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## Introduction

- The stratum corneum (SC) is the outermost skin layer and consists of corneocytes embedded in a lipid matrix, primarily containing ceramides, free fatty acids and cholesterol.<sup>1</sup>
- Ceramides are structurally highly diverse lipids classified based on their sphingoid base and fatty acid chain.<sup>2</sup>
- Alterations in the SC ceramide profile have been observed in various skin diseases.<sup>3,4</sup>
- Changes in the SC ceramide composition may also be present in Mycosis Fungoides (MF), and thus worth investigating its potential as future non-invasive biomarker.

### Objectives

To characterize the SC ceramide profile in lesional and non-lesional skin of MF patients.

## Materials and methods

- 21 early-stage (Ia/Ib) MF patients (52.9±14.3 years, 9 female) were included in the study.
- Assessments were performed on a lesional and a contralateral non-lesional site.
- Skin permeability was assessed by measuring trans-epidermal water loss (TEWL).
- SC was harvested by tape stripping for ceramide lipidomics.
- Ceramide analysis was performed by liquid chromatography-mass spectrometry and quantitative data was obtained after correction with SquameScan values.<sup>5</sup>

## Results

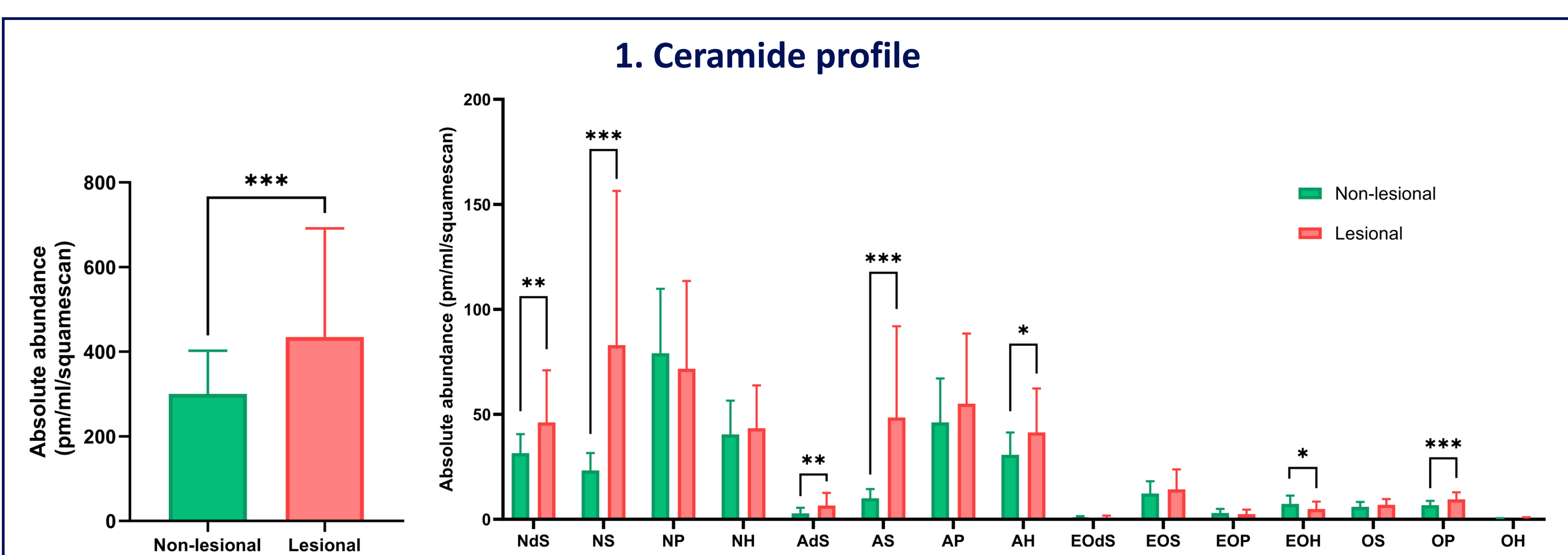


Figure 1: Comparison of absolute abundance of total ceramides in lesional and non-lesional SC.

Figure 2: Comparison of absolute abundance of ceramide subclasses in lesional and non-lesional SC.

