Reply to Gifford et al.: Symmorphosis in chronic heart failure patients?

**Reply to the Editor:** We thank Gifford and colleagues for their comment (3) and agree that the correlation between mitochondrial oxidative capacity and VO\(_{2\text{max}}\) among our chronic heart failure (CHF) patients is not significant \([r = 0.47, P = 0.11(5)]\). However, we disagree with their conclusion that the slope is "effectively 0/1" and that VO\(_{2\text{max}}\) and mitochondrial oxidative capacity are dissociated in CHF patients. The fact that significance was not reached in this subgroup may also be due to insufficient statistical power, which appears to be the case.

In the dissertation of Bekedam (1), group data of 18 CHF patients (including our CHF subgroup) showed that significance was reached \([r = 0.53, P < 0.05]\). Note that in this thesis individual data were not presented (1) and therefore were not included in our analysis (5). Hence, similar to controls and cyclists, CHF patients also conform to the concept of symmorphosis. Therefore, impaired peripheral oxygen supply in CHF not only reduces VO\(_{2\text{max}}\) but also leads to a similar reduction in mitochondrial oxidative capacity.

The observed dysmorphosis in trained subjects by Gifford et al. (2) was not confirmed in our larger sample containing a wider range of VO\(_{2\text{max}}\) (5). We did not intend to suggest that Gifford et al. (2) based their results, challenging symmorphosis, on only four subjects. In our view, six of the trained subjects fitted the (extrapolated) relationship between VO\(_{2\text{max}}\) and mitochondrial capacity of the untrained subjects rather well (cf. Fig. 4 in Ref. 2). There are many possible explanations for this discrepancy in results (2, 5); however, a comparison of the reported data does not allow conclusions in this respect.

Muscle fiber SDH activity does not explain all the variance in VO\(_{2\text{max}}\), indicating that other determinants of VO\(_{2\text{max}}\) are also important. Note that the correlation between SDH activity and VO\(_{2\text{max}}\) in single muscle fibers is very strong under well-controlled hyperoxic experimental conditions \([r = 0.98, P < 0.001(4)]\). Therefore, differences in oxygen supply related to the O\(_2\) cascade from atmosphere to mitochondria may add to the unexplained variance in VO\(_{2\text{max}}\). In the CHF patients, 62% of the variance in VO\(_{2\text{max}}\) is explained by a combination of SDH activity, myocardial ejection fraction and lung diffusion capacity \([r^2 = 0.62, P < 0.01(1)]\). Hence, the factors contributing to the unexplained variance in the relationship between mitochondrial oxidative capacity of skeletal muscle and VO\(_{2\text{max}}\) are important both clinically as well as in sports science and warrant further research.

**DISCLOSURES**

No conflicts of interest, financial or otherwise, are declared by the author(s).

**AUTHOR CONTRIBUTIONS**


**REFERENCES**


