ORIGINAL ARTICLE

The long-term evolution of melanocytic nevi among high-risk adults

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Abstract

Background There is little understanding regarding the long-term natural history of melanocytic nevi among adults.

Objective The objective of the study was to describe the long-term natural history of individual nevi located on the torso of high-risk patients.

Methods All patients attending Memorial Sloan Kettering Cancer Center (MSKCC) who underwent two total body photography (TBP) sessions 15+ years apart were included ('retrospective' group). To account for a potential selection bias, we also included consecutive patients who had TBP 15+ years ago and consented to undergo follow-up TBP ('prospective' group). We compared baseline and follow-up torso images on the TBPs and evaluated the number of total, new and disappearing nevi; number of seborrheic keratoses and actinic keratoses; each nevus' diameter at both time points; each nevus' colour change; the presence of clinical atypia; and when dermoscopy was available, the dermoscopic features at each time point.

Results One hundred six patients were included in the study. Although the average age of the patients was 40 at baseline TBP, most patients developed new nevi between imaging sessions (median 16.4 years) with an average of 2.6 (SD = 4.8) nevi per participant. The average number of disappearing nevi was 0.3 (SD = 0.6). In addition, 62/106 (58%) patients had an absolute increase, and 9/106 (8%) patients had an absolute decrease in their total nevus count. Roughly half (49%: 1416/2890) of the nevi that could be evaluated at both time points increased in diameter by at least 25%. Only 6% (159/2890) of nevi shrunk in diameter by at least 25%. Patients with a history of melanoma had a higher rate of disappearing nevi, and their nevi were more likely to grow. Most nevi demonstrated no significant dermoscopic changes.

Conclusions High-risk patients acquire new nevi throughout life with very few nevi disappearing over time. Contrary to prior reports, most nevi in adults increase in diameter, while few nevi shrink.

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Conflict of Interest

None declared.

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Introduction

Nevus phenotype is a strong risk marker for melanoma. A meta-analysis by Gandini *et al.*[1] observed that the risk of melanoma increases with higher nevus counts. Hence, clinicians face the challenge of finding 'a needle in a haystack'—identifying melanoma in patients with many nevi. While change is an important clue for melanoma development,[2] nevi also change over time.[3] To detect changes indicating malignancy, we must study the behaviour of nevi.

Little is known regarding the long-term natural history of melanocytic nevi. Numerous cross-sectional and longitudinal studies suggest that nevus counts are associated with age, but the relationship is not linear.[4,5] Total nevus counts tend to increase until the 4th decade of life before decreasing in the elderly. The prevailing explanation for this age-related effect has been that people develop new nevi in early life and lose nevi in later life. In fact, this nevus volatility has been observed in paediatric cohorts—over a follow-up period of 3–7 years, up to 75% of

patients had new nevi, and 28% had nevi that disappeared.[6,7] In later life, there could be a shift, whereby disappearing nevi exceed new nevi.

However, in adult cohorts, data on change in nevus counts with age has been inconclusive.[8–15] An account for the conflicting data could be that the association between nevus counts and age is an artefact of cross-sectional studies, and differences in ultraviolet radiation (UV) exposure across birth cohorts may explain the disparity in nevus counts by age.[13] Furthermore, longitudinal studies have not correlated changes in nevus counts with patient and nevus factors.[9,11,14–17] A study that does not track individual nevi may ignore the possibility that different types of nevi may have different trajectories. An exogenous pathway of development, related to UV exposure, may apply to junctional nevi that peak in midlife and then regress. In contrast, an endogenous pathway, unrelated to UV exposure, may apply to intradermal nevi that appear in youth and persist indefinitely.[18]

A study that longitudinally tracks long-term changes in individual nevi in adults is needed. Total body photography (TBP) provides the opportunity to clinically monitor individual nevi. TBP acquires high-resolution overview images and is typically used in patients with high risk for melanoma.[19] The goal of the present study was to describe long-term changes, in overall nevus count and in individual nevi, among adult patients undergoing serial TBP at a high-risk pigmented lesion clinic. These data could help clinical practice recognize banal changes in nevi over time and shed new light on nevus biology.