Lesional skin showed an increase in total ceramide abundance (figure 2) and an altered SC ceramide composition (figure 3) compared to non-lesional skin with:

- Increase in CER[NdS], CER[NS], CER[AS], CER[AdS], CER[OP]
- Reduction of CER[EOH]

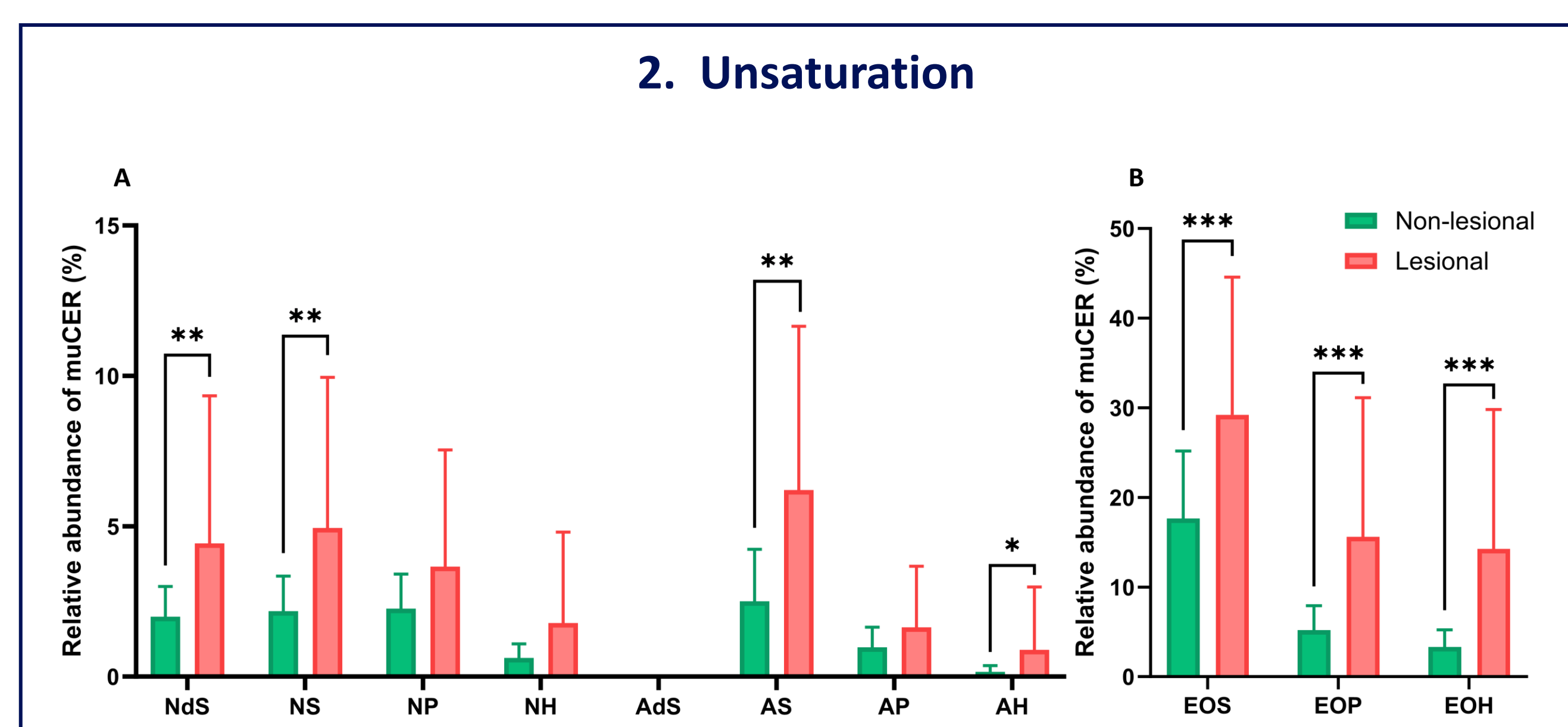


Figure 3: Comparison of relative abundance of mono-unsaturated ceramides (muCER) per ceramide class in lesional and non-lesional SC. (A) Non-EO ceramides (B) EO-ceramides

A higher degree of unsaturation was observed in lesional skin compared to non-lesional skin:

- Unsaturation in CER[NdS], CER[NS], CER[AS], CER[AH] and CER[EO] is significantly higher.

