Association of Lynch Syndrome with Breast Cancer: An Exploratory Analysis Using Claims Data

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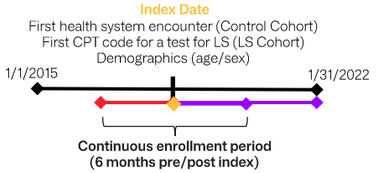
Study Summary

Study Question: Do patients with Lynch Syndrome have higher rates of breast cancer than those who do not have Lynch Syndrome in retrospective claims data?

Study Design:



Study Results: Lynch Syndrome is strongly associated with diagnosis of breast cancer

	Odds ratio (95%CI)	p-value
Any breast cancer	9.72 (8.00, 11.81)	<0.0001
In situ breast cancer	10.35 (7.61, 14.07)	<0.0001
Malignant breast cancer	10.04 (8.23, 12.24)	<0.0001

CI: Confidence interval

Conclusion: Results show a significantly strong association of Lynch Syndrome with skin cancers. Retrospective claims data is useful for conducting exploratory epidemiology studies in diseases that are not well understood.

Background

- Lynch syndrome (LS) is among the most common hereditary cancer syndromes, occurring in about 1 in 279 people. However, it is highly underdiagnosed; only 5%–10% of individuals with LS are aware that they have the disease.[1]
- LS is associated with increased risk of a variety of cancers, including colorectal, endometrial, ovarian, stomach, urinary tract, and pancreatic, among others. In individuals with LS who develop cancer, the cancer typically occurs in their forties or fifties.[2]
- LS is caused by mutations in DNA mismatch repair genes in the EPCAM cell adhesion molecule gene. Inherited mutations in these genes affect DNA mismatch repair, a process that fixes errors when DNA is copied.[3]
- Diagnosis of LS requires genetic testing; however, there is no specific ICD code designating LS diagnosis.[4]

Objective

- There has been considerable debate as to the role of LS in breast cancer. While some studies suggest that breast cancer should be included as a LS-linked cancer, definitive evidence is lacking. The objective of this study was to use administrative claims data to determine the statistical strength of association of LS with breast cancer.

Methods

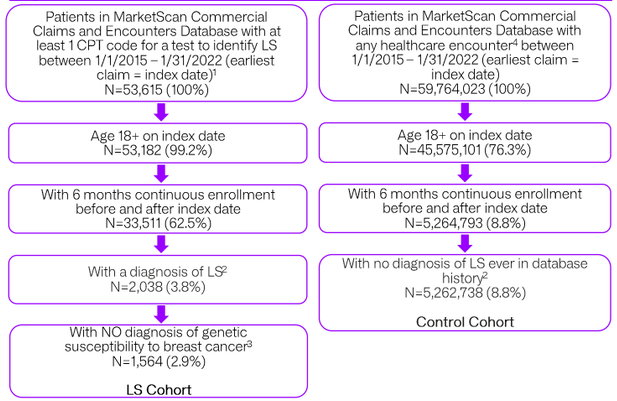
Study Design and Data Source

- This study employed a retrospective observational cohort design (2015-2022) using U.S. insurance claims data within the Merative™ MarketScan® Commercial Claims and Encounters Database.
- The MarketScan data was accessed using Treatment Pathways 4.0, an online analytic platform.

Outcomes

- Prevalence of breast cancer (ICD-9/ICD-10 diagnoses) was compared between patients with tests (CPT codes) and diagnoses (ICD-9/ICD-10) indicating probable LS ("LS Cohort") and patients without LS ("Control Cohort").
- Patients with diagnoses indicating genetic susceptibility to breast cancer specifically (e.g., ICD-9/ICD-10 V84.01/ Z15.01 for BRCA1, BRCA2 mutations) were excluded.
- Adjustment was made to cancer prevalence rates in the Control Cohort to approximate the sex/age distribution of the LS Cohort; this was accomplished for male/female categorization in five age brackets (18-39, 40-49, 50-59, 60-69, and 70+ years).
- Strength of association between LS and breast cancer was evaluated using odds ratios (OR) with 95% confidence intervals (95%CI).
- Patient demographics were measured on the index date.

