Table of contents

LIST OF STUDIES

As for many other studies initiated before/during the corona crisis, study III and IV were substantially delayed due to various corona related reasons. Consequently, data collection and study initiation were delayed making for final collection of data a few weeks prior to the deadline of this thesis causing the manuscripts (particularly study IV) to not be at their final stage.

I. **TIPPING THE SCALE: EFFECTS OF PHYSICAL ACTIVITY AND BODY COMPOSITION ON CARDIAC PARAMETERS IN POSTMENOPAUSAL WOMEN (SUBMITTED)**

II. **INTENSIFIED TRAINING AUGMENTS CARDIAC FUNCTION, BUT NOT BLOOD VOLUME, IN MALE YOUTH NATIONAL ICE HOCKEY TEAM PLAYERS (IN 2ND ROUND OF REVIEW)**

III. **EXERCISE- ECHOCARDIOGRAPHY FOR IMPROVED ASSESSMENT OF DIASTOLIC FILLING DYNAMICS (Manuscript in preparation)**

IV. **CARDIAC ADAPTATIONS TO ONE YEAR WITH SUPERVISED ENDURANCE TRAINING (Manuscript in preparation)**

LIST OF PAPERS NOT INCLUDED

I. Belval LN, Cramer MN, Moralez G, Huang Dpt M, Watso JC, Fischer M, Crandall CG. **Burn size and environmental conditions modify thermoregulatory responses to exercise in burn survivors.** J Burn Care Res. 2024 Jan 5;45(1):227-233. doi: 10.1093/jbcr/irad128. PMID: 37615621.

II. Nørregaard LB, Wickham KA, Ehlers T, Rocha MP, Fischer M, Lundberg Slingsby MH, Cheung SS, Evans PA, Bangsbo J, Hellsten Y. **Exercise training induces thrombogenic benefits in recent but not late postmenopausal females.** Am J Physiol Heart Circ Physiol. 2023 Aug 1;325(2):H346-H361. doi: 10.1152/ajpheart.00054.2023. Epub 2023 Jun 30. PMID: 37389949.

III. Jessen S, Lemminger A, Backer V, Fischer M, Di Credico A, Breenfeldt Andersen A, Bangsbo J, Hostrup M. **Inhaled formoterol impairs aerobic exercise capacity in endurance-trained individuals: a randomised controlled trial.** ERJ Open Res. 2023 Apr 24;9(2):00643-2022. doi: 10.1183/23120541.00643-2022. PMID: 37101738; PMCID: PMC10123513.

IV. Huang M, Watso JC, Belval LN, Cimino FA, Fischer M, Jarrard CP, Hendrix JM, Laborde CH, Crandall CG. **Low-dose fentanyl does not alter muscle sympathetic nerve activity, blood pressure, or tolerance during progressive central hypovolemia.** Am J Physiol Regul Integr Comp Physiol. 2022 Jan 1;322(1):R55-R63. doi: 10.1152/ajpregu.00217.2021. Epub 2021 Dec 1. PMID: 34851734; PMCID: PMC8742719.

V. Fischer M, Moralez G, Sarma S, MacNamara JP, Cramer MN, Huang M, Romero SA, Hieda M, Shibasaki M, Ogoh S, Crandall CG. **Altered cardiac β1 responsiveness in hyperthermic older adults.** Am J Physiol Regul Integr Comp Physiol. 2022 Sep 12. doi: 10.1152/ajpregu.00040.2022. Epub ahead of print. PMID: 36094450.

VI. Fischer M, Secher NH. **Results for World Rowing Federation and Olympic events** 1893-2019. Res Sports Med. 2022 Jan-Feb;30(1):101-107. doi: 10.1080/15438627.2021.1895780. Epub 2021 Mar 2. PMID: 33653181.

VII. Huang M, Watso JC, Belval LN, Cimino FA, Fischer M, Jarrard CP, Hendrix JM, Laborde CH, Crandall CG. **Low-dose fentanyl does not alter muscle sympathetic nerve activity, blood pressure, or tolerance during progressive central hypovolemia.** Am J Physiol Regul Integr Comp Physiol. 2022 Jan 1;322(1):R55-R63. doi: 10.1152/ajpregu.00217.2021. Epub 2021 Dec 1. PMID: 34851734; PMCID: PMC8742719.

