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Sex-Based Differences in Clinicopathological Features and Surgical Outcomes of Clinical Stage I Solid NSCLC in Japan

Insights from a Single-Institution Study

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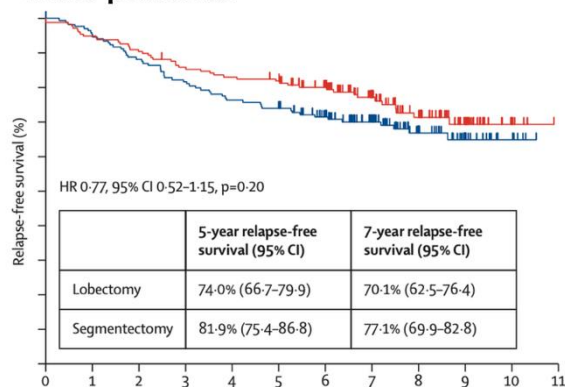
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Background & Purpose

- Segmentectomy is increasingly performed for NSCLC ≤ 2 cm, following the JCOG0802/WJOG4607L trial.
- A post-hoc analysis showed segmentectomy was associated with significantly higher recurrence than lobectomy in female patients with radiologically solid (CTR=1) NSCLC.

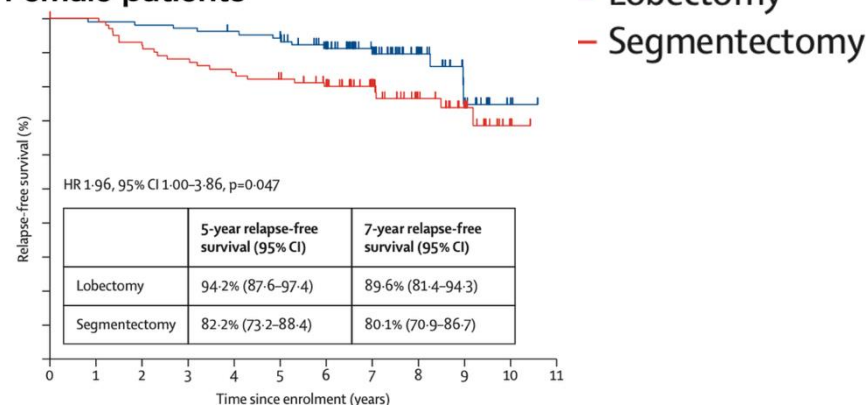
Pure solid tumor (CTR=1) size ≤ 2 cm

Male patients



170	161	149	138	129	124	106	82	45	20	8	0
(0)	(1)	(0)	(0)	(0)	(1)	(14)	(22)	(34)	(24)	(12)	(8)
177	168	160	151	146	143	121	85	54	27	6	0
(0)	(0)	(0)	(1)	(0)	(1)	(19)	(32)	(26)	(26)	(21)	(6)

Female patients



104	103	102	101	99	97	81	59	30	13	3	0
(0)	(0)	(0)	(0)	(1)	(0)	(13)	(21)	(29)	(14)	(10)	(3)
102	101	93	89	85	82	75	51	31	20	4	0
(0)	(1)	(0)	(0)	(0)	(1)	(5)	(24)	(18)	(10)	(15)	(4)

(Hattori et al., Lancet Respir Med 2024)

Purpose: To clarify sex-based differences in clinicopathological features and surgical outcomes of clinical stage I solid NSCLC in a Japanese cohort.

