Table S1 Femoral mid-shaft trait values of controls and animals treated with treadmill exercise at the end of the experiment.

Trait	Control	Exercise	P-value
I_{max}	0.535 ± 0.074	0.614 ± 0.089	0.004
I_{min}	0.320 ± 0.041	0.364 ± 0.050	0.005
I_{max}/I_{min}	1.68 ± 0.18	1.69 ± 0.17	0.74

Values are means ± SD. I_{max} and I_{min} are size-standardized by the product of body mass and bone length X 1000.

Table S2 Femoral mid-shaft trait values of controls and animals treated with hindlimb unloading at baseline and after the treatment period.

Trait	Control at baseline	Control after treatment	P-value: control at baseline vs. after treatment	Unloading at baseline	Unloading after treatment	P-value: unloading at baseline vs. after treatment	P-value: control vs. unloading
I_{max} (mm^4)	0.241 ± 0.044	0.261 ± 0.044	<0.0001	0.217 ± 0.046	0.213 ± 0.035	0.34	<0.0001
I_{min} (mm^4)	0.136 ± 0.022	0.152 ± 0.024	<0.0001	0.120 ± 0.023	0.121 ± 0.020	0.40	<0.0001
I_{max}/I_{min}	1.78 ± 0.13	1.72 ± 0.12	0.007	1.81 ± 0.11	1.76 ± 0.12	0.002	0.64

Values are means ± SD.

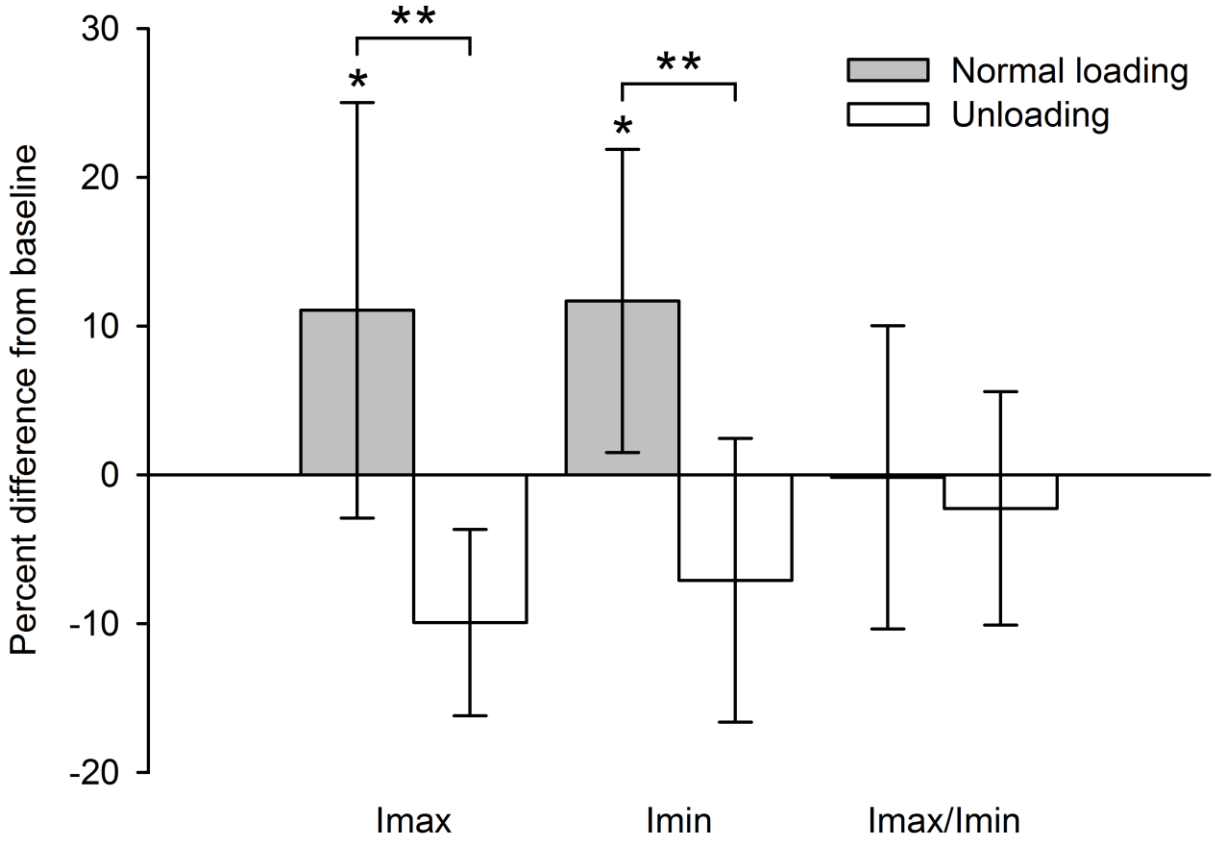

Fig. S1 Change in femoral mid-shaft traits in growing controls and animals treated with hindlimb unloading. Bars equal mean percent change relative to mean baseline values and whiskers equal the standard deviation. Single asterisks indicate statistically significant ($P<0.05$) change within experimental groups relative to baseline values. Double asterisks indicate significant differences between experimental groups. Female C57BL/6J mice (n=34) were acquired from The Jackson Laboratory. At 9 weeks of age, animals were divided into a baseline group (n=10), an unloading group (n=12), and a control group (n=12). Unloading was induced for 2 weeks by hindlimb elevation through tail suspension. Baseline and experimental groups were euthanized at 9 and 11 weeks of age, respectively, and right femora were extracted. Femora were scanned at a 10-μm^3 voxel size (55 kVp, 145 μA, 200-ms integration time) using a Scanco μCT 40 scanner. The volume of interest was a 780-μm-long region of the mid-shaft. μCT image processing followed the same protocol as the two experiments described in the main text. Significant changes within experimental groups were determined with independent samples t-tests (i.e., experimental group means versus baseline group means), as were significant differences between experimental groups (i.e., control group means versus unloading group means). Consistent with the results of the second experiment described in the main text, normal growth of I_{max} and I_{min} were significantly retarded by unloading, but the shaft bending strength index was not significantly affected.