VIII. Cramer MN, Huang MU, Fischer M, Moralez G, Crandall CG. **Thermoregulatory Responses with Size-matched Simulated Torso or Limb Skin Grafts.** Med Sci Sports Exerc. 2021 Oct 1;53(10):2190-2195. doi: 10.1249/MSS.0000000000002694. PMID: 33935232; PMCID: PMC8440327.

IX. Olsen LN*, Fischer M*, Evans PA, Gliemann L, Hellsten Y. **Does Exercise Influence the Susceptibility to Arterial Thrombosis? An Integrative Perspective.** Front Physiol. 2021 Feb 23;12:636027. doi: 10.3389/fphys.2021.636027. PMID: 33708141; PMCID: PMC7940832. Review article.

X. Sejersen C, Fischer M, Mattos JD, Volianitis S, Secher NH. **Fluctuations in cardiac stroke volume during rowing.** Scand J Med Sci Sports. 2021 Apr;31(4):790-798. doi: 10.1111/sms.13901. Epub 2020 Dec 22. PMID: 33280195.

XI. Craig G Crandall, Matthew N Cramer, Mu Huang, Gilberto Moralez, Luke Belval, Joseph C Watso, Mads Fischer. **Burn Survivors Can Exercise for 30 Min, Even in the Heat, Without a Risk of Excessive Hyperthermia**, *Journal of Burn Care & Research*, Volume 41, Issue Supplement_1, March 2020, Pages S48-S49, https://doi.org/10.1093/jbcr/iraa024.079

XII. Fischer M*, Cramer MN*, Huang MU, Belval LN, Watso JC, Cimino FA, Crandall CG. **Burn Injury Does Not Exacerbate Heat Strain during Exercise while Wearing Body Armor.** Med Sci Sports Exerc. 2020 Oct;52(10):2235-2241. doi: 10.1249/MSS.0000000000002375. PMID: 32936596; PMCID: PMC7503202. * These authors have contributed equally to this work.

ABSTRACT (ENGLISH)

The capacity to modulate cardiac output to meet an increased metabolic rate or respond to changes in vascular pressures is crucial for optimal exercise performance as well as to adapting to environmental or pathological stress. While heart rate alterations contribute to the adjustment of cardiac output, the adaptations in maximal cardiac output primarily occur through functional and morphological adaptations that impact stroke volume. Our research aimed to elucidate the functional changes that occur with short- and long-term training interventions as well as the effects on cardiac function with acute exercise and exercise training. The studies in this thesis include various 'healthy' subjects ranging from sedentary individuals with a peak oxygen uptake of 18 ml/kg/min to elite athletes with 78 ml/kg/min. In postmenopausal women, we found that cardiac mass and function, when matched for lean body mass, were not different between sedentary individuals and well-trained subjects. In addition, classical markers associated with improved cardiac function showed some association with fitness, but not at group levels. However, a clear discrepancy was evident in the estimated stroke volume needed for the measured maximal oxygen uptake (VO_2max), suggesting that resting cardiac function were inadequate at revealing the functional capacity of the trained hearts. This indicates a more complex interplay between physical fitness and cardiac dimensions than previously recognized, underscoring the importance of selecting appropriate metrics for assessing cardiac adaptations. This novel finding underpins the pitfalls of echocardiographic assessment of cardiac function in otherwise healthy individuals. This assessment may be improved by assessing cardiac function during acute stress which challenges cardiac function. A strong association between functional markers and heart rate were found and revealed that the morphological adaptations of the athletes' hearts are not reflected when stressed in relation to relative workloads (i.e. normalized to heart rate) but instead are reflected with absolute workloads (i.e. normalized to absolute power output watt). Additionally, filling rate emerged as a valuable tool for distinguishing between

trained and untrained individuals. Lastly, the studies revealed that training interventions, both in untrained and highly trained subjects, can yield alterations with just a few weeks of exercise training. In untrained subjects, improvements in cardiac function were predominantly evident during stress at absolute load (75w) intensities, with limited effects observed when assessed by relative workloads (i.e., heart rate 140 BPM). In conclusion, this thesis reveals that even a brief period of exercise training can enhance cardiac function in both sedentary and highly trained individuals. Importantly, the findings highlight that current indexing practices result in skewed comparisons due to limited insights from the assessment of resting cardiac function. Furthermore, exercise stress testing emerges as valuable in enhancing functional assessment, especially when evaluating differences between groups.