Methods & Patient Selection

- **Design:** Retrospective, single-institution study
— Kobe University Hospital (2017–2023)
- **Inclusion:** Clinical stage I NSCLC (UICC 8th edition), complete surgical resection
- **Exclusion:** Multiple lung cancers, malignancy within 5 years, preoperative therapy
- Tumors classified as solid (CTR=1) or non-solid ($0 \leq \text{CTR} < 1$); recurrence-free survival (RFS) compared between lobectomy and sublobar resection, by sex

	Male	Female
Solid (CTR=1)	251	168
Non-solid ($0 \leq \text{CTR} < 1$)	94	141
Total	345	309

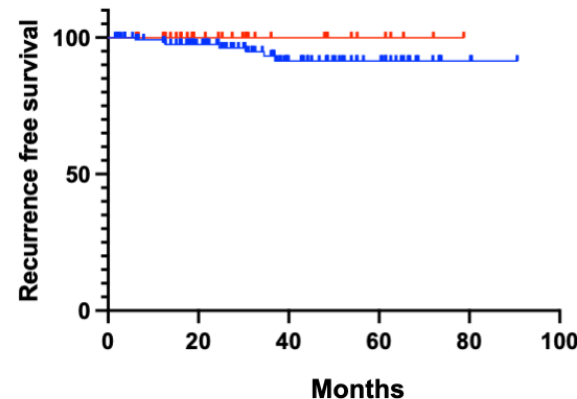
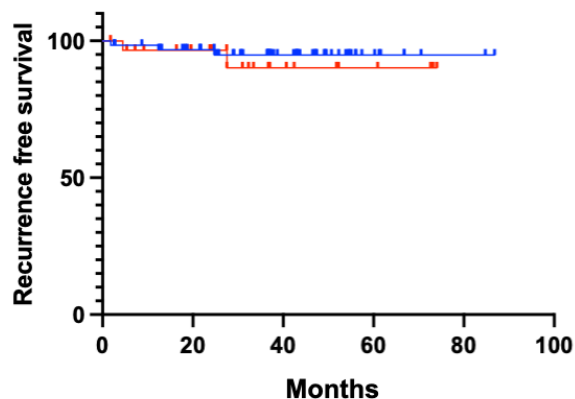
N = 654 patients retrospectively reviewed

Results: Recurrence-Free Survival by Sex

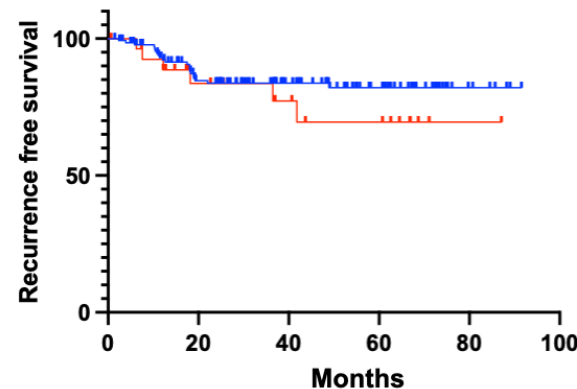
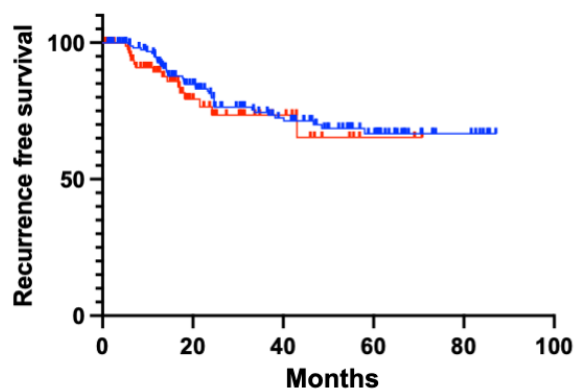
Male patients