Figure 1. Patient Selection



[1]CPT codes include: 81288, 81292, 81293, 81294, 81295, 1296, 81297, 81298, 81299, 81300, 81301, 81317, 81318, 81319, 81435, 81436, 0101U, 0130U, 0158U, 0161U, 0162U, 0238U
[2]LS diagnosis codes include: ICD-9-CM V84.09, Genetic susceptibility to other malignant neoplasm; ICD-10-CM Z15.09, Genetic susceptibility to other malignant neoplasm
[3]Diagnosis codes for genetic susceptibility to malignant neoplasm of the breast include : ICD-9-CM V84.01; ICD-10-CM Z15.01
[4]Healthcare encounters include inpatient or outpatient medical encounters or pharmacy claims

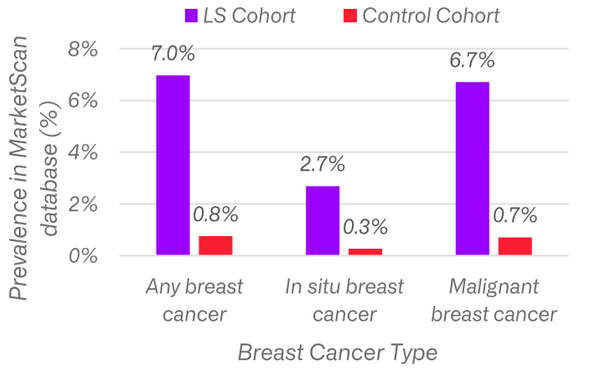
Results

- We identified 2,038 patients tested and likely diagnosed with LS in the LS Cohort and 5,262,738 patients without LS in the Control Cohort. (Figure 1)
- After adjustment for age and sex, large differences in breast cancer prevalence were found between cohorts, corresponding with significantly ($p<0.0001$) strong association between LS and all breast cancer types examined.

Results, continued

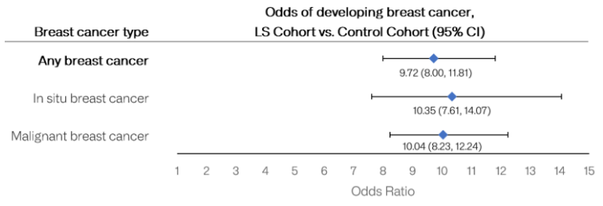
- Prevalence of "any breast cancer" in the LS Cohort was 6.97% versus 0.76% in the Control Cohort (OR = 9.72, 95%CI [8.00, 11.81]) (Figures 2 & 3).
- Statistically significant results for association were also found the malignant and in situ breast cancer subtypes (Figures 2 & 3).

Figure 2. Age- and sex-adjusted prevalence of various types of breast cancers



In situ breast cancer codes include ICD-9-CM: 233.0; ICD-10-CM: D05.x
Malignant breast cancer diagnosis codes include ICD-9-CM: 174.x; ICD-10-CM: C50.x
"Any breast cancer" includes patients with any of the above diagnoses (it is possible for patients to have >1 breast cancer type)

Figure 2. Age- and sex-adjusted odds ratios for development of various types of breast cancers



CI: Confidence interval; LS: Lynch Syndrome

Limitations

This analysis has conventional limitations of claims-based analyses:

- No specific diagnosis codes exist for LS; the estimates of probable LS diagnosis herein are based on combinations of CPT codes and ICD-9/ICD-10 diagnosis codes commonly assigned to LS in real-world practice.
- The analysis presented here does not include results of genetic testing (only that the test was administered), nor does it distinguish which of the five DNA mismatch repair genes is affected; our analyses consider them in pooled fashion.
- Exact 1:1 matched cohort comparisons were not feasible with the data analysis tool used in this study; instead, LS patients were compared to the broad population of all patients without LS using weighted averages based on age and sex. No multivariable analysis was employed; thus no adjustments were made for other potential factors influencing the results.
- LS is 90%–95% underdiagnosed. Therefore, the Control Cohort may have included patients who have LS. However, this is estimated to be only 0.3% of the sample (~17,000 patients).
- Only patients covered by commercial insurance or Medicare supplemental insurance were included in data, and results may not represent all U.S. patients (i.e., uninsured, Medicaid).

Conclusions

- This study demonstrates the value and power of retrospective claims data for conducting exploratory epidemiology studies in diseases that are not well understood.
- The number of cancer types associated with LS is growing, prompting clinicians to redefine LS, at risk populations, screening needs, and diagnostic criteria.
- An association of LS with breast cancer has been long suspected, but there have been insufficient data to make a definitive connection. This study may help answer questions on this issue, as results indicate that there a significantly strong association of LS with breast cancer.
- These findings suggest that women diagnosed with LS may benefit from increased and more targeted breast cancer screening.

References

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Disclosure

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