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ERRATUM

Natural history of Type 2 and 3 spinal muscular atrophy: 2-year NatHis-SMA study

The article by Annoussamy et al. (2021)[1] was published with several errors:

FF_{T2} should be replaced by *FF* throughout the text, and CSA changes expressed in cm^2 should be expressed in mm^2. The corrected version of the affected text follows:

Abstract:
Objective: To characterize the natural history of spinal muscular atrophy (SMA) over 24 months using innovative measures such as wearable devices, and to provide evidence for the sensitivity of these measures to determine their suitability as endpoints in clinical trials. Methods: Patients with Type 2 and 3 SMA (N = 81) with varied functional abilities (sitters, nonsitters, nonambulant, and ambulant) who were not receiving disease-modifying treatment were assessed over 24 months: motor function (Motor Function Measure [MFM]), upper limb strength (MyoGrip, MyoPinch), upper limb activity (ActiMyo®), quantitative magnetic resonance imaging (fat fraction [*FF*] mapping and contractile cross-sectional area [C-CSA]), pulmonary function (forced vital capacity [FVC], peak cough flow, maximum expiratory pressure, maximum inspiratory pressure, and sniff nasal inspiratory pressure), and survival of motor neuron (SMN) protein levels. Results: MFM32 scores declined significantly over 24 months, but not 12 months. Changes in upper limb activity could be detected over 6 months and continued to decrease significantly over 12 months, but not 24 months. Upper limb strength decreased significantly over 12 and 24 months. FVC declined significantly over 12 months, but not 24 months. *FF* increased over 12 and 24 months, although not with statistical significance. A significant increase in C-CSA was observed at 12 but not 24 months. Blood SMN protein levels were stable over 12 and 24 months. Interpretation: These data demonstrate that the MFM32, MyoGrip, MyoPinch, and ActiMyo® enable the detection of a significant decline in patients with Type 2 and 3 SMA over 12 or 24 months.

Introduction, last paragraph:
Here, we present data of a 24-month observational natural history study, which may be one of the last in SMA due to an increasing number of patients receiving SMA treatment as a result of the recent approval of disease-modifying treatments. Data from the MFM are presented to characterize the disease course over 24 months in patients with Type 2 and 3 SMA. Further assessments include muscle strength (digital measures assessed by performance in grip and pinch strength tests through wearable devices), fat fraction (*FF*), and pulmonary function tests for the identification of (1) prognostic variables of SMA, (2) best-outcome measures for future treatment studies, and (3) SMN biomarkers.

Methods section, Protocol subsection, first paragraph:
Outcomes assessed during the study include motor function (MFM), upper limb strength (MyoGrip, MyoPinch), upper limb activity (ActiMyo®), quantitative magnetic resonance imaging (MRI) (*FF* mapping and muscle contractile cross-sectional area [C-CSA]), pulmonary tests (forced vital capacity [FVC], peak cough flow [PCF], maximum expiratory pressure [MEP], maximum inspiratory pressure [MIP], and sniff nasal inspiratory pressure [SNIP]), and measurement of blood SMN protein levels. These outcomes were evaluated at baseline and then every 6 months (±28 days) for the 24-month duration of the study, except for the MRI assessment (performed annually in two French centers). The full protocol for this trial has been published previously.[19] One-year ActiMyo® data are only available for a limited number of patients due to lack of availability of ActiMyo® devices at the time (Month 6, $n = 25$ [ambulant, $n = 6$; nonambulant, $n = 19$]; Month 12, $n = 17$ [ambulant, $n = 4$; nonambulant, $n = 13$]; Month 18, $n = 7$ [ambulant, $n = 1$; nonambulant, $n = 6$]; Month 24, $n = 2$ [ambulant, $n = 1$; nonambulant, $n = 1$]).

Methods section, MRI muscle assessment subsection:
FF maps were derived from quantitative water-fat imaging obtained using a 3-point Dixon 3D gradient echo sequence; the Dixon-based regions of interest were used in combination with the *FF* mapping to provide the C-CSA, as previously described.[19] These assessments were carried out in one study site with a limited number of patients. *FF* and C-CSA were calculated separately for arms, forearms, legs, and thighs based on outputs for different muscle groups (see supplemental material for more detailed information).

