

# The Mechanical Properties of Skin in Osteogenesis Imperfecta

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**Background:** Skin mechanics may be affected by several dermatological and systemic conditions. The skin can act as a marker of generalized disease. Osteogenesis imperfecta (OI) is a heritable disorder characterized by fragile bones caused by a generalized disorder of collagen. The dermis has a relative increase of argyrophil and elastic fibers and a deficiency of adult collagen. The collagen defect is well described, but functional changes in tissue mechanics have not been studied in the skin. The functional changes may reflect general changes and may give insight into the pathogenesis of clinical problems in these patients.

**Objective:** To examine skin mechanics (elasticity, distensibility, and hysteresis) in patients with OI.

**Methods:** Ten patients with OI (mean  $\pm$  SD age, 45.9  $\pm$  11.5 years) and 24 age-matched control subjects (mean  $\pm$  SD age, 43.3  $\pm$  13.8 years) were studied. The suction cup technique was used (Dermaflex; Cortex Technology, Hadsund, Denmark).

**Results:** Significant differences between the patients and controls were found in all measurements ( $P < .002$ ). Skin elasticity was decreased in patients vs controls (55.5% [range, 50.9%-60.1%] vs 73.8% [range, 70.3%-77.2%]). Similarly, distensibility was decreased (2.10 mm [range, 1.85-2.35 mm] vs 2.50 mm [range, 2.37-2.63 mm]), as was hysteresis (0.19 mm [range, 0.15-0.23 mm] vs 0.28 mm [range, 0.27-0.30 mm]).

**Conclusions:** The skin of patients with OI is more stiff and less elastic than normal skin. It is speculated that similar differences may be found in other tissues in patients with OI. The results potentially offer a quantitative standardized measure of OI, which may further our understanding of the underlying physical problems of these patients, provide better case definitions, and assist in predicting the prognosis of patients with OI.

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QUANTIFICATION IS of great help in the evidence-based clinical management of disease. Classification of disease denotes its genetic, anatomical, and molecular levels, while quantification of disease assists in the clinical management of its severity, risks, and prognosis. Osteogenesis imperfecta (OI) is a well described disease involving the major connective tissues of the body, such as bone, skin, cartilage, and blood vessels. Osteogenesis imperfecta causes a generalized decrease in bone mass (osteopenia and bone brittleness).<sup>1</sup> The disorder is frequently associated with blue sclerae, dental abnormalities (dentinogenesis imperfecta), progressive hearing loss, and a positive family history. Most patients with OI have several deletions, insertions, and point mutations in 1 of 2 structural genes coding for type I procollagen.<sup>2</sup> The same mutation, however, does not always produce the same disease phenotype in terms of severity of the condition or its clinical course.<sup>3</sup>

In families with OI, some members are clinically severely affected, whereas others with the identical mutation have only a mild disorder. This study was undertaken to characterize the mechanical properties of the skin in patients with OI and to determine whether they can be used as a functional measure of the underlying abnormality and correlated to disease severity.

## RESULTS

No abnormalities of skin elasticity or fragility were apparent in the clinical examination of the patients' skin. However, there were significant differences between the patients and controls in all suction cup measurements. Skin elasticity was 55.5%  $\pm$  4.6% in the patients and 73.8%  $\pm$  3.5% in the controls ( $P < .001$ ). The distensibility was 2.10  $\pm$  0.25 mm in the patients and 2.50  $\pm$  0.13 mm in the controls ( $P < .001$ ). Hysteresis was 0.19  $\pm$  0.04 mm in the patients and 0.28  $\pm$  0.01 mm in the controls ( $P < .001$ ) (**Table**).

A linear relationship was found between standing height and skin elasticity

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## MATERIALS AND METHODS

Ten patients with OI (8 with type I [3 men and 5 women] and 2 with type III<sup>†</sup> [1 man and 1 woman]) and 24 control subjects (14 men and 10 women) were studied. The mean  $\pm$  SD age of the patients was  $45.9 \pm 11.5$  years and of the controls,  $43.3 \pm 13.8$  years. The study was in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants.

Skin mechanics were studied using the suction cup technique (Dermaflex; Cortex Technology, Hadsund, Denmark).<sup>5,6</sup> A 100-mm probe (suction cup) is attached to the skin with an adhesive ring, and a vacuum is applied in 4 cycles of 6 seconds each. Two variables were studied: *distensibility*, reflecting the elevation (in millimeters) of the skin surface in the suction cup following the first application of suction, and *hysteresis*, measuring the change in maximum elevation following successive suction cycles (the "creep" phenomenon). *Elasticity* is the relative retraction following the first suction.

Healthy controls were recruited from the staff of the Department of Dermatology, Bispebjerg Hospital, Copenhagen, Denmark. None of the controls had signs or a history of generalized dermatological or connective tissue disease. For 3 hours before skin measurement, subjects refrained from moisturizer use or exposure to water to avoid externally induced changes of skin mechanics.<sup>7</sup>

Standing height was measured to the nearest 1.0 cm, using a stadiometer. Standing height has been suggested as an overall measure of disease severity in OI by Lund et al.<sup>8</sup>

Comparisons between patients and controls and between patient groups were done by independent *t* tests. All tests were 2-tailed, and  $P < .05$  was considered significant. Regression by the least squares method was used for fitting the height and skin elasticity measurements. These calculations were performed using commercially available software (SPSS version 10.0; SPSS Inc, Chicago, Ill). Data are given as mean  $\pm$  SD.

in patients with OI ( $r^2=0.37$ ;  $P=.06$ ): percentage of skin elasticity =  $(30.90 + 0.17) \times$  height in centimeters.