Methods

Ethics

The study was approved by the Institutional Review Board at Memorial Sloan Kettering Cancer Center (MSKCC) under protocols 99-099 and 17-078.

Patient recruitment

At MSKCC, most pigmented lesion clinic patients undergo digital TBP during their follow-up. We reviewed all charts of patients who underwent the initial TBP at MSKCC prior to 1/1/2005. Patients who subsequently received a follow-up TBP more than 14 years after the initial TBP session were included ('retrospective' group). To account for bias in the selection of patients for the second TBP, we recruited an additional cohort of consecutive patients scheduled to be seen in a dermatology clinic with TBP more than 14 years prior but with no follow-up TBP. These patients consented to undergo a follow-up TBP as part of the study ('prospective' group). Patients were excluded if their original TBP images were not of sufficient quality to measure nevus size.

Demographic information, as well as personal and family history of skin cancer, were retrieved from the patients' clinical charts and interviews. Baseline and follow-up TBP digital image sets were synchronously compared side by side on two screens. In a previous study,[20] we found that counting and measuring nevi ≥4 mm on flat surfaces of the body had better reproducibility and made it easier to identify solar lentigines and seborrheic keratoses. Therefore, only nevi ≥4 mm (at any time point) on the torso were included in the current study. The borders of the torso were defined as follows: upper front = clavicles; upper back = tip of shoulders; lower border = iliac crests.

Image analysis

Torso images, divided into four parts (chest, abdomen, upper and lower back) were compared between the baseline and follow-up TBP for the following: (i) patient-level observations—presence of individual nevi at each time point for calculating total, new, disappearing and excised nevi; number of seborrheic keratoses and actinic keratoses (diagnosed based on clinical/dermoscopic features); (ii) nevus-level observations—diameter at both time points (mm); colour change (lighter/darker/same); and presence or absence of clinical atypia at either time point.

Nevus tracking

Due to technological improvements during the study, the baseline TBP was comprised of 2D images (DermaGraphix®& VECTRA, Canfield Imaging, Parsippany, NJ, USA), while the follow-up TBP consisted of 3D images (VECTRA, Canfield Imaging). All TBP images were acquired by trained clinical photographers using standardized lighting, image storage, patient postures and camera distance and orientation. Prior to the session, patients were instructed to trim body hair and remove jewellery and undergarments. The images used for this study depicted patients in a standing position with their upper limbs parallel to their torso.

Diameter measurements on 2D images were performed manually using ImageJ software (National Institutes of Health, Bethesda, MD, USA) which was calibrated to the dermoscopy images. Measurements on 3D images were performed automatically using VECTRA software on a parallel screen simultaneously. The diameter of each nevus at the most current TBP session was compared with its diameter at the first TBP, and per cent change was calculated. In a prior study, we found that ImageJ manual measurements of nevi were reproducible between observers and correlate well with automated measurements made by VECTRA 3D.[20] Still, to account for measurement inaccuracy, a nevus was considered growing or shrinking if it showed at least a ±25% change in diameter.

Dermoscopic nevus tracking

When a dermoscopic image was available, we noted each nevus' main dermoscopic features at the centre and at the periphery and noted any dermoscopic between the two imaging sessions. Dermoscopic 'fading' was defined as (i) pigment network and/or globules disappearing or (ii) pigment network becoming lighter

in colour, patchier in distribution or having thinner lines. Dermoscopic 'enhancement' was defined as (i) pigment network and/or globules appearing and (ii) pigment network becoming darker, more widespread in the lesion or showing thicker lines. All comparisons were made on non-polarized images, as the older images were all non-polarized.

