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

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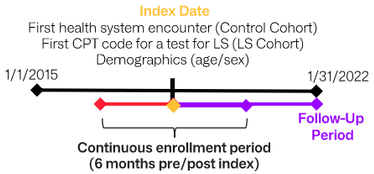
Study Summary

Study Question: Do patients with Lynch Syndrome have higher rates of skin 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 skin cancer

	Odds ratio (95%CI)	p-value
Any Skin Cancer	5.81 (5.01, 6.74)	<0.0001
Malignant melanoma	8.52 (5.97, 12.16)	<0.0001
Basal cell carcinoma	4.09 (3.36, 4.99)	<0.0001
Squamous cell carcinoma	7.42 (5.76, 9.56)	<0.0001
Sebaceous cell carcinoma	N/A	N/A
Merkel cell carcinoma	N/A	N/A
Other/unspecified malignant neoplasm of skin	5.47 (4.67, 6,41)	<0.0001

CI: Confidence interval; N/A, not analyzed due to insufficient sample size

Conclusion: Results show a significantly strong association of LS 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 40s or 50s.[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.

Objective

- Although the rare Muir-Torre variant of LS is associated with higher risk of certain skin tumors, no definitive studies have been conducted to determine whether LS generally confers increased risk of skin cancer. The objective of this study was to determine the statistical strength of association of LS with various skin cancers.

Methods

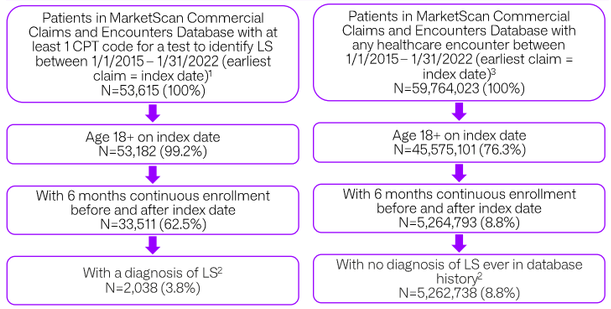
Study Design and Data Source

- 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 skin cancer (ICD-9/ICD-10 diagnoses) occurring any time after index 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").
- 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 skin 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]Healthcare encounters include inpatient or outpatient medical encounters or pharmacy claims

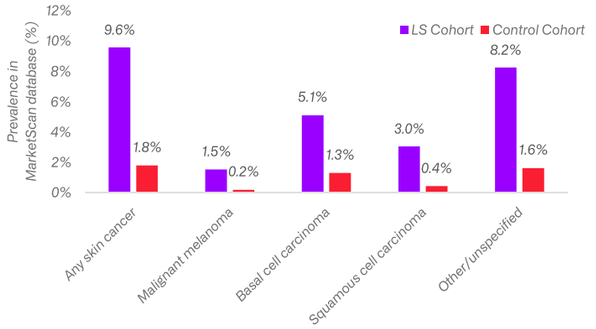
Results

- 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 skin cancer prevalence were found between cohorts, corresponding with significantly (p<0.0001) strong association between LS and all skin cancer types.

Results, continued

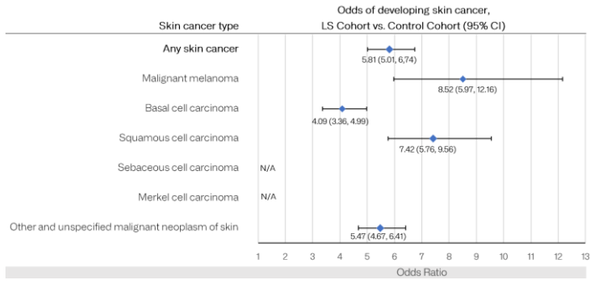
- Prevalence of "any skin cancer" was 9.57% (LS Cohort) vs. 1.79% (Control Cohort; OR = 5.81, 95%CI [5.01, 6.74]). (Figures 2 & 3)
- The strongest association was for malignant melanoma: 1.52% (LS Cohort) vs. 0.18% (Control Cohort; OR = 8.52, 95%CI [5.97, 12.16]). (Figures 2 & 3)
- Statistically significant results for association were also found for squamous and basal cell carcinomas and other/unspecified skin cancers.

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



Malignant Melanoma diagnosis codes include ICD-9-CM: 172.x; ICD-10-CM: C43.x
Basal cell carcinoma diagnosis codes include ICD-9-CM: 173.x1; ICD-10-CM: C44.x1x
Squamous cell carcinoma diagnosis codes include ICD-9-CM: 173.x2; ICD-10-CM: C44.x2x
Other/unspecified diagnosis codes include those with codes specified as "other and unspecified malignant neoplasm of skin", "Other specified malignant neoplasm of skin", "Merkel cell carcinoma", and "sebaceous cell carcinoma"
"Any skin cancer" includes patients with any of the above diagnoses (it is possible for patients to have >1 skin cancer type)

Figure 3: Age- and sex-adjusted odds ratios for development of various types of skin cancers



CI: Confidence interval; N/A, not analyzed due to insufficient sample size

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.
- Evidence linking LS with most cutaneous malignancies is lacking, although a topic of current research interest. Our results show a significantly strong association of LS with skin cancers.
- With LS being a CDC "Tier 1" genomic condition, consideration should be given to add skin cancer screening to the roster of other cancer screenings for LS patients.

References

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Disclosure

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