

P3211: Should Multifocal Pulmonary Neuroendocrine Proliferation be Included as a Prognostic Factor for Lung Carcinoids?

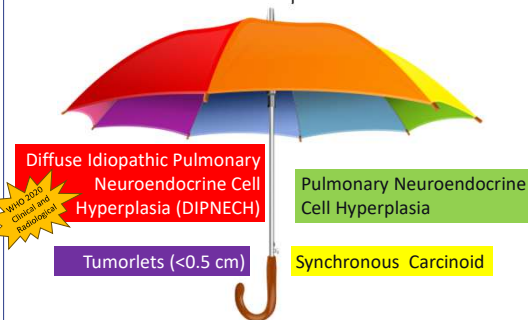
D. Bianchi^{1,2}, S. Ceccarelli³, I. Pacilio⁴, G. Vitaggio⁵, C. Bonelli¹, J. Vannucci³, S. Nicotra⁴, A. Stefani⁵, M. Paci¹, P.L. Filosso⁵, F. Puma³, N. Daddi⁴

¹Thoracic Surgery Unit, AUSL-IRCCS Reggio Emilia, IT | ²PhD Program in Cardio-Nephrothoracic Sciences, University of Bologna, IT | ³University of Perugia, IT | ⁴IRCCS S. Orsola-Malpighi University Hospital, Bologna, IT | ⁵University of Modena and Reggio Emilia, IT

Correspondence: daniel.bianchi@ausl.re.it

INTRODUCTION

Multifocal pulmonary neuroendocrine proliferation (**MNEP**) — defined as the coexistence of ≥ 2 bronchopulmonary neuroendocrine tumors or their precursors



- **underexplored clinical entity** whose prognostic significance remains poorly defined.
- We aimed to determine the **prevalence** of multifocal presentation in a large multicenter national cohort and to assess its **independent impact on survival outcomes** after surgical resection.

? **Key question:** Does multifocality independently worsen survival in resected pulmonary carcinoids?

METHODS

Design: Retrospective multicenter study with prospectively collected data
Population: 313 patients with R0 resection for bronchopulmonary carcinoid (TC or AC) — national thoracic surgery consortium
MNEP definition: ≥ 2 carcinoid lesions or one of their precursors
Endpoints: Overall survival (OS) and disease-free survival (DFS)
Statistics: Kaplan-Meier + log-rank test; multivariable Cox regression adjusting for histotype, pN stage, type of resection, age, sex, tumor diameter, and Charlson Comorbidity Index

DISCUSSION AND CONCLUSION

Actionable Take-Away Message

- MNEP occurs in **~30%** of surgically resected carcinoids — substantially higher than previously reported
- In our series multifocality does **not independently worsen** OS or DFS after complete resection
- AC histotype** and **pN stage** — not multifocality — are the dominant prognostic drivers
- TC-predominant MNEP follows an **indolent course** and requires extended follow-up

Clinical Implications

These findings support **parenchyma-sparing surgery** with thorough lymphadenectomy and systematic pathological assessment of surrounding parenchyma, even in sublobar resections, to optimize staging and preserve future surgical options.

Future Directions

Prospective multicenter studies are needed to validate these findings and establish a **dedicated staging system** for this emerging clinical entity.

REFERENCES & ACKNOWLEDGEMENTS

- Caplin ME, et al. Pulmonary neuroendocrine (carcinoid) tumours. *Lancet*. 2015;386:1999–2012.
- Filosso PL, et al. Outcome and prognostic factors in bronchial carcinoids. *J Thorac Oncol*. 2013;8:1282–8.
- Pelosi G, et al. Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia. *J Thorac Oncol*. 2015;10:1402–10.
- Rindi G, et al. TNM staging of neuroendocrine neoplasms. *J Natl Cancer Inst*. 2012;104:764–77.
- WHO Classification of Tumours Editorial Board. *Thoracic Tumours*. 5th ed. IARC; 2021.

Artificial Intelligence (AI) use disclaimer. AI tools (Claude, Anthropic) were used to support statistical visualization and figure preparation. All clinical content, analyses, and interpretations were independently verified by the authors, consistent with ACCME Standards for Integrity and Independence.

