Lobar versus Sublobar Resection in the Elderly for Early Lung Cancer: A Meta-Analysis

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Background

- In 1995, Ginsberg and Rubinstein demonstrated a threefold increase in local recurrence rates and a 75% increased risk of overall recurrence in sub lobar resection compared with lobectomy for patients undergoing resection in stage 1A NSCLC.

- Difficult situation in elderly with high risk factors.

- Hence surgeons moved away from lobectomy in such patients to offer alternative treatment options for early stage lung cancer.

- Cancer and Leukemia Group B (CALGB 140503) and the Japan Clinical Oncology Group (JCOG 0802): Prospective, randomized, multi-institutional phase III trials

Aim

- Compare lobectomy and sublobar resection in elderly patients with stage 1 NSCLC.

- Primary outcomes :
✓ Overall survival
✓ Recurrence

- Secondary outcomes :
✓ Perioperative mortality,
✓ Disease- free survival (DFS), and,
✓ Cancer-specific survival (CSS).

- Literature: EMBASE, The Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library, PubMed, Scopus and Web of Science from inception to 17 May 2020

Inclusion Criteria

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Elderly patients (defined as age 65) with clinical stage 1 NSCLC who underwent lobectomy or sublobar resection and reported postoperative outcomes such as :

- ✓ Operative mortality (OM),
- ✓ Overall Survival (OS),
- ✓ Cancer Specific Survival(CSS),
- ✓ Disease Free Survival (DFS), and,
- ✓ Recurrence of cancer (inclusive of local and overall).

Exclusion Criteria

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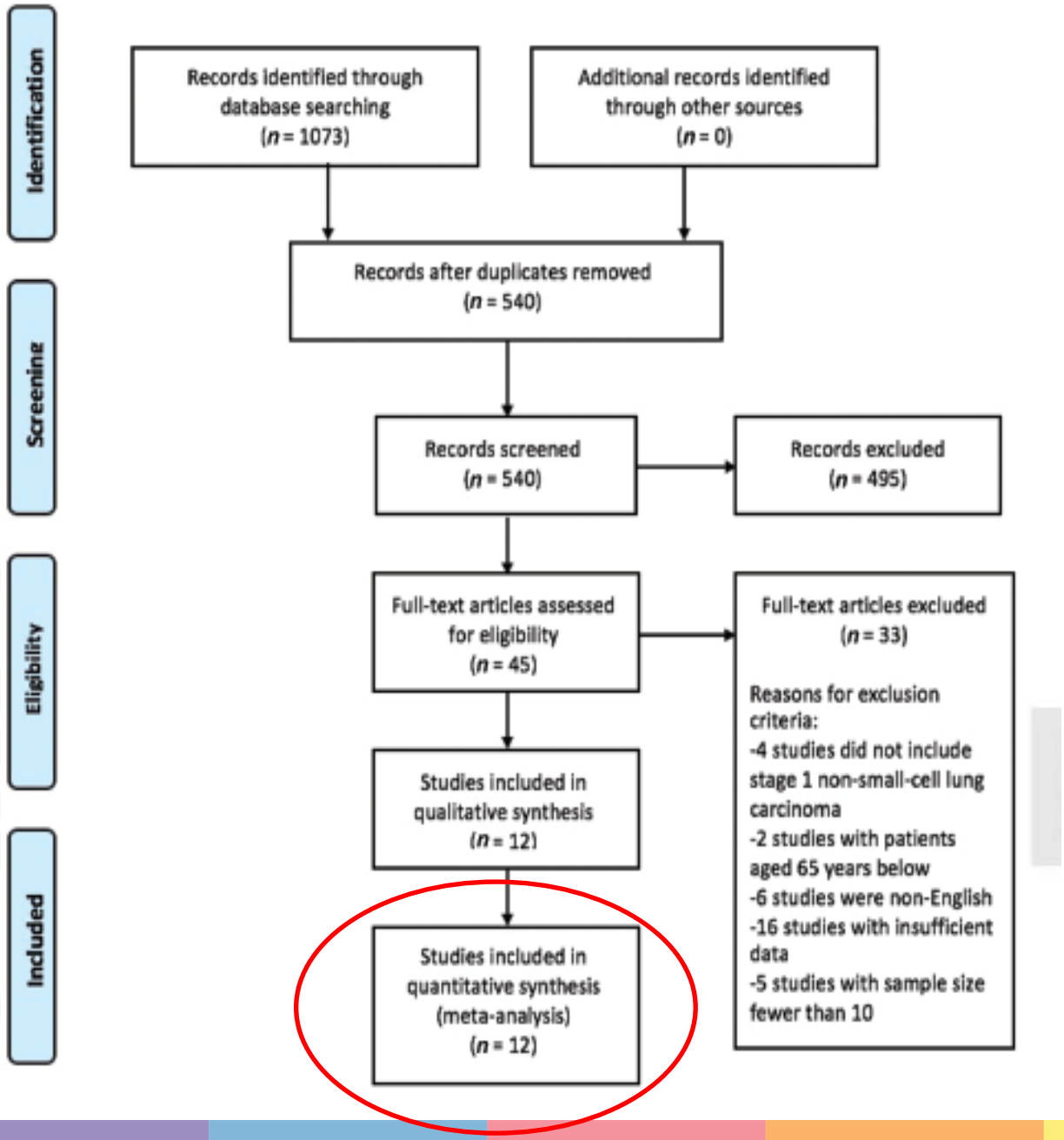
- Non-English papers.
- Studies that did not segregate the outcomes based on lobectomy and sublobar resection.
- Studies that lacked critical and necessary data, case reports, abstracts from conference papers, commentaries.
- Studies with sample size fewer than 10.