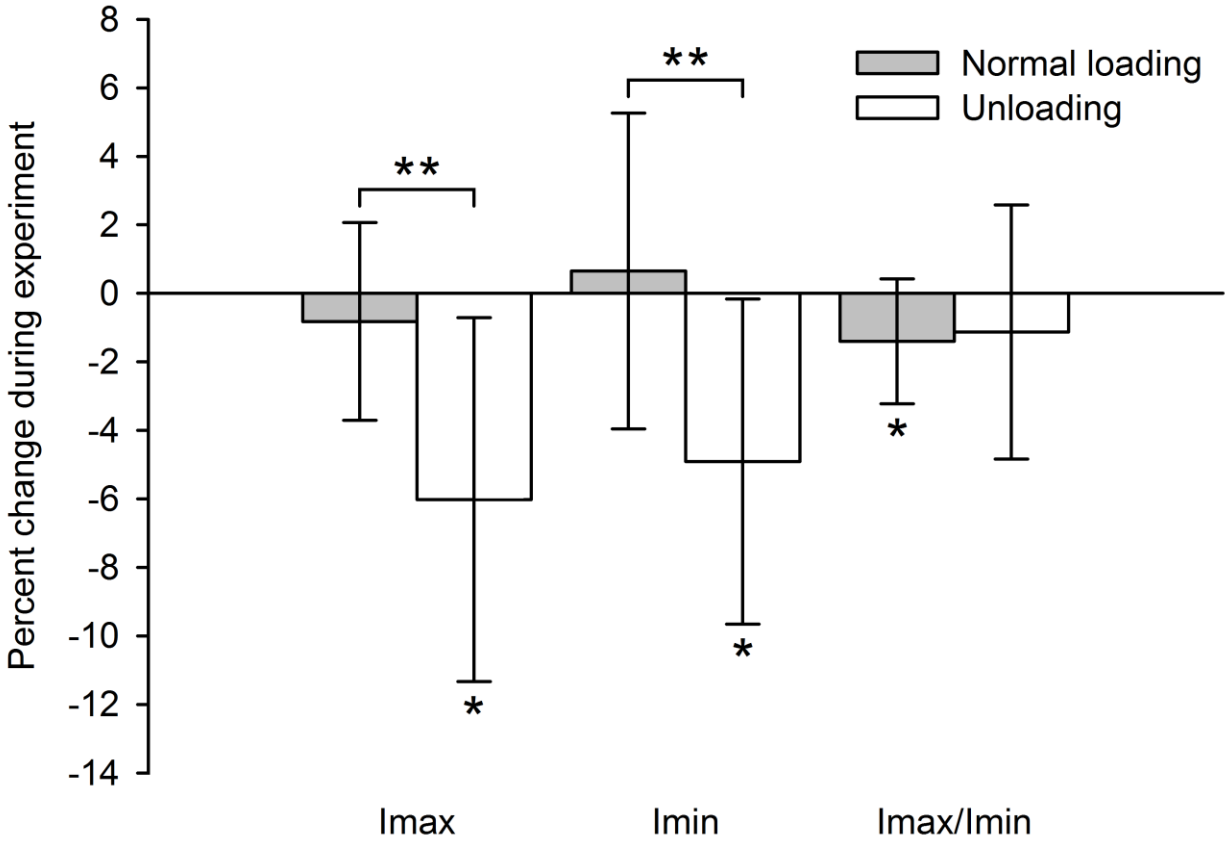

Fig. S2 Longitudinal change in femoral mid-shaft traits in skeletally mature adult controls and animals treated with hindlimb unloading. Bars equal mean percent change relative to baseline values and whiskers equal the standard deviation. Single asterisks indicate statistically significant ($P<0.05$) longitudinal change within groups during the experiment. Double asterisks indicate significant differences between groups at the end of the experiment, determined by statistical analyses that controlled for baseline variation (i.e., ANCOVA; see main text for details). Male C57BL/6J mice (n=20) were acquired from The Jackson Laboratory. At 28 weeks of age, animals were divided into an unloading group (n=11) and a control group (n=9). Unloading was induced for 2 weeks by hindlimb elevation through tail suspension. Immediately prior to and after the unloading period, all animals underwent *in vivo* µCT scanning using a Scanco VivaCT 75 scanner to track longitudinal changes in shaft structure in the right femur. A 600-µm-long mid-shaft volume was scanned at a 20.5-μm^3 voxel size (45 kVp, 177 µA, 200-ms integration time). µCT image processing followed the same protocol as the two experiments described in the main text. Unloading led to significant diminishment of I_{max} and I_{min} compared to the morphological stasis displayed by controls, but the shaft bending strength index was not significantly altered by unloading.