RESULTS

Of **313 patients, 92 (29.4%)** presented with MNEP. The cohort was predominantly female (70.3%) with TC histotype in 80.8% of cases. MNEP patients were significantly **older** ($p=0.023$), had a higher **comorbidity burden** ($p<0.001$), **smaller** primary tumor diameter ($p=0.042$), and were more frequently **female** (87.0% vs 63.3%, $p<0.001$). No significant differences were observed in pN stage, surgical approach, or histotype distribution between groups.

At a median follow-up of **126.7 months**: 13 deaths (14.1%) and 10 recurrences (10.9%) in the MNEP group versus 23 deaths (10.4%) and 20 recurrences (9.0%) in the unifocal group.

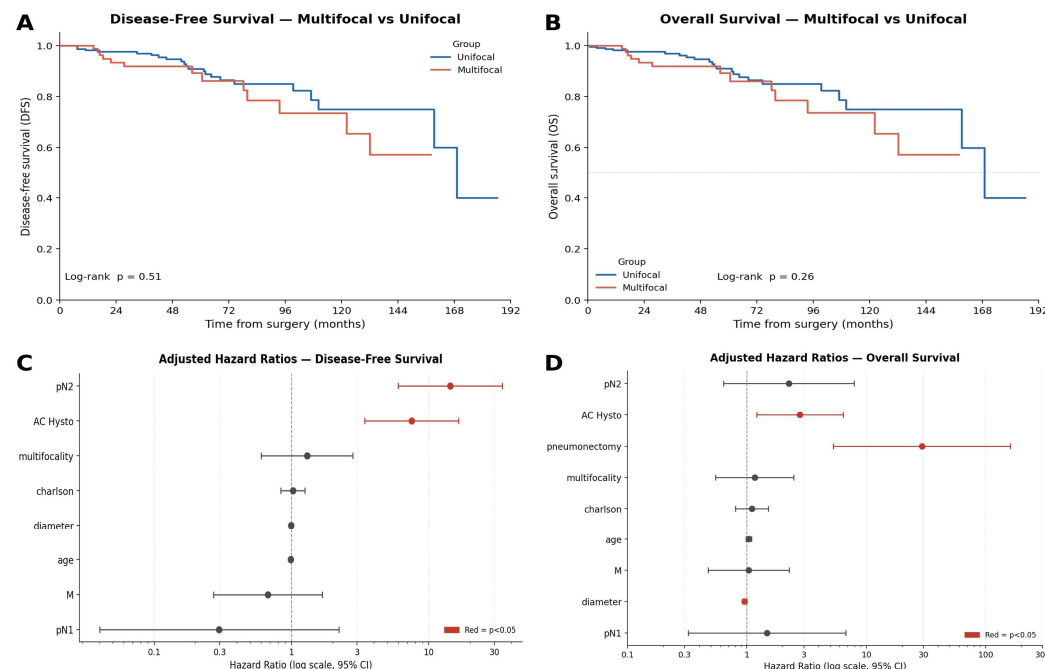
OS
log-rank $p = 0.261$ (NS)

DFS
log-rank $p = 0.511$ (NS)

On multivariable Cox regression, MNEP was **not** an independent predictor of OS (HR=1.16) or DFS (HR=1.30). Independent prognostic factors were:

DFS
AC histotype HR = 7.5 (95% CI 3.4–16.5)
pN2 HR = 14.3 (95% CI 6.0–34.2)

OS
Pneumonectomy HR = 29.2 (95% CI 5.3–161.1)



- Kaplan-Meier curves for Disease-Free Survival (DFS) in multifocal vs unifocal tumors (Log-rank $p = 0.51$).
- Kaplan-Meier curves for Overall Survival (OS) in multifocal vs unifocal tumors (Log-rank $p = 0.26$).
- Forest plot of adjusted Hazard Ratios for Disease-Free Survival. Red dots indicate $p < 0.05$.
- Forest plot of adjusted Hazard Ratios for Overall Survival. Red dots indicate $p < 0.05$.