Identification
Screening
Eligibility
Included
Records identified through database searching (n = 1073)
Additional records identified through other sources (n = 0)
Records after duplicates removed (n = 540)
Records screened (n = 540)
Records excluded (n = 495)
Full-text articles assessed for eligibility (n = 45)
Full-text articles excluded (n = 33)
Reasons for exclusion criteria:
-4 studies did not include stage 1 non-small-cell lung carcinoma
-2 studies with patients aged 65 years below
-6 studies were non-English
-16 studies with insufficient data
-5 studies with sample size fewer than 10
Studies included in qualitative synthesis (n = 12)
Studies included in quantitative synthesis (meta-analysis) (n = 12)

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Results

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			Heterogeneity		
5-Year OS	10 Trials, 2,615 Patients	HR - 0.80 [0.66,0.96]	Acceptable	**p- 0.03**	**Lobectomy:20% lower risk of death**
Overall Recurrence	6 Trials, 892 Patients	OR-0.80 [0.51,1.27]	Acceptable	p-0.35	**higher in sublobar resection**
Local Recurrence	5 Trials, 848 Patients	OR-0.32 [0.15, 0.68]	Acceptable	**p-0.003**	**higher in sublobar resection**
30-Day OM	6 Trials, 2,491 Patients	OR-2.84 [0.82, 9.85]	Statistical	p-0.10	**higher in patients undergoing lobectomy**
5-Year CSS	4 Trials, 2,974 Patients	HR-0.84 [0.68, 1.03],	Statistical	p-0.10	**Lobectomy: 16% lower risk of death (in context of CSS)**
5-Year DFS	4 Trials, 715 Patients	HR-0.80 [0.63, 1.03]	Acceptable	p- 0.08	**Lobectomy: 20% lower risk of death**

Subgroup Analysis

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			Heterogeneity		
5-Year OS in Stage 1ATumors	3 Trials, 182 Patients	HR-1.19 [0.74, 1.92	Acceptable	p-0.48	No statistically significant difference in 5 year OS
5-Year OS in Stage 1B Tumors	2 Trials, 38 Patients	HR-0.34 [0.13, 0.88	Acceptable	p-0.03	Lobectomy: 66% lower risk of death