Statistical analysis

Primary patient-level outcomes were total count of new and disappearing nevi. Poisson regression was used to assess the rate of new nevi per 15 years and to evaluate the association of that rate with other clinical factors. Each Poisson model included covariates for patient group, age, sex and counts of baseline and disappearing nevi. Similarly, logistic regression models were fit to analyse the occurrence of at least one disappearing nevus, and adjusted odds ratios were derived. Patient group and baseline nevus count were accounted for in each model, as was patient age when analysing personal and familial histories of melanoma and counts of actinic and seborrheic keratoses. The primary nevus-level outcomes were change in maximum diameter and likelihoods of increased and decreased maximum diameter by at least 25%. As groups of nevi are nested within patients, nevus-level outcomes were analysed using a generalized estimating equations (GEE) approach with an exchangeable correlation structure to account for the lack of independence between nevi. Each model contained covariates for patient group and baseline diameter. Additionally, the model included a continuous covariate for ordinal patient age (20–34, 35–45, >45) when analysing the relationship between nevus diameter change and personal and familial histories of melanoma.

Results

Of 836 patients who underwent TBP at MSKCC prior to 1/1/2005, 66 had a follow-up TBP that met the inclusion criteria. Sixty-three additional consecutive patients were seen for follow-up dermatology visits and consented to undergo a follow-up TBP for the study. Of these, 19 patients were excluded due to inability to measure nevi due to lack of calibrated dermoscopy images, two for being younger than 18 at baseline and two for having received immunotherapy during follow-up. A total of 106 patients participated in the study, with a median follow-up time of 16.4 years (range 14.2–19.8). All patients had Fitzpatrick skin type of I or II. In total, 71 (67%) patients had a history of melanoma, 50 (47%) had their first melanoma before and 21 (20%) after their baseline TBP (Table 1).

Forty-nine patients were included in the 'retrospective' group that received their follow-up TBP prior to the study and 57 in the 'prospective' group that received their follow-up TBP as part of the study. The patients in the 'retrospective' group and in the 'prospective' group were similar in terms of age and history of melanoma. Patients in the 'retrospective' group had a higher average baseline nevus count (36 vs. 23, $P = 0.017$).

Table 1 Characteristics of patients enrolled in the study

Characteristic	*n*	col %
Total patients	106	100%
Sex		
Male	58	55%
Female	48	45%
Personal history of melanoma (first primary)		
Never	35	33%
During follow-up	21	20%
Before follow-up	50	47%
Family history of melanoma		
No	59	56%
Yes	44	42%
Unknown	3	3%
	Mean	**SD**
Age at baseline	40.6	10.1
Years between baseline and follow-up	16.8	1.5
Torso nevi at baseline	29.2	27.4
Actinic keratoses at baseline or follow-up	0.5	2.2
Seborrheic keratoses at baseline or follow-up	14.5	23.1
New nevi at follow-up	2.6	4.8
Disappearing nevi at follow-up	0.3	0.6

Patient tracking

Excluding lesions that were excised, 62/106 (58%) patients had an absolute increase in their nevus count and 9/106 (8%) patients had an absolute decrease in their nevus count over the follow-up period. Sixty-nine patients (65.1%, 95% CI 55.6–73.5%) had new nevi that appeared on the torso, and the average number of new nevi on the torso was 2.6 (Table 2).

The average number of new nevi was higher among young patients and decreased with age; however, we observed new nevi even in a patient who was the oldest in the sample at baseline imaging (Fig. 1). New nevi appeared more commonly among male patients. Women had 46% fewer new nevi than men per 15 years ($P = 0.001$). In addition, patients with a higher baseline nevus count and patients with at least one nevus that disappeared had more new nevi.

Twenty-seven patients (25.5%, 95% CI 18.1–34.5%) had at least one nevus that disappeared. The number of disappearing nevi ranged from 0 to 3 per patient. The disappearance of nevi was not related to age and this phenomenon was uncommon even among the oldest participants (Fig. 2). The average number of disappearing nevi was higher among patients with a higher baseline nevus count; however, this was not statistically significant.

Patients with a history of melanoma were less likely to acquire new nevi and more likely to have disappearing nevi compared to patients with no history of melanoma.

The number of seborrheic keratoses and actinic keratoses on the torso ranged from 0 to 190 and 0 to 19, respectively and was positively associated with age.