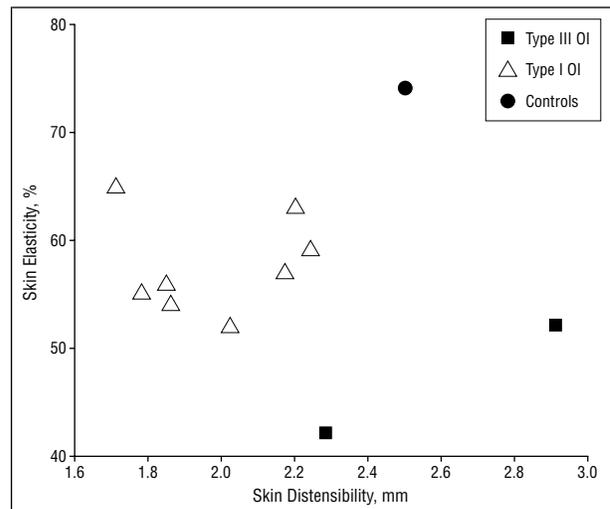
The patients were divided into groups according to OI type. Consequently, 8 had type I and 2 had type III. Patients with type III had a lower skin elasticity than those with type I ( $47.00 \pm 7.70$  mm vs  $57.60 \pm 4.50$  mm). However, patients with type I had a much lower skin distensibility ( $1.98 \pm 0.21$  mm vs  $2.60 \pm 0.45$  mm). Hysteresis was greater in patients with type III ( $0.25 \pm 0.05$  mm vs  $0.18 \pm 0.05$  mm).

### COMMENT

The mechanical properties of the skin in patients with OI are abnormal. In the present study, all 10 patients with OI had decreased elasticity, distensibility, and hysteresis compared with controls. These changes differ from age-related changes, which have been described as in-

### Characteristics of Patients With Osteogenesis Imperfecta

Sex/ Age, y	Height, cm	Elasticity, %	Distensibility, mm	Hysteresis, mm
M/52	153	57	2.17	0.17
M/36	110	52	2.91	0.28
M/55	152	56	1.85	0.21
M/41	165	55	1.78	0.14
F/57	136	59	2.24	0.24
F/27	163	65	1.71	0.10
F/56	153	54	1.86	0.20
F/41	167	52	2.02	0.15
F/60	147	63	2.20	0.23
F/34	100	42	2.28	0.21



Skin distensibility and elasticity associated with patients' osteogenesis imperfecta (OI) type vs those of controls.

creased distensibility and viscosity (similar to hysteresis).<sup>9</sup> Collagen is the only fibrous protein that has high tensile strength and tensile properties.<sup>10,11</sup> Therefore, altered elastic properties may be interpreted as a reflection of abnormalities in dermal collagen and, possibly, as an indication of general changes in body collagen. The findings of this study suggest that the skin is stiffer and less elastic in patients with OI, which may reflect the connective tissue abnormalities that underlie the general clinical presentation of the disease, such as bone brittleness. The correlation between elasticity and distensibility appeared to be altered between type I (mild to moderate disease, minimal bone deformity, and autosomal dominant inheritance) and type III (severe disease, progressive bone deformity, and autosomal recessive inheritance), suggesting additional means of distinguishing different types of OI, based on mechanical abnormalities of the skin (**Figure**). The current sample size, however, does not allow for meaningful analysis of subgroups.

Osteogenesis imperfecta can be a severely debilitating disease, and a method is needed to predict the prognosis in individual patients. The disease is classified into 4 types, but in clinical practice it may be difficult to distinguish between them. This is especially the case in child-

hood, when the need for a predictive prognosis is the greatest. The problem is compounded by the fact that, even if the genetic type is known, it is often not possible to predict the clinical outcome.<sup>3</sup> Current classification does not provide the necessary data for prediction of future impairment. Lund and coworkers<sup>8</sup> have found that a relative reduction in standing height appears to correlate with OI type and the type of collagen defect. However, this may be viewed as an explanatory rather than a predictive association.<sup>8</sup> When changes in the skin elasticity were compared with adult height, a near-significant correlation was found, supporting this association.

Other connective tissue diseases, such as Marfan syndrome or progressive systemic scleroderma, are known to involve skin and other organs. In these cases, changes in the mechanical properties of the skin are paralleled by similar changes in internal organs (eg, slack skin and aneurysms in Marfan syndrome, fibrosis of the skin and lungs in progressive systemic scleroderma). This makes it possible for a dermatological examination of a patient to contribute to the diagnosis. It is hypothesized that a more quantitative approach may be of further use in establishing the magnitude of the impairment and in offering prognostic information to the patient.<sup>12</sup>

In the present study, abnormal changes in the mechanical properties of the skin of patients with OI reflected the functional changes of connective tissue. Although difficult to interpret because of the small number of patients studied, differences were found between subtypes of OI, suggesting that additional information may be gathered by biophysical studies. These findings suggest that in vivo measurement of the mechanical properties of skin may be a relevant, prognostic factor in the clinical assessment of OI.

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