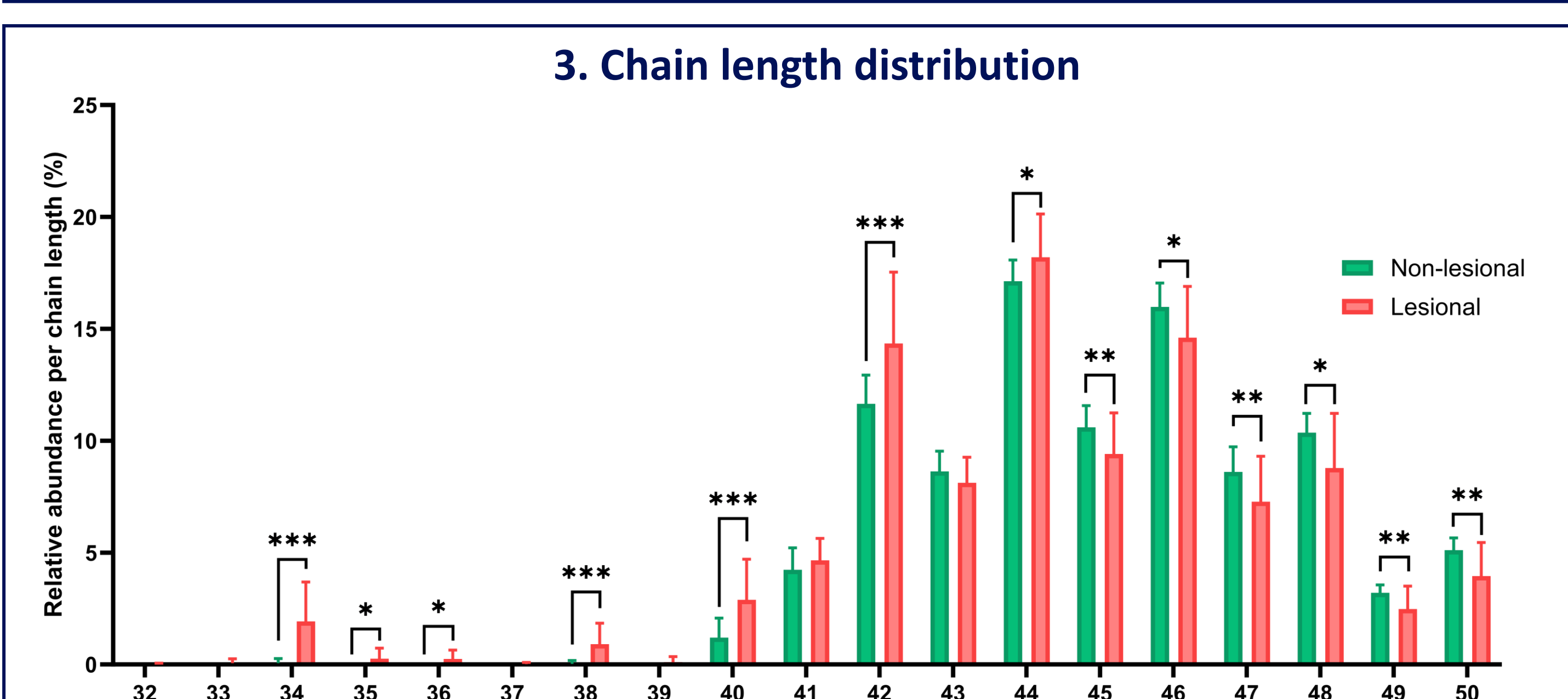


Figure 4: Comparison of relative abundance of CER chain lengths in lesional and non-lesional SC.

Ceramide elongation seems impaired in MF lesions:

- Lesional skin showed an increase in short-chain ceramides C32 to C44.
- Especially short-chain ceramides of 34 carbons (C34) were increased in lesional skin and remained almost undetected in non-lesional skin.
- Relative abundance of C45-C50 was higher in non-lesional skin.

