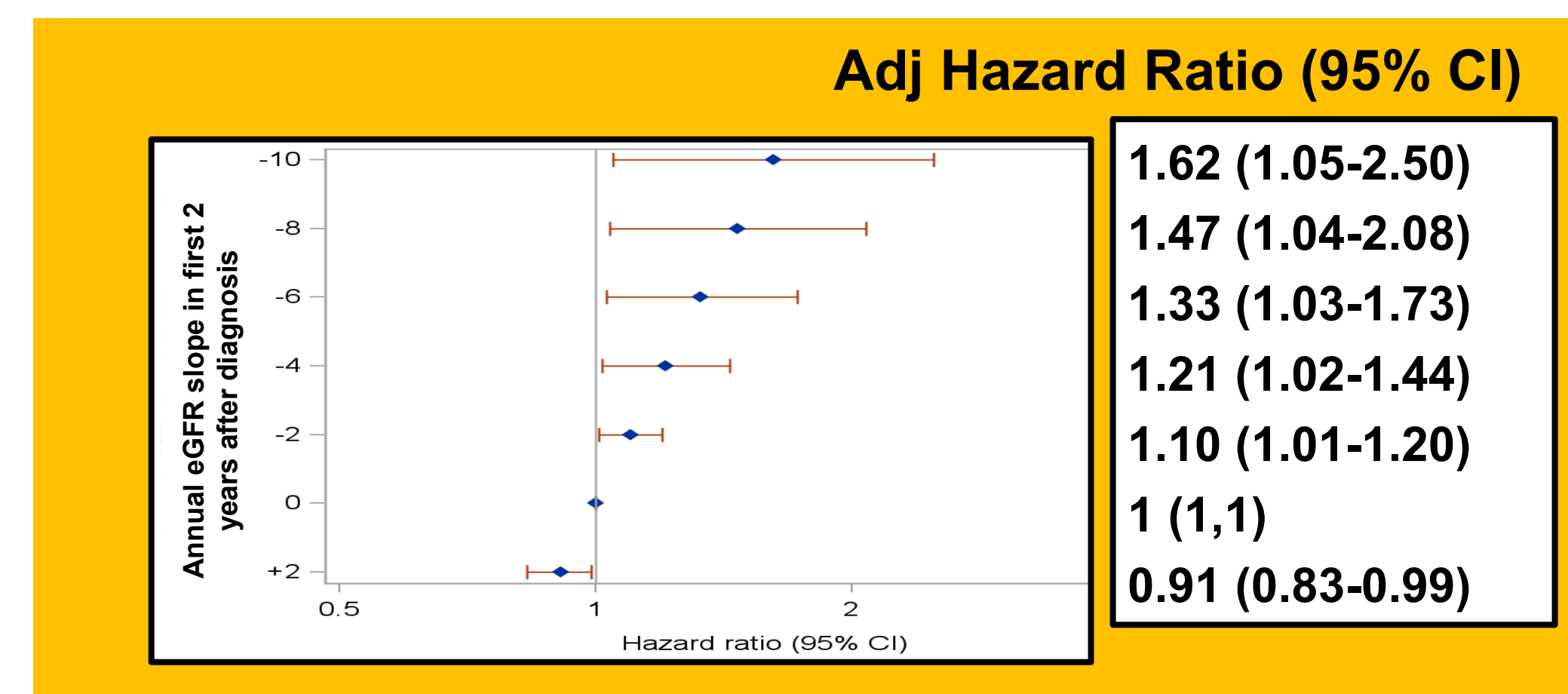


Figure 3. Forest plot changes in UPCR at 1 year & kidney failure (left). Time to kidney failure by UPCR at 1 year (right)

