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Androgenetic alopecia is associated with increased scalp hardness

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The physical properties of a tissue, including hardness, play an important role in development, homeostasis and disease pathogenesis.[1] For hair follicles, physical properties of the surrounding tissue regulates hair morphogenesis and growth.[2] However, little is known about the role of tissue hardness in hair loss diseases. Androgenetic alopecia (AGA) is caused by androgen and susceptible genetic background. The disease process of AGA is also modified by other factors.[3, 4] We hypothesized that AGA was associated with scalp hardness and thus this study was conducted to confirm the hypothesis.

Subjects with AGA and without other alopecia were enrolled from our Dermatology Clinic. The control non-AGA subjects were healthy volunteers without any alopecia. The study protocol was approved by the Institutional Review Board of National Cheng Kung University Hospital. The scalp hardness was measured by Durometer (Model DD-4, Type OO, Rex®), which quantified the hardness as 0-100 and reflected the average hardness of the epidermis, dermis and upper subcutis. The hardness of scalp was measured at 15 designated anatomical points (Fig. 1a-b) before any treatment of alopecia was initiated. Student's t-test, with Bonferroni correction when required, was used for comparison between subgroups. Generalized estimating equation (GEE) model was utilized to analyze the association between variables.

Eighty male subjects, including 57 male-pattern AGA and 23 non-AGA subjects, and 80 female subjects, including 54 female-pattern AGA and 26 non-AGA, were enrolled. There was no difference in the mean age and BMI between AGA and non-AGA subjects. In non-AGA subjects, the scalp hardness was the highest at the frontal area and the lowest at the occipital area (Fig. 1c-d). The scalp hardness in male and female non-AGA subjects was comparable, except the crown area where male subjects had higher hardness than female subjects. The GEE model showed that sex, age and BMI was not associated with scalp hardness.

In male subjects, the hardness at the frontal and vertex scalp was significantly higher in

AGA subjects (Fig. 1e), compared to non-AGA subjects. The scalp hardness at the frontal and vertex scalp was also higher in subjects with higher AGA severity (Fig. 1f). GEE model showed that increased scalp hardness was associated with higher risk and increased severity of AGA (Table 1).

In female subjects, however, there was no significant difference in the scalp hardness between female AGA and non-AGA subjects (Fig. 1g). The vertex scalp of subjects with grade 3 AGA had higher hardness than subjects without AGA (Fig. 1h). GEE model showed no association between scalp hardness and AGA occurrence or severity (Table 1).

Our data showed that the AGA-prone scalp (frontal and vertex scalp) correlated with higher hardness, while the AGA-resistant scalp (temporal and occipital scalp) correlated with lower hardness. Male AGA subjects had higher hardness at the AGA-affected scalp than non-AGA subjects. The above findings suggest an association between AGA and scalp hardness. The interaction between the scalp hardness and hair follicles in AGA are complicated. Transforming growth factor β1 (TGF-β1) is the key growth inhibitor of the hair epithelium in AGA.[5] On the other hand, TGF-β1 also induces tissue fibrosis and increased tissue hardness.[6] Perifollicular fibrosis had actually been identified in AGA.[7, 8] Fibrosis of the tissue can in turn activate latent TGF-β1,[9] and further inhibits the hair epithelium growth. TGF-β1 also potentiated the sensitivity of androgen receptor in the DP cells from the bald scalp.[10]

In conclusion, there was a pattern distribution of scalp hardness. The occurrence of AGA and AGA severity was positively correlate with scalp hardness in men. Further investigation is required to identify the underlying mechanism and to look for a new therapeutic strategy.

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Table 1 The association of scalp hardness with the occurrence and severity of AGA by GEE test[†]

Sex	Outcome	Independent variable	OR	95% CI	P-value
Male	AGA vs. non-AGA	Hardness	1.11	1.04 – 1.19	**0.003**
	AGA grade (0-1, 2-4, and 5-7)		1.11	1.03 – 1.19	**0.004**
Female	AGA vs. non-AGA	Hardness	1.04	0.96 – 1.13	0.32
	AGA grade (0, 1, 2, and 3)		1.07	0.997 – 1.14	0.061

Bold indicates statistical significance at $P < 0.05$.