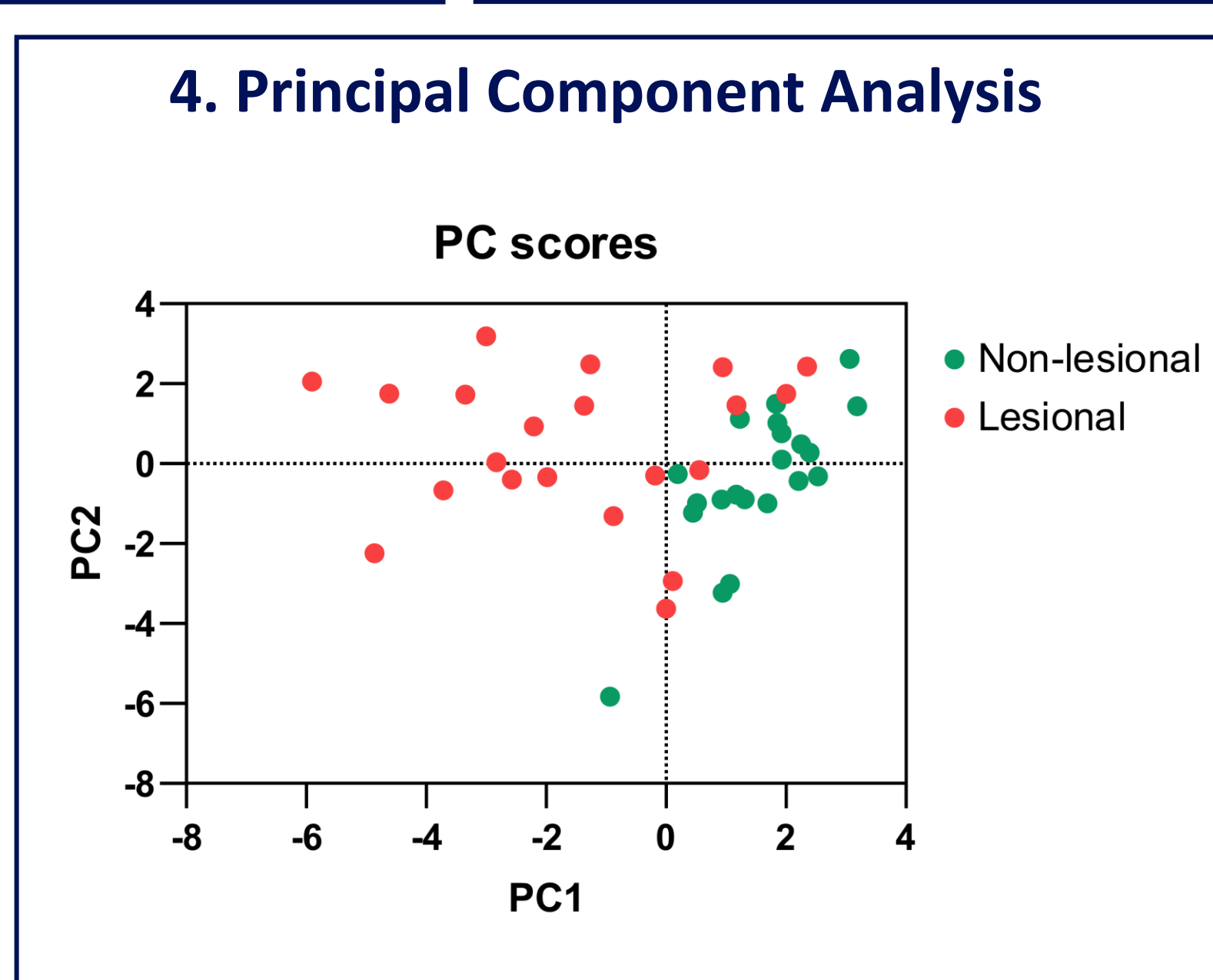


Figure 5: Principal component analysis of ceramide subclasses for lesional and non-lesional SC.

Principal component analysis of ceramide subclasses revealed two distinct populations for lesional and non-lesional skin, indicating that lesional skin differs from non-lesional skin.