RESUMÈ (DANSK)

Evnen til at regulere hjertets minutvolumen for at imødekomme ændringer i stofskifte eller reagere på ændringer i vaskulære tryk er afgørende for optimal fysisk præstation under træning samt tilpasning til miljømæssige eller patologiske stressfaktorer. Mens ændringer i puls frekvensen bidrager til justeringen af minutvolumen, sker forbedringer af maksimal minutvolumen primært gennem funktionelle og morfologiske tilpasninger, der påvirker slagvolumen. Vores forskning sigtede mod at belyse de funktionelle ændringer, der opstår med kortvarige og langvarige træningsinterventioner samt effekterne på hjertefunktionen ved akut træningsstress og vedvarende træning. Studierne i denne afhandling omfatter forskellige 'sunde' individer, for hvem deres fysiske aktivitetsniveau spænder fra utrænede individer med en maksimal iltoptagelse på 18 ml/kg/min til eliteatleter med iltoptagelse op til 78 ml/kg/min. Hos kvinder der har passeret overgangsalderen, fandt vi, at hjertemuskelmasse og funktion, når der blev matchet for fedtfri kropsmasse, ikke var signifikant forskellige mellem utrænede og veltrænede. Derudover viste klassiske markører forbundet med forbedret hjertefunktion en vis

sammenhæng med kondition, men ikke på gruppeniveau. Imidlertid var der en tydelig diskrepans i det anslåede slagvolumen, der var nødvendigt for det målte maksimale iltforbrug (VO_2max), hvilket antyder, at hvilende hjertefunktion ikke var tilstrækkelig til at belyse de trænede hjerters funktionelle kapacitet. Dette indikerer et mere komplekst samspil mellem fysisk kondition og hjertedimensioner end tidligere beskrevet, hvilket understreger vigtigheden af at vælge passende målemetoder til vurdering af hjertetilpasninger. Dette nye fund understreger faldgruberne ved ekkokardiografisk vurdering af hjertefunktion hos ellers sunde individer. Denne vurdering kan forbedres ved at vurdere hjertefunktionen under akut stress, som udfordrer hjertefunktionen. En stærk sammenhæng mellem funktionelle markører og hjertefrekvens blev fundet og afdækkede, at de funktionelle tilpasninger af atleters hjerter ikke afspejles, når de stresses i forhold til relative arbejdsbelastninger (dvs. normaliseret til hjertefrekvens), men i stedet afspejles med absolutte arbejdsbelastninger (dvs. normaliseret til absolut arbejdsbelastning i watt). Desuden fremkom fyldningshastigheden som et værdifuldt værktøj til at skelne mellem trænede og utrænede individer. Endelig afslørede studierne, at træningsinterventioner, både i utrænede og højt trænede individer, kan medføre ændringer med bare få ugers motionstræning. Hos utrænede emner var forbedringer i hjertefunktionen overvejende tydelige under stress ved absolut belastning (75w) intensiteter, med begrænsede effekter, når vurderet ved relative arbejdsbelastninger (dvs. hjertefrekvens 140 slag/min). Sammenfattende understreger denne afhandling, at selv en kort periode med motionstræning kan forbedre hjertefunktionen hos både stillesiddende og veltrænede individer. Fundene fremhæver, at nuværende indekseringspraksisser i kardiologi resulterer i forfejlede sammenligninger på grund af begrænsede indsigter fra vurderingen af hvilende hjertefunktion og kropssammensætning. Desuden fremstår 'stress-test' som værdifuld i at forbedre funktionel vurdering, især når man evaluerer forskelle mellem grupper.