Table 2 Patient tracking: new and disappearing nevi on the torso of 106 patients

	Overall	New nevi count				Adjusted rate ratio (95% CI)†,‡	*P*-value†,‡	Disappearing nevi count			Adjusted odds ratio (95% CI)§	*P*-value§
		0	1–3	≥4	Average			0	≥1	Average		
	n (col %)	*n* (row %)	*n* (row %)	*n* (row %)				*n* (row %)	*n* (row %)			
Total patients	106 (100)	37 (35)	46 (43)	23 (22)	2.6	N/A	N/A	79 (75)	27 (25)	0.3	N/A	N/A
Cohort												
Retrospective	49 (46)	13 (27)	22 (45)	14 (29)	3.4	1.0 (referent)	0.710	32 (65)	17 (35)	0.5	1.0 (referent)	0.115
Prospective	57 (54)	24 (42)	24 (42)	9 (16)	1.9	1.05 (0.8–1.38)		47 (82)	10 (18)	0.2	0.47 (0.18–1.19)	
Total torso nevi at baseline												
1–10	27 (25)	19 (70)	8 (30)	0 (0)	0.5	1.0 (referent)	<0.001¶	25 (93)	2 (7)	0.1	1.0 (referent)	0.068¶
10–20	29 (27)	12 (41)	14 (48)	3 (10)	1.4	1.92 (1.05–3.75)		21 (72)	8 (28)	0.3	4.31 (0.93–31.09)	
20–40	23 (22)	4 (17)	15 (65)	4 (17)	1.9	2.3 (1.25–4.49)		15 (65)	8 (35)	0.4	7.25 (1.53–53.54)	
≥40	27 (25)	2 (7)	9 (33)	16 (59)	6.5	5.65 (3.2–10.8)		18 (67)	9 (33)	0.5	4.71 (1.01–34.21)	
Number of disappearing nevi at follow-up												
0	79 (75)	29 (37)	34 (43)	16 (20)	2.1	1.0 (referent)	<0.001	—	—	—	—	—
≥1	27 (25)	8 (30)	12 (44)	7 (26)	4.0	1.8 (1.39–2.34)		—	—	—	—	—
Number of new nevi at follow-up												
0	37 (35)	—	—	—	—	—	—	29 (78)	8 (22)	0.2	1.0 (referent)	0.391¶
1–3	46 (43)	—	—	—	—	—	—	34 (74)	12 (26)	0.3	0.74 (0.23–2.38)	
4 or more	23 (22)	—	—	—	—	—	—	16 (70)	7 (30)	0.5	0.51 (0.1–2.33)	
Age at baseline												
<35	33 (31)	5 (15)	11 (33)	17 (52)	5.5	1.0 (referent)	<0.001¶	27 (82)	6 (18)	0.3	1.0 (referent)	0.270¶
35–45	43 (41)	14 (33)	24 (56)	5 (12)	1.4	0.3 (0.22–0.4)		29 (67)	14 (33)	0.4	3.89 (1.21–14.35)	
>45	30 (28)	18 (60)	11 (37)	1 (3)	0.9	0.22 (0.14–0.33)		23 (77)	7 (23)	0.3	2.11 (0.57–8.34)	
Sex												
Male	58 (55)	13 (22)	26 (45)	19 (33)	3.7	1.0 (referent)	<0.001	44 (76)	14 (24)	0.3	1.0 (referent)	0.089
Female	48 (45)	24 (50)	20 (42)	4 (8)	1.2	0.54 (0.39–0.74)		35 (73)	13 (27)	0.3	2.57 (0.89–8.04)	
Personal history of melanoma (first primary)												
Never	35 (33)	11 (31)	13 (37)	11 (31)	3.7	1.0 (referent)		31 (89)	4 (11)	0.1	1.0 (referent)	
During follow-up	21 (20)	7 (33)	7 (33)	7 (33)	2.9	0.57 (0.41–0.78)	<0.001	13 (62)	8 (38)	0.4	4.85 (1.17–23.26)††	0.035††
Before follow-up	50 (47)	19 (38)	26 (52)	5 (10)	1.6	0.56 (0.41–0.76)	<0.001	35 (70)	15 (30)	0.4	3.43 (0.99–14.41)††	0.066††
Family history of melanoma												
No	59 (56)	26 (44)	24 (41)	9 (15)	1.9	1.0 (referent)		46 (78)	13 (22)	0.3	1.0 (referent)	0.871††
Yes	44 (42)	10 (23)	21 (48)	13 (30)	3.5	1.04 (0.79–1.36)	0.353	31 (70)	13 (30)	0.4	1.08 (0.4–2.86)††	
Unknown	3 (3)	1 (33)	1 (33)	1 (33)	2.3			2 (67)	1 (33)	0.3		