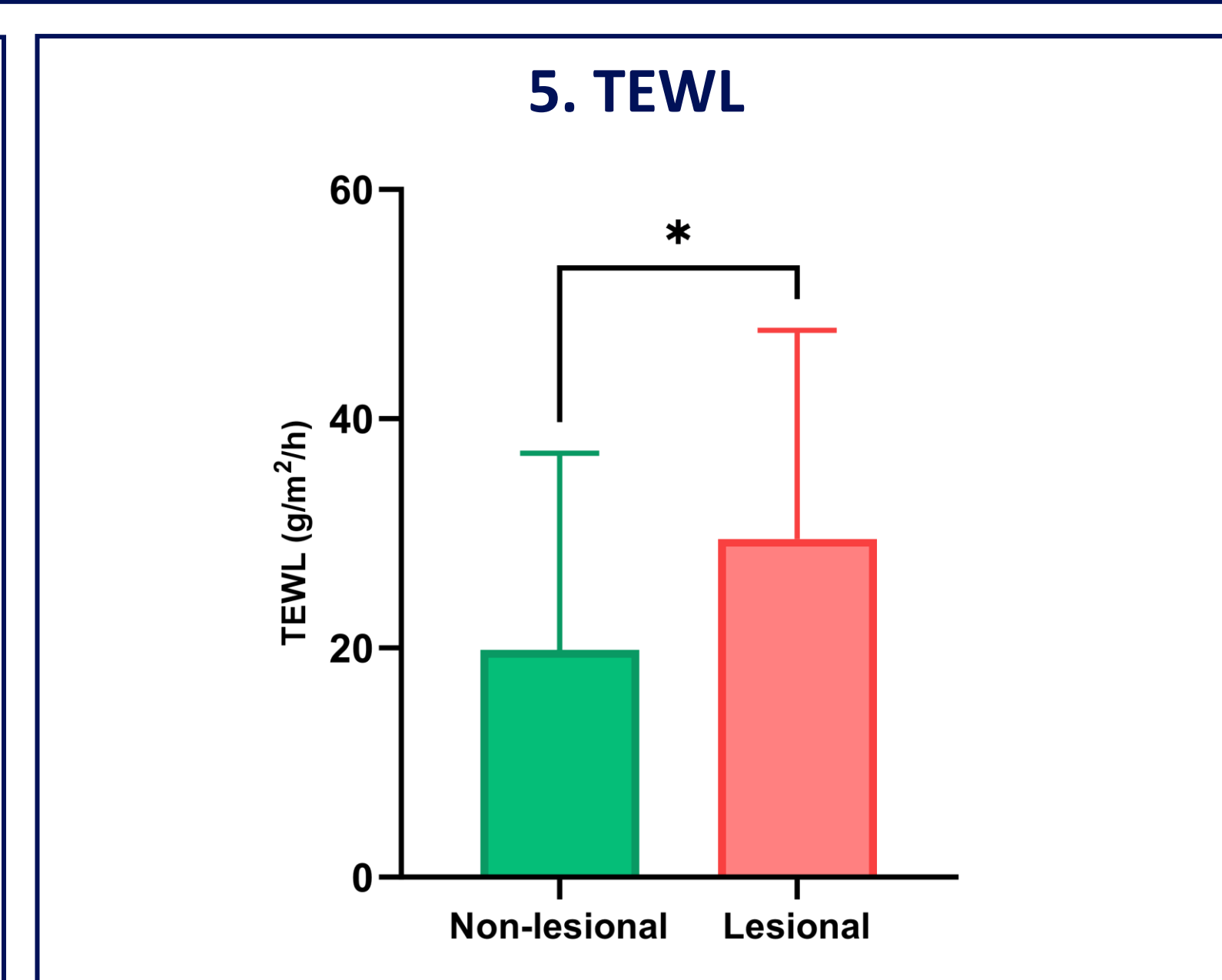


Figure 6: Comparison of TEWL values of non-lesional and lesional skin.

TEWL was significantly increased in lesional skin compared to non-lesional skin. However, no correlation to ceramide profile (CER abundance, carbon chain length, degree of unsaturation, ceramide ratios) was observed.

### Conclusion

- The SC ceramide profile in MF significantly differs between lesional and non-lesional skin.
- Further research should investigate whether these changes correlate to disease severity and progression.

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### Acknowledgements:

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