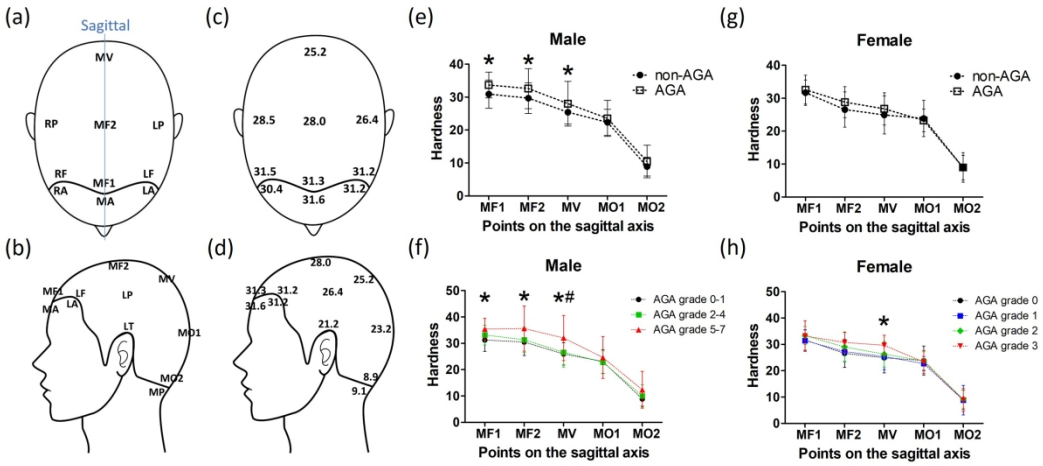
[†]The GEE model was adjusted for age, BMI and anatomical locations on the scalp.

AGA, Androgenetic alopecia; BMI, body mass index; CI, confidence interval;

OR, odds ratio.

FIGURE LEGEND

Figure 1 The distribution of skin hardness on the non-AGA scalp and the comparison of scalp hardness between AGA and non-AGA subjects. (a, b) The top and lateral view of the scalp showing the designated points for measurement of skin hardness (LA, left-anterior; LF, left-frontal; LP, left-posterior; LT, left-temporal; MA, mid-anterior; MF1, mid-frontal 1; MF2, mid-frontal 2; MV, mid-vertex; MO1, mid-occipital 1; MO2, mid-occipital 2; MP, mid-posterior; RA, right-anterior; RF, right-frontal; RP, right-parietal point). (c, d) The skin hardness of each designated point on the scalp of non-AGA patients. (e) The scalp hardness along the sagittal axis in male AGA and non-AGA subjects. The AGA subjects had significant higher scalp hardness at the frontal (MF1 and MF2) and vertex (MV) scalp, compared to the non-AGA subject (MF1, 33.7 ± 3.9 vs. 30.9 ± 4.3; MF2, 32.6 ± 6.1 vs. 29.7 ± 4.7; MV, 28.0 ± 6.8 vs. 25.4 ± 3.6) (*$P < 0.05$). Data was presented in mean ± standard deviation (SD). (f) The scalp hardness in male subjects with none to minimal AGA (grade 0-1), mild to moderate AGA (grade 2-4) and severe AGA (grade 5-7). The scalp hardness of frontal (MF1, MF2) and vertex (MV) scalp in the severe AGA subjects was significantly higher than the none to minimal AGA subjects (MF1, 35.4 ± 4.1 vs. 31.2 ± 4.3; MF2, 35.6 ± 8.6 vs. 30.5 ± 5.1; MV, 32.0 ± 8.6 vs. 25.9 ± 4.2) (*$P < 0.05$). Subjects with severe AGA had higher scalp hardness at the vertex area than subjects with none to minimal AGA (32.0 ± 8.6 vs. 26.6 ± 5.6) (#$P < 0.05$). Data was presented in mean ± SD. (f) The scalp hardness along the sagittal axis in female AGA and non-AGA subjects. There was no significant difference of scalp hardness in each point. Data was presented in mean ± SD. (h) The scalp hardness in female subjects with grade 1, 2 and 3 female-pattern AGA and without AGA (grade 0). The hardness of vertex scalp in grade 3 AGA subjects was significantly higher than subjects without AGA (grade 0) (29.7 ± 3.8 vs. 24.9 ± 5.8) (*$P < 0.05$). Data was presented in mean ± SD.



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