Table 2 *Continued*

	Overall	New nevi count				Adjusted rate ratio (95% CI)†,‡	*P*-value†,‡	Disappearing nevi count			Adjusted odds ratio (95% CI)§	*P*-value§
		0	1–3	≥4	Average			0	≥1	Average		
	n (col %)	*n* (row %)	*n* (row %)	*n* (row %)				*n* (row %)	*n* (row %)			
Torso actinic keratoses at baseline or follow-up												
0	91 (86)	29 (32)	40 (44)	22 (24)	2.8	1.0 (referent)	0.044	67 (74)	24 (26)	0.4	1.0 (referent)	0.693††
≥1	15 (14)	8 (53)	6 (40)	1 (7)	0.9	0.57 (0.31–0.95)		12 (80)	3 (20)	0.2	0.75 (0.15–2.81)††	
Torso seborrheic keratoses at baseline or follow-up												
0	16 (15)	5 (31)	3 (19)	8 (50)	4.6	1.0 (referent)	0.051¶	12 (75)	4 (25)	0.4	1.0 (referent)	0.191¶,††
1–10	48 (45)	16 (33)	24 (50)	8 (17)	2.7	0.76 (0.56–1.04)		34 (71)	14 (29)	0.4	1.05 (0.26–4.76)††	
≥10	42 (40)	16 (38)	19 (45)	7 (17)	1.6	0.7 (0.49–1.01)		33 (79)	9 (21)	0.2	0.39 (0.07–2.21)††	

†Normalized for 15-year follow-up.
‡Model includes covariates for study cohort, baseline count, disappearing nevi, age and sex.
§Base model includes covariates for study cohort and baseline count.
¶*P*-values for trend.
††Base model includes additional covariate for age.

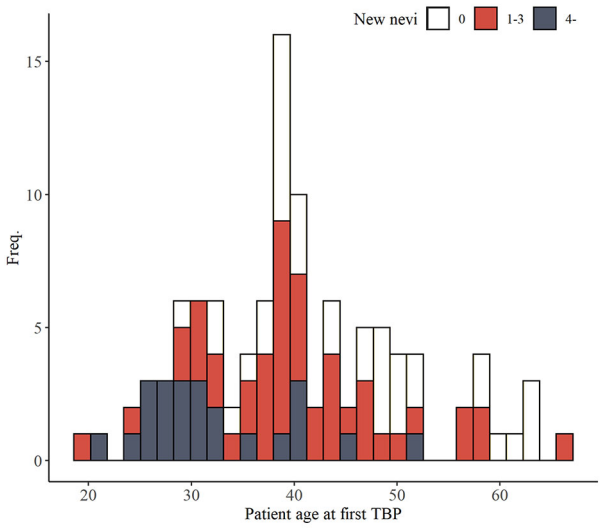

Figure 1 Count of new nevi on the torso compared with age at first TBP session.

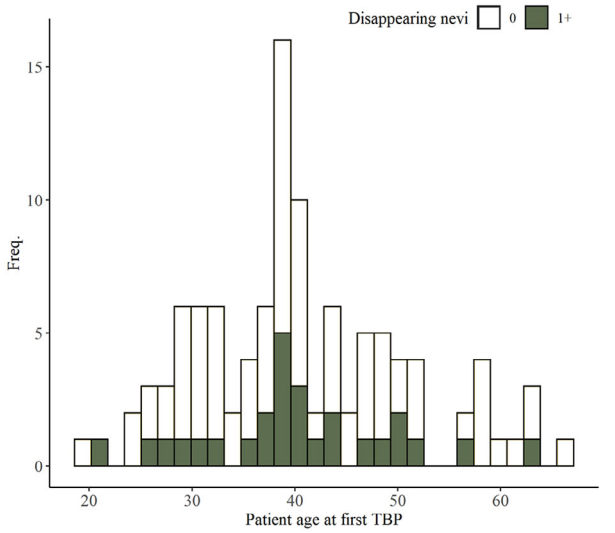

Figure 2 Count of disappearing nevi on the torso compared with age at first TBP session.

