

Reduced lower limb muscle strength and volume in patients with Type 2 diabetes in relation to neuropathy, intramuscular fat and vitamin D levels

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Word Count: 475

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Initial Decision MiR-DCi16-0020

We thank Treiber et al for sharing their data in relation to a greater prevalence of painful neuropathy and slower walking speeds in their patients taking a statin [1]. They suggest that some of the differences observed in our study could be explained by treatment with statins. We have utilised our data to assess if statins may contribute to lower limb weakness or muscle atrophy and neuropathy.

We have compared our study parameters between T2DM patients on a statin (n=16) to those who were not on a statin (n=4; Table 1). The interpretation of our data is limited and cautious because of the small number of patients not on a statin and also the lack of matching for age, weight and BMI. Nevertheless, muscle strength of the lower limb (knee extensors and ankle plantar flexors) did not differ significantly. Muscle volumes for the knee extensors (P=0.04) and flexors (P=0.09) were lower, with no difference in the ankle plantar (P=0.21) and dorsiflexor (P=0.24) muscle volumes of T2DM patients on a statin compared to patients not on a statin.

Diabetic patients on a statin were older and it is well known that muscle mass declines as a result of ageing due to a reduction in skeletal muscle fibre number, size and length [2]. Whilst it has been suggested that a reduction in muscle size can result in reduced motor neuron unit activation and decreased muscle force and power generation [2], this was not observed in the present study. Another possible explanation is that the older individuals on a statin have a reduction in physical activity, which particularly affects the antigravity muscles such as the knee extensors. Reduced muscle size, reduced muscle activation capacity and ageing are of course highly correlated with reduced muscle strength [3], but in the present study there was no difference between those patient taking a statin compared to those not on a statin.

The loss of muscle mass is also associated with diabetic neuropathy, and in the present study vibration perception threshold (VPT) (P=0.0001) and NDS (P=0.09) were significantly higher indicative of neuropathy in diabetic patients on a statin compared to patients not on a statin, similar to the findings of Treiber et al. Of course whether or not a T2DM patient is on a statin will always be confounded by age, cardiovascular risk and the presence of other microvascular complications [4]. Furthermore, contrary to the studies cited by Trieber and colleagues, a recent large study has shown that treatment with statins may prevent the development of diabetic neuropathy [5]. And of course whether or not a patient is taking a statin depends on whether they can tolerate it, particularly in relation to vitamin D deficiency [6]. A large prospective study is required to establish the potential relationship between statin use, muscle volume and strength and indeed walking ability and falls in diabetes.

References

1. Treiber, G., et al., *Reduced muscle strength : may statins play a role?* Diabetes Care (Online Letter- comment), 2016.
2. Lexell, J., C.C. Taylor, and M. Sjostrom, *What is the cause of the ageing atrophy? Total number, size and proportion of different fiber types studied in whole vastus lateralis muscle from 15- to 83-year-old men.* J Neurol Sci, 1988. **84**(2-3): p. 275-94.
3. Narici, M.V. and C.N. Maganaris, *Plasticity of the muscle-tendon complex with disuse and aging.* Exerc Sport Sci Rev, 2007. **35**(3): p. 126-34.
4. Brownrigg, J.R., et al., *Microvascular disease and risk of cardiovascular events among individuals with type 2 diabetes: a population-level cohort study.* Lancet Diabetes Endocrinol, 2016.
5. Nielsen, S.F. and B.G. Nordestgaard, *Statin use before diabetes diagnosis and risk of microvascular disease: a nationwide nested matched study.* Lancet Diabetes Endocrinol, 2014. **2**(11): p. 894-900.
6. Michalska-Kasiczak, M., et al., *Analysis of vitamin D levels in patients with and without statin-associated myalgia - a systematic review and meta-analysis of 7 studies with 2420 patients.* Int J Cardiol, 2015. **178**: p. 111-6.

Table 1. Clinical demographics and measures of neuropathy, muscle strength and volume in T2DM patients treated with or without a statin.

Variables	T2DM-No Statin (n=4/20)	T2DM- Statin (n=16/20)	P value
Age (years)	50±13.4	66±7.5	0.09
Body mass (kg)	97.6±18.8	79.1±16.7	0.14
BMI (kg/m ²)	32.7±5.6	28.5±3.4	0.24
VPT (Hz)	5.3±1.3	15.7±8.4	0.0001
NDS (0-10)	1.2±1.8	3.5±2.5	0.09
Muscle strength (Nm/kg)			
Knee extensors	1.4±0.4	1.3±0.5	0.47
Ankle plantar flexors	0.8±0.3	0.6±0.2	0.28
Muscle volume (cm³)			
Knee extensors	1370.9±316.1	873.7±356.2	0.04
Knee flexors	705.1±199.3	473.4±204.8	0.09
Ankle plantar flexors	882.0±323.3.7	629.9±155.2	0.21
Ankle dorsiflexors	253.9±83.9	192.4±39.6	0.24

Data are expressed as Mean ± SD. BMI: Body mass index; VPT: Vibration perception threshold; NDS: Neuropathy disability score.