Specific site of metastasis in stage IV triple-negative breast cancer: a national registry analysis of survival outcomes and treatment patterns

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INTRODUCTION

- Metastatic sites in triple-negative breast cancer (TNBC) differ widely in prognosis, yet existing studies have grouped sites broadly or examined only single organs.
- TNBC with brain, lung, or liver involvement reflects aggressive biology and limited therapeutic options.
  - Brain metastases indicate rapid progression and limited CNS penetration of systemic agents.
  - Liver involvement often signals high-volume visceral spread and poor outcomes.
  - Lung involvement shows a wider range of behavior and may carry better prognosis when isolated.
- Lack of detailed, site-specific survival estimates limits accurate prognostic discussions for patients.
- Traditional categories such as “single” or “multiple” metastases mask heterogeneity in overall survival (OS).

This study examined site-specific metastatic groups in de-novo stage IV TNBC using national data to define survival and treatment differences.

METHODS AND MATERIALS

- **Data Source:** National Cancer Database, 2010–2020.
- **Population:** Women ≥40 at diagnosis with de-novo stage IV TNBC.
- **Metastatic Groups:** Brain only, Lung only, Liver only, Brain + Lung, Brain + Liver, Lung + Liver, Brain + Lung + Liver.
- **Treatments Assessed:** Chemotherapy, radiation, and surgery to the primary breast tumor.

Analyses:

- Kaplan-Meier for median OS, six-month OS, and one-year OS.
- Multivariate Cox regression modeled two-year OS adjusted for age, comorbidity, race/ethnicity, facility type, and diagnosis year.

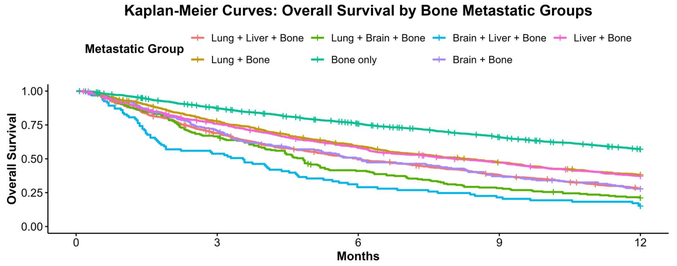


Table 1. Overall Survival and Treatment Patterns by Metastatic Group

Metastatic Group	n	Median OS (months) ↑	6-month OS (%)	1-year OS (%)	Chemotherapy (%)	Radiation (%)	Surgery (%)
Brain + Liver	142	**3.6**	30.3	17.3	57.0	60.6	6.3
Brain + Lung + Liver	276	**3.8**	34.9	13.1	62.0	68.8	6.5
Brain + Lung	501	**6.0**	50.0	29.2	64.5	69.9	9.0
Brain only	544	**6.7**	52.5	30.8	61.8	64.5	16.2
Lung + Liver	1,127	**7.3**	54.3	34.0	67.4	19.3	14.8
Liver only	1,800	**11.2**	66.6	47.6	75.7	18.9	21.7
Lung only	3,058	**12.7**	71.7	51.8	73.9	21.3	27.1

RESULTS

Cohort Summary

- 119,373 stage IV breast cancer cases identified.
- Of these, 13,345 (11.2%) were TNBC.
- After exclusions, 7,448 women comprised the final cohort.

Overall Survival (OS)

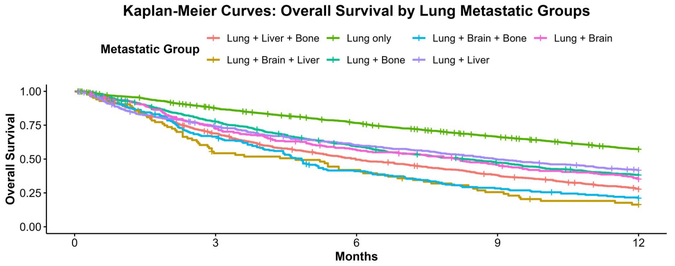
- Median OS: 3.6 months (Brain + Liver) to 12.7 months (Lung only).
- One-year OS: 13.1% (Brain + Lung + Liver) to 51.8% (Lung only).

Adjusted Two-Year OS (Cox Regression, Hazard of Mortality) vs. Brain Only

- Lung only: aHR 0.55 (95% CI 0.49–0.61, p<0.001)
- Liver only: aHR 0.69 (95% CI 0.62–0.77, p<0.001).
- Brain + Liver: aHR 1.67 (95% CI 1.37–2.03, p<0.001).
- Brain + Lung + Liver: aHR 1.72 (95% CI 1.47–2.01, p<0.001).

Treatment Patterns

- Chemotherapy: 57.0% (Brain + Liver) to 75.7% (Liver only).
- Radiation: Highest with brain involvement, 60.6% to 69.9%.
- Breast Surgery: 6.3% (Brain + Liver) to 27.1% (Lung only).



DISCUSSION

- Survival varied sharply by metastatic pattern, with lung-only disease showing the longest survival and brain or liver involvement showing the shortest.
- Combined organ involvement showed the poorest outcomes and likely indicated high-volume disease.
- Lung-only metastasis may reflect lower-burden visceral spread compared to liver or CNS sites.
- Advanced visceral spread, especially to the brain or liver, impairs critical organ function and drives rapid physiologic decline.
- Mortality in metastatic TNBC is largely driven by progressive organ failure from uncontrolled metastatic burden rather than local breast disease complications.
- Treatment selection differences across metastatic sites may influence survival independently of tumor biology.
- **Limitations**: Retrospective design, no recurrence data, and lack of molecular profiling.
- **Strengths:** Large national sample, modern diagnostic period, and detailed site-specific stratification.

CONCLUSIONS

- Metastatic site at diagnosis was a major determinant of OS and treatment patterns in de-novo stage IV TNBC.
- Lung-only metastasis showed the most favorable outcomes, while brain or liver involvement predicted worse OS, especially when combined.
- Findings support more accurate prognostic counseling and better-informed treatment discussions for patients with newly diagnosed metastatic TNBC.

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