Nevus tracking

Serial assessments were performed for all nevi imaged, including those for which there was no dermoscopy available. Of these, most nevi (80.4%) did not significantly change in colour during the follow-up period, while 15.6% of the nevi became lighter and 3.9% became darker (Table 3).

All but three patients experienced at least one growing nevus and 59 patients (55.7%) had at least one shrinking nevus on

Table 3 Nevus tracking: nevus diameter changes of 2890 nevi

	Overall	Diameter increased by at least 25%			Diameter decreased by at least 25%		
	n (col %)	*n* (row %)	Adjusted odds ratio (95% CI)†	*P*-value†	*n* (row %)	Adjusted odds ratio (95% CI)†	*P*-value†
Total nevi	2890 (100)	1416 (49)	N/A	N/A	159 (6)	N/A	N/A
Cohort							
Retrospective	1667 (57.68)	771 (46)	1.0 (referent)	0.601	105 (6)	1.0 (referent)	0.228
Prospective	1223 (42.32)	645 (53)	1.08 (0.8–1.47)		54 (4)	0.75 (0.47–1.19)	
Total torso nevi at baseline							
1–10	151 (5.22)	89 (59)	1.0 (referent)	0.544§	6 (4)	1.0 (referent)	0.002§
10–20	388 (13.43)	172 (44)	0.64 (0.34–1.18)		37 (10)	2.13 (0.75–6.05)	
20–40	585 (20.24)	226 (39)	0.52 (0.29–0.93)		46 (8)	1.7 (0.59–4.85)	
≥40	1766 (61.11)	929 (53)	0.94 (0.55–1.62)		70 (4)	0.74 (0.27–2.06)	
Number of disappearing nevi at follow-up							
0	1865 (64.53)	911 (49)	1.0 (referent)	0.362	74 (4)	1.0 (referent)	0.002
≥1	1025 (35.47)	505 (49)	1.16 (0.85–1.58)		85 (8)	2.1 (1.31–3.37)	
Number of new nevi at follow-up							
0	480 (16.61)	221 (46)	1.0 (referent)	0.653§	33 (7)	1.0 (referent)	0.254§
1–3	1246 (43.11)	564 (45)	0.86 (0.57–1.31)		72 (6)	0.89 (0.46–1.7)	
4 or more	1164 (40.28)	631 (54)	1.09 (0.7–1.7)		54 (5)	0.69 (0.36–1.35)	
Age at baseline							
<35	1095 (37.89)	537 (49)	1.0 (referent)	0.519§	61 (6)	1.0 (referent)	0.744§
35–45	1059 (36.64)	539 (51)	0.98 (0.69–1.39)		64 (6)	1.27 (0.74–2.2)	
>45	736 (25.47)	340 (46)	0.87 (0.58–1.3)		34 (5)	0.86 (0.45–1.66)	
Sex							
Male	2148 (74.33)	1087 (51)	1.0 (referent)	0.199	108 (5)	1.0 (referent)	0.220
Female	742 (25.67)	329 (44)	0.81 (0.58–1.12)		51 (7)	1.4 (0.82–2.38)	
Personal history of melanoma (first primary)							
Never	837 (28.96)	322 (38)	1.0 (referent)		47 (6)	1.0 (referent)	
During follow-up	724 (25.05)	381 (53)	2.36 (1.6–3.48)	<0.001¶	32 (4)	0.83 (0.45–1.54)	0.564¶
Before follow-up	1329 (45.99)	713 (54)	2.55 (1.83–3.57)	<0.001¶	80 (6)	1.32 (0.78–2.24)	0.298¶
Family history of melanoma							
No	1240 (42.91)	584 (47)	1.0 (referent)	0.394¶	62 (5)	1.0 (referent)	0.654¶
Yes	1596 (55.22)	816 (51)	1.14 (0.84–1.56)		93 (6)	1.12 (0.68–1.86)	
Unknown	54 (1.87)	16 (30)			4 (7)		
Colour change							
No Change	2312 (80)	1213 (52)	1.0 (referent)		65 (3)	1.0 (referent)	
Lighter	452 (15.64)	109 (24)	0.51 (0.4–0.65)	<0.001	93 (21)	5.65 (3.91–8.15)	<0.001
Darker	112 (3.88)	90 (80)	2.01 (1.23–3.28)	0.005	0 (0)	0 (0–0)	<0.001
Unknown	14 (0.48)	4 (29)			1 (7)		
Atypical at baseline							
No	2691 (93.11)	1346 (50)	1.0 (referent)	0.052	143 (5)	1.0 (referent)	
Yes	194 (6.71)	68 (35)	0.67 (0.45–1)		16 (8)	1.31 (0.76–2.24)	0.330
Unknown	5 (0.17)	2 (40)			0 (0)		