Risk of Bias

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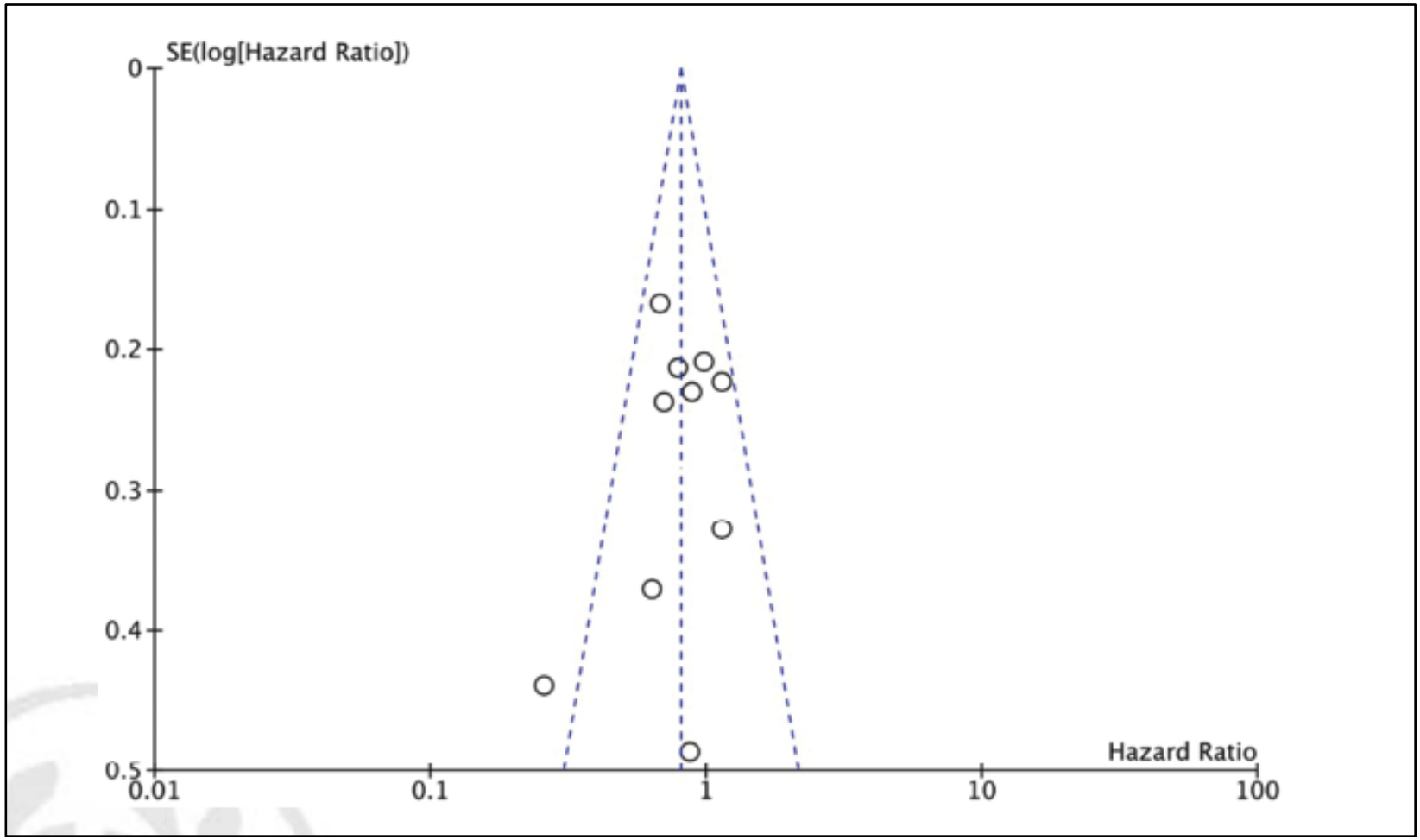
Funnel plot: no publication bias in this meta-analysis



Points

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- Subgroup analysis :

✓ Stage 1A : No significant difference in 5-year OS
✓ Stage 1B: Significant improvement favoring lobectomy.

- Suggestion: For patients with stage 1A cancers, Sublobar resection : Viable alternative in high risk patients.

- ✓ Sublobar Resection for larger tumor sizes ⟹ decreased resection margins ⟹ higher risk of recurrence.
- ✓ Lack of discrimination between segmentectomy and wedge resection.
- ✓ Spread through air spaces ⟹ Impact frequency of recurrence after limited resection for stage 1 lung adenocarcinomas.
- ✓ Suggest: In elderly but otherwise fit patients with Stage IB onwards – Lobectomy still preferable

- Limited resection : less postoperative morbidity and mortality compared with a lobectomy.
- Hence Sublobar Resection: better 30-day OM
- Suggests: Sublobar Resection may be justified in elderly patients with increased comorbidities and poor lung reserves.

Limitations

1. All but one of our included studies were retrospective in nature, with no RCTs available

2. Definition of “elderly” varied from paper to paper

3. No differentiation between wedge resection and segmentectomy as they were not always separately defined in the studies

Conclusion

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- Survival and Local Recurrence in Stage 1 NSCLC: Lobar resection Superior to Sub lobar resection.
- If Clinically feasible : Elderly patients should be offered lobectomy.
- Subgroup analysis : Stage 1A tumors: sub lobar resection is noninferior for OS. Provides a viable alternative that can mitigate surgical risks in unfit patients with Stage IA.
- Further RCTs are required to justify sublobar resection for elderly patients

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Thank You

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