Female patients

$0 \leq \text{CTR} < 1$



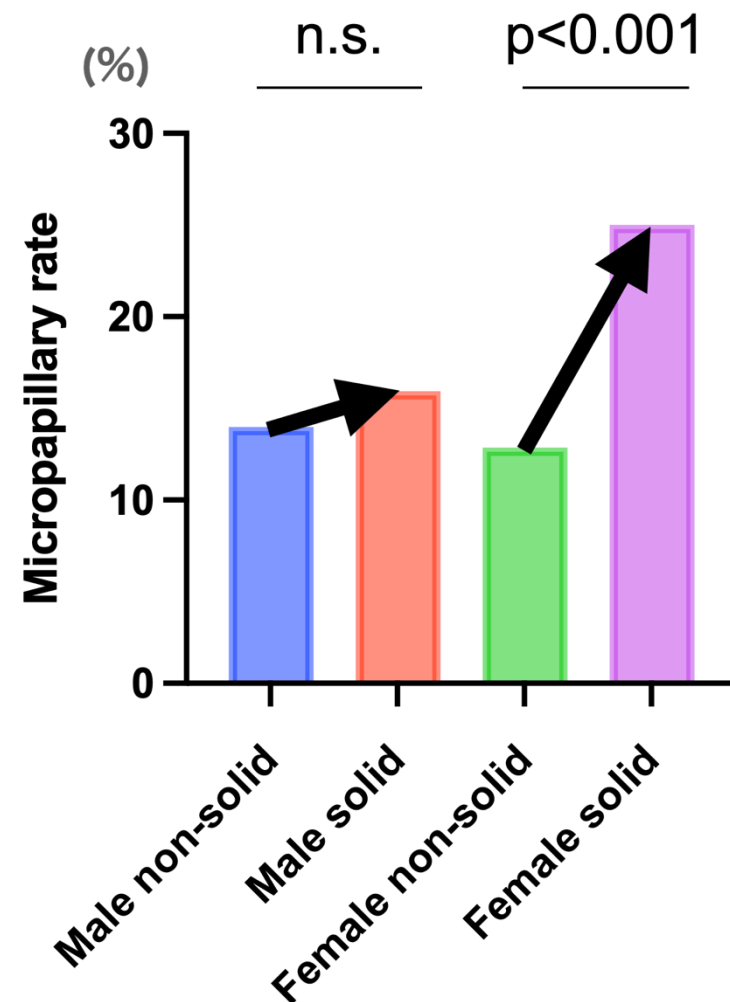
CTR=1



In CTR = 1, Female patients, 5-year RFS: 82.1% (lobectomy) vs 72.7% (sublobar) $P=0.394$
Lobectomy tended to be associated with better RFS compared to sublobar resection

Results: Micropapillary Component

- A solid radiological appearance (CTR=1) is associated with a higher rate of micropapillary component in female patients, but not in male patients — suggesting a sex-specific relationship between tumor consolidation and micropapillary histology.