†Base model includes covariates for study cohort and baseline diameter.
‡Normalized for 15-year follow-up.
§*P*-values for trend.
¶Base model includes additional covariate for age.

their torso. Of all nevi included in this study, 49% (1416 of 2890) grew and 6% (159 of 2890) shrunk in diameter by at least 25% during follow-up. The average change in diameter was 1 mm (SD = 1.7).

The nevi of patients with a history of melanoma were more likely to increase in size. The nevi of patients with at least one disappearing nevus were more likely to decrease in size compared to patients without a disappearing nevus. Likelihood of

nevus size decrease was positively associated with total count of baseline torso nevi. In terms of individual nevus characteristics, nevi that became lighter in colour were more likely to decrease in size, while nevi that became darker were more likely to increase in size.

The number of new and disappearing nevi, as well as the likelihood of growth and shrinkage of nevi, were similar in all four sections of the torso (chest, abdomen, upper and lower back).

Dermoscopic nevus tracking

Patients had numerous nevi imaged using total body photography (2890, see Table 1), which were included in nevus counts and nevus tracking, but only 773 were evaluated for dermoscopic change (dermoscopic nevus tracking) due to the availability of dermoscopic images at both time points for comparison. Most nevi (76%) did not have major dermoscopic changes (Table 4).

Fading at the centre of the lesion was noted in 15% of nevi that grew compared with 35% of nevi that shrunk ($P < 0.001$). Dermoscopic features of enhancement at the centre of the lesion were less common and were noted in only 4% of nevi that grew vs. 2% of nevi that shrunk.

Discussion

The current study includes the largest group reported to date and the longest follow-up of individual patients as well as individual nevi between time points. This study may provide important insights regarding the natural evolution of nevi in high-risk patients and help clinicians when deciding to biopsy a new or growing nevus in a high-risk patient.

While some of our findings likely reflect true biological behaviours of nevi, others likely reflect clinical practice: Clinicians are more likely to excise new nevi in patients with a history of melanoma, which may explain why melanoma patients had fewer new nevi in this study; clinicians are also more likely to excise a growing nevus if it is atypical, which may explain why atypical nevi were less likely to grow in this study; finally, it is reasonable that nevi with major dermoscopic changes were more likely to be excised, which could have contributed to the relatively unchanged dermoscopy of nevi in the study.

In terms of nevus counts, our results suggest that patients continue to acquire new nevi and most patients experience an overall increase in nevus counts over time. This finding is consistent with previous studies with shorter follow-up periods that reported new nevi in 10–33% of adults.[9,11,14] Indeed, the current study describes long-term changes that occur over a time period much longer than the average follow-up done in most pigmented lesion clinics. However, this observation is important to incorporate into clinical practice as new melanocytic lesions are easily identified with the increasing use of TBP, but many are likely to be benign and not require biopsy. Unlike previous studies,[11,17] we observed a very limited number of disappearing nevi (max. 3), even in older participants. The discrepancy between our findings and previous studies may be related to asynchronous nevus tracking, in which the observers may have missed nevi that faded in colour over time but have not completely regressed.[20]

Very few studies have reported on the size change of multiple nevi over a long period of time. Abbott *et al.*[10] reported that during 12 months of follow-up, 16% of nevi changed, 36% of which grew in diameter. Banky *et al.*[12] reported 329 changed nevi per 1000 patient-years, 67% of which changed in size. In the current study, we found that nevi commonly grew in diameter over time rather than shrank. Out of 106 patients, only four patients did not present any nevus that grew in diameter by more than 25%. This growth decreases as patients aged.