Results section, MRI muscle assessment subsection:
Overall, there was an increase in *FF* at Months 12 and 24 that was not statistically significant: median arm *FF* increased by 0.60% at Month 12 ($n = 16$; [Wilcoxon test $P = 0.501$]; SRM: 0.23) and decreased by 0.51% at Month 24 ($n = 9$; [$P = 0.767$]; SRM: 0.18); median forearm *FF* increased by 0.87% ($n = 13$; [$P = 0.422$]; SRM: 0.35) at Month 12 and by 1.34% at Month 24 ($n = 10$; [$P = 0.203$]; SRM: 0.39); median thigh *FF* increased by 2.11% at Month 12 ($n = 7$; [$P = 0.398$]; SRM: 0.36) and by 4.49% at Month 24 ($n = 3$; [$P = 0.109$]; SRM: 10.68); median leg *FF* increased by 2.91% at Month 12 ($n = 7$; [$P = 0.063$]; SRM: 0.87) and by 2.58% at Month 24 ($n = 3$; [$P = 0.109$]; SRM: 1.40) (Table 2, Figs. S4 and S5).

There was an overall statistically significant increase in muscle C-CSA at Month 12, with no significant increase at Month 24: median arm C-CSA increased by 42.62 mm^2 at Month 12 ($n = 16$; [Wilcoxon test $P = 0.017$]; SRM: 0.69) and by 22.87 mm^2 at Month 24 ($n = 9$; [$P = 0.110$]; SRM: 0.45); median forearm C-CSA increased by 27.31 mm^2 at Month 12 ($n = 13$; [$P = 0.039$]; SRM: 0.72) and by 26.77 mm^2 at Month 24 ($n = 10$; [$P = 0.059$]; SRM: 0.73); median thigh C-CSA increased by 169.88 mm^2 at Month 12 ($n = 7$; [$P = 0.043$]; SRM: 1.01) and by 178.36 mm^2 at Month 24 ($n = 3$; [$P = 0.285$]; SRM: 0.66); median leg CCSA increased by 91.14 mm^2 at Month 12 ($n = 7$; [$P = 0.018$]; SRM: 0.82) and by 308.18 mm^2 at Month 24 ($n = 3$; [$P = 0.285$]; SRM: 0.87) (Table S5, Fig. S5).

Results section, Correlations between clinical outcome measures subsection, last paragraph:
MFM32 was also highly correlated with muscle-imaging measurements. MFM32 was most positively correlated with thigh C-CSA (Spearman = 0.813, $P = 0.026$). High negative correlations were found between MFM32 and forearm *FF* (Spearman = −0.868, $P < 0.001$) and MFM32 and leg *FF* (Spearman = −0.815, $P = 0.025$).

Discussion, 7th paragraph:
Although an increase in the *FF* data was observed at Months 12 and 24 for all SMA types, it was not considered statistically significant. This may be due to the low number of participants available at Month 24 (arm *FF*, $n = 9$; forearm *FF*, $n = 10$; thigh *FF*, $n = 3$; leg *FF*, $n = 3$). An unexpected significant increase in muscle C-CSA was observed at 12 months, possibly due to patient growth; however, no significant increase was observed at 24 months. This is in line with previous findings, where the data also revealed a significant correlation between muscle-imaging assessments such as *FF* and muscle C-CSA and motor function assessments such as the MFM.[39] Taken together, this suggests that although muscle imaging alone may not serve as a suitable marker of disease progression in SMA, it has the potential to serve as a valuable outcome measure in clinical trials in the context of other assessments of motor function.

Supporting Information, caption to Figure S5:

Figure S5. *FF* and C-CSA changes in thigh and leg according to age.

In Table 2, all values should have been multiplied by 100. The corrected table follows:

Table 2. *FF* changes over 12 and 24 months.

FF changes (%)	Arm	Forearm	Thigh	Leg
Changes from baseline at Month 12				
N	16	13	7	7
Mean	0.90	1.15	0.93	1.94
SD	3.83	3.26	2.55	2.23
Median	0.60	0.87	2.11	2.91
Min	−4.33	−2.46	−3.56	−2.17
Max	12.84	9.09	3.85	3.97
P-value*	0.501	0.422	0.398	0.063
SRM	0.23	0.35	0.36	0.87
Changes from baseline at Month 24				
N	9	10	3	3
Mean	0.85	1.61	4.38	3.00
SD	4.70	4.11	0.41	2.15
Median	−5.51	1.34	4.49	2.58
Min	−5.56	−4.71	3.93	1.09
Max	7.03	9.03	4.73	5.32
P-value*	0.767	0.203	0.109	0.109
SRM	0.18	0.39	10.68	1.40

FF, fat fraction; SO, standard deviation; SRM, standardized response means.
**P*-value from Wilcoxon test.

We apologize for these errors.

Reference

1. Annoussamy M, Seferian AM, Daron T. Natural history of Type 2 and 3 spinal muscular atrophy: 2-year NatHis-SMA study. Ann Clin Transl Neurol 2021;8:359–373.