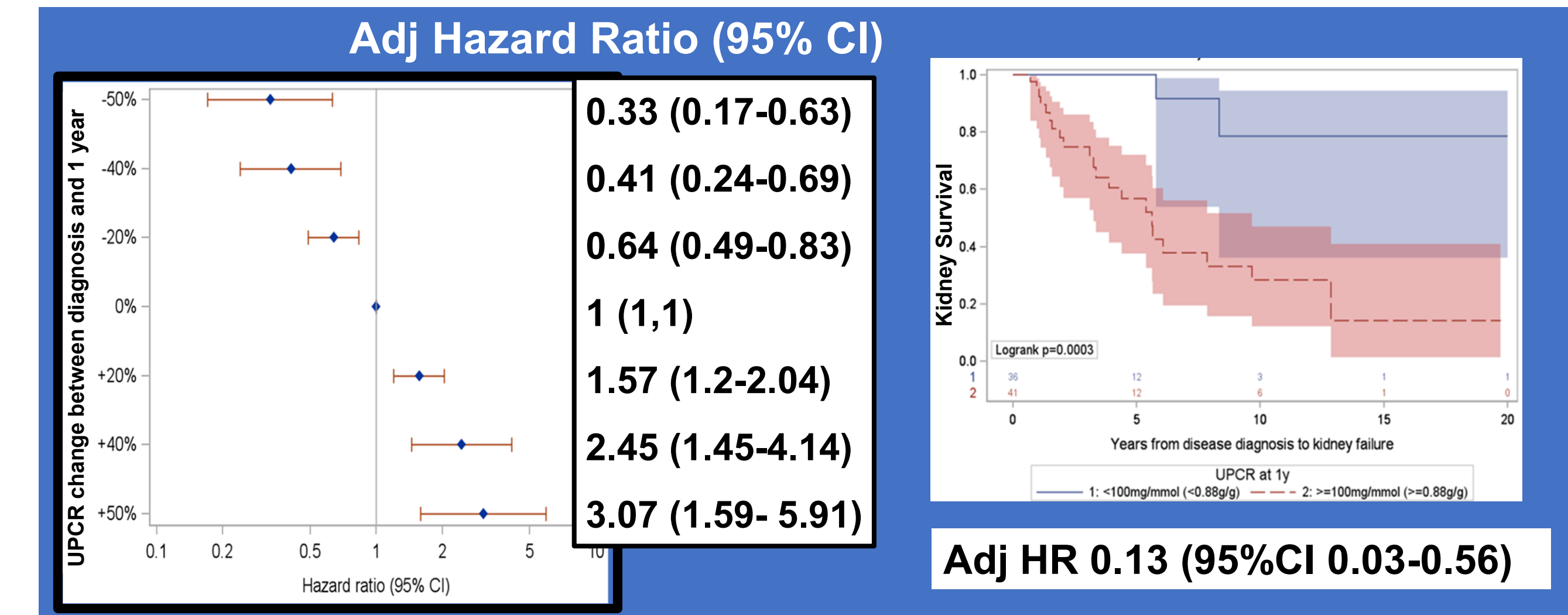


Table 2. Proteinuria changes in first year after diagnosis & risk of kidney failure

C3G & IC-MPGN		50% ↓UPCR			50mg/mmol ↓Time Averaged UPCR		
Timepoint from	Timepoint to	N	Adjusted HR	P value	N	Adjusted HR	P value
Diagnosis	6 months	49	1.09 (0.73 - 1.63)	0.67	42	0.94 (0.90 - 0.99)	0.01
Diagnosis	1 year	39	0.33 (0.17 - 0.63)	<0.001	43	0.66 (0.53 - 0.83)	<0.001
6 months	1 year	43	0.85 (0.76 - 0.94)	0.002	51	0.71 (0.59 - 0.85)	<0.001

DISCUSSION

- There was no significant difference in median time to kidney failure between C3G and IC-MPGN (p=0.31; median follow-up 6.2 years (IQR 2.1-11.3))
- eGFR slope early in disease was associated with progression to kidney failure
- Baseline proteinuria did not predict risk of kidney failure but changes at 1 year were a powerful predictor.
- UPCR <100mg/mol at 1 year (irrespective of cause) was associated with a substantially lower risk of kidney failure - Adj HR 0.13 (95% CI 0.03-0.56)
- Limitations- real world data and limited/ lack of medication data

CONCLUSION

Using a range of metrics this study demonstrates that proteinuria a short time after diagnosis is a powerful prognostic tool and provides further evidence of its potential as an accessible endpoint in C3G/ IC-MPGN.