Nevi appear to have a growth limitation as their diameter change was limited to 2 mm, and we know the vast majority of even-growing nevi do not progress to malignancy.[21] However, our findings imply that the process of nevus senescence, mediated by p-16 and the p14-p53-p21 pathway,[22] may be more dynamic than previously thought, and one must remember that long-term changes appear in nevi and do not necessarily point to malignancy. The disappearance of nevi in the current study

Table 4 Dermoscopic nevus tracking

				Diameter change					
		Overall (*N* = 773)		Decrease (*N* = 43)		No significant change (*N* = 373)		Increase (*N* = 357)	
Dermoscopic change	Location	*N*	%	*N*	%	*N*	%	*N*	%
Any	Any	189	24	17	40	104	28	68	19
Fading	Any	166	21	17	40	94	25	55	15
Fading	Centre	153	20	15	35	85	23	53	15
Fading	Periphery	108	14	14	33	71	19	23	6
Enhance	Any	40	5	2	5	19	5	19	5
Enhance	Centre	27	3	1	2	10	3	16	4
Enhance	Periphery	16	2	1	2	9	2	6	2

was not accompanied by a halo or apparent inflammation, suggesting the most common mechanism was fading pigment.[17]

Traits of nevus volatility are associated with each other. In the current study, patients with a higher baseline nevus count and a higher number of disappearing nevi were also more likely to have a higher number of new nevi. In addition, it appears that nevus volatility is associated with melanoma. While we assume that new nevi were more likely to be excised in patients with a history of melanoma, these patients had more disappearing nevi, and their nevi were more likely to grow in diameter. The idea that melanoma patients have more 'volatile nevi' was previously suggested by Abbott *et al.*,[10] but the underlying mechanism remains unclear. One possible explanation is that patients who develop melanoma harbour a genetic predisposition for melanocytic proliferation, which also affects the melanocytes in their nevi. Another reason could be that the development of melanoma induces systemic effects, such as immunological, which lead to changes in the patient's nevi. Our observation that patients developing melanoma prior to the baseline TBP had relatively similar nevus evolution compared with patients developing melanoma during follow-up supports the first explanation (genetic predisposition).

In terms of dermoscopy, previous studies on children and adults found that most nevi do not show major dermoscopic changes over time.[23–26] In the current study, dermoscopic nevi patterns and structures stayed relatively stable during follow-up. About a third of nevi that shrunk in diameter were likely to present the features of dermoscopic 'fading', and features of dermoscopic 'enhancement' were uncommon. However, as mentioned above, this can also be attributed to clinical practice, since nevi that showed major dermoscopic changes were more likely to be excised by the clinician.

Limitations

This was a retrospective single institution study, and the 'retrospective' group were 'preselected' to receive a second TBP for clinical care. We tried to address this bias by adding the 'prospective' group, who were consecutive patients attending follow-up. The study participants were high-risk patients, which limits applicability to the general population. The study was also limited to nevi on the torso ≥4 mm in diameter, which increased the validity of the measurements but may impact applicability to total nevus counts. Some patients experienced changes in body size and shape between the TBP sessions, which may have affected their nevi size. Finally, longer follow-up periods may show additional changes.

Conclusions

High-risk adult patients continue to acquire new torso nevi throughout life, thus the appearance of a new melanocytic lesion in old age is not enough to determine that it is malignant, and if it is not an outlier,[27] has no melanoma-specific dermoscopic structure[28] and shows dermoscopic features that fit with the body location and the patient's age,[29] follow-up may be considered. In addition, most nevi display limited growth in diameter, which is not associated with malignancy.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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