25.0% of solid tumors in female patients had a micropapillary component

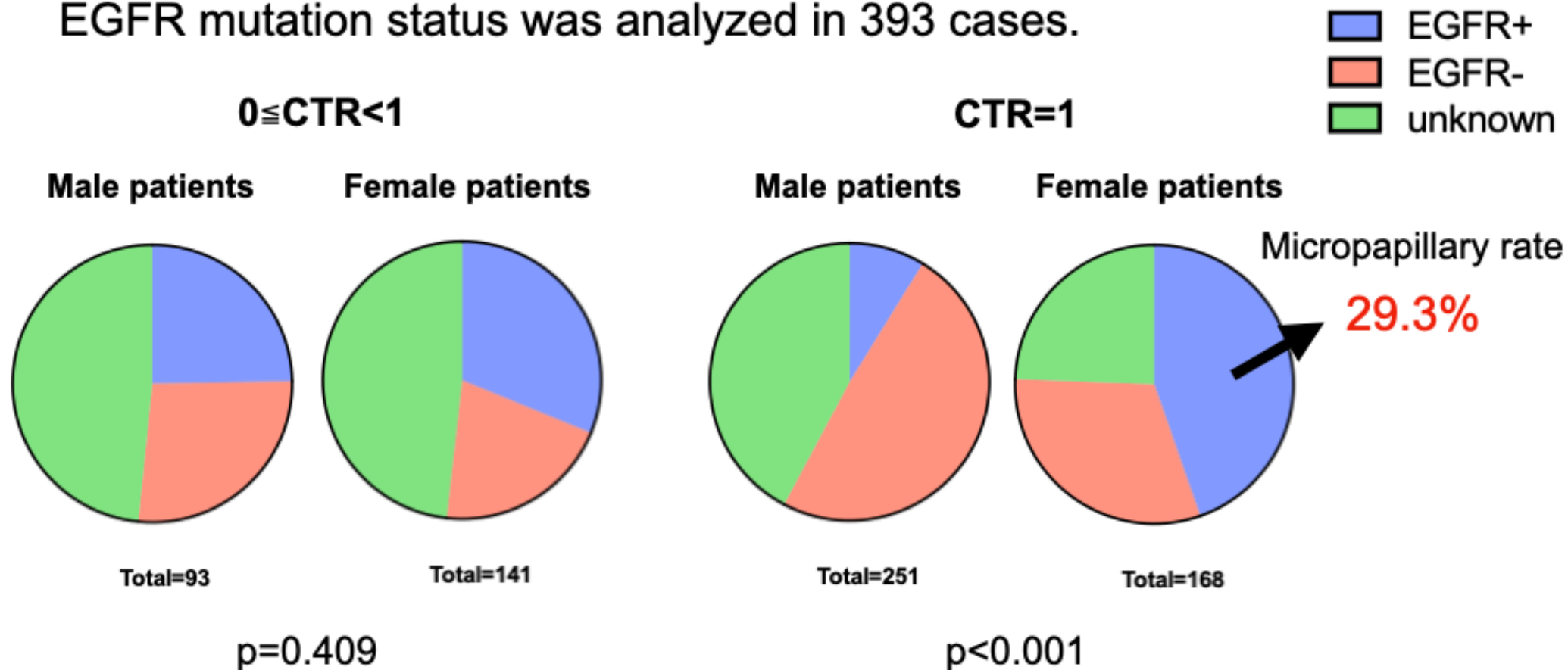
Results: Univariable and Multivariable analysis for Micropapillary Component in CTR =1 patients

	Univariable analysis			Multivariable analysis		
Variables	Odds Ratio	95% CI	P-value	Odds Ratio	95% CI	P-value
Gender (Female)	1.76	1.08-2.86	0.023	1.10	0.55-2.19	0.798
Radiological solid tumor size	1.03	0.99-1.03	0.099	–	–	–
PET SUV max	0.97	0.92-1.03	0.302	–	–	–
Preoperative CEA level	1.01	0.98-1.05	0.535	–	–	–
Smoking history (Ever)	0.59	0.36-0.97	0.037	0.95	0.48-1.90	0.895
%FEV1.0	1.01	1.00-1.03	0.045	1.01	0.99-1.02	0.318
EGFR mutation status (positive)	2.68	1.59-4.50	<0.001	2.33	1.29-4.21	0.005

EGFR mutation status is independently associated with the presence of micropapillary component in CTR = 1 patients

Results: EGFR mutation status and micropapillary component

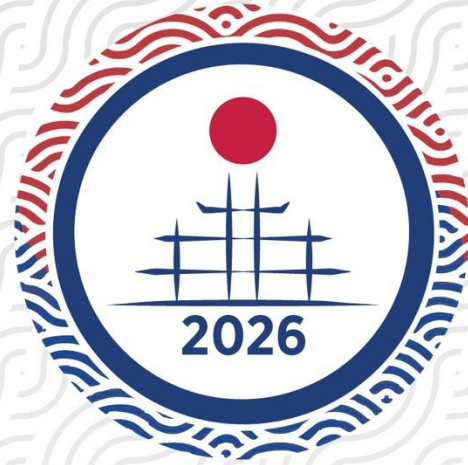
EGFR mutation status was analyzed in 393 cases.



29.3% of EGFR-mutant solid tumors in female patients had a micropapillary component

Conclusion

- Female patients with clinical stage I solid NSCLC show distinct tumor biology — higher rates of EGFR mutation and micropapillary component — compared with male patients.
- These biological differences may explain the poorer segmentectomy outcomes observed in female solid-tumor patients in JCOG0802/WJOG4607L.



Thank You.