

LJMU Research Online

Nie, J, Zhang, H, He, Y, Cao, W, Liu, Y, Kong, Z and George, KP

The impact of high-intensity interval training on the cTnT response to acute exercise in sedentary obese young women.

<http://researchonline.ljmu.ac.uk/id/eprint/9743/>

Article

Citation (please note it is advisable to refer to the publisher's version if you intend to cite from this work)

Nie, J, Zhang, H, He, Y, Cao, W, Liu, Y, Kong, Z and George, KP (2018) The impact of high-intensity interval training on the cTnT response to acute exercise in sedentary obese young women. Scandinavian Journal of Medicine and Science in Sports. ISSN 1600-0838

LJMU has developed **LJMU Research Online** for users to access the research output of the University more effectively. Copyright © and Moral Rights for the papers on this site are retained by the individual authors and/or other copyright owners. Users may download and/or print one copy of any article(s) in LJMU Research Online to facilitate their private study or for non-commercial research. You may not engage in further distribution of the material or use it for any profit-making activities or any commercial gain.

The version presented here may differ from the published version or from the version of the record. Please see the repository URL above for details on accessing the published version and note that access may require a subscription.

For more information please contact researchonline@ljmu.ac.uk

<http://researchonline.ljmu.ac.uk/>

The impact of high-intensity interval training on the cTnT response to acute exercise in sedentary obese young women

Jinlei Nie¹, Haifeng Zhang^{2,3}, Yuxiu He², Wenling Cao², Yang Liu², Zhaowei Kong⁴, Keith George⁵

¹ School of Physical Education and Sports, Macao Polytechnic Institute, Macao

² Physical Education College, Hebei Normal University, Shijiazhuang, Hebei, China

³ Provincial Key Lab of Measurement and Evaluation in Human Movement and Bio-Information, Shijiazhuang, Hebei, China

⁴ Faculty of Education, University of Macau, Macao

⁵ Research Institute for Sport and Exercise Sciences, Liverpool John Moores University, Liverpool, UK

Address for Correspondence:

Prof. Haifeng Zhang

Physical Education College, Hebei Normal University, No. 20 Road East. 2nd Ring South, Yuhua District, Shijiazhuang, Hebei, 050024, China

Tel: +86-311-8078 7773

E-mail: h.zhang.hbnu@gmail.com

zhanghaifeng@hebtu.edu.cn

Running Head: high-intensity exercise and cardiac troponin

Abstract

Aims: This study characterized (1) the cardiac troponin T (cTnT) response to three forms of acute high-intensity interval exercise (HIE), and (2) the impact of 12 weeks of HIE training on the cTnT response to acute exercise in sedentary obese young women. **Methods:** Thirty-six sedentary women were randomized to traditional HIE training (repeated 4-min cycling at 90% $\dot{V}O_{2\max}$ interspersed with 3-min rest, 200 kJ/session), work-equivalent sprint interval exercise (SIE) training (repeated 1-min cycling at 120% $\dot{V}O_{2\max}$ interspersed with 1.5-min rest) or repeated sprint exercise (RSE) training (40×6 -s all-out sprints interspersed with 9-s rest) group. cTnT was assessed using a high sensitivity assay before and immediately, 3 and 4 h after the 1st (PRE), 6th (EARLY), 20th (MID), and 44th (END) training session, respectively. **Results:** cTnT was elevated ($P < 0.05$) after all forms of acute interval exercise at the PRE and EARLY assessment with cTnT response higher ($P < 0.05$) after HIE (307%) and SIE (318%) than RSE (142%) at the PRE assessment. All forms of acute interval exercise at MID and END had no effect on the cohort cTnT concentration post-exercise (all $P > 0.05$). **Conclusion:** For sedentary obese young women, both HIE and SIE, matched for total work, induced a similar elevation in cTnT after acute exercise with a smaller rise observed after RSE. By the 44th training session, almost no post-exercise cTnT elevation was observed in all three groups. Such information is relevant for clinicians as it could improve medical decision-making.

Key Words: cardiac troponin T; cardiac biomarker; high-intensity interval training; sprint interval exercise; repeated sprint exercise

Introduction

There is a burgeoning evidence base that cardiac troponin (cTn, cTnT, and/or cTnI), a biomarker pathognomic for cardiomyocyte damage¹, is elevated after continuous prolonged exercise². There are very few data describing the cTn response to high-intensity interval exercise (HIE)³. HIE typically involves repeated bouts of relatively intense exercise interspersed by short periods of recovery and is growing in popularity in cardiac rehabilitation, health, and fitness applications⁴. Concerns related to the safety of HIE have been expressed due to the high cardiac demand and uptake in “at risk” groups⁵. The interpretation of any cTn appearance following acute HIE is likely to be complicated due to potential variance in different forms of HIE, training status and cardiac risk, etc. Further insights into the acute cTn response to different forms of HIE and what adaptation, if any, occurs in the exercise-related cTn response with training could potentially inform clinical decision-making regarding the evaluation of interval type exercise-associated cTn elevation.

A common classification scheme subdivides interval exercise into HIE (“near maximal” efforts) and sprint interval exercise (SIE; “supramaximal” efforts)⁴. Although it has been established that exercise duration and intensity are essential factors in mediating the cTn response to moderate intensity continuous exercise⁶, we do not know whether HIE and SIE would result in different cTn responses, if matched for total work accomplished. In addition, repeated sprint exercise (RSE) where activity is “all-out” but only lasts for 3 to 7 s is a particularly intense form of SIE with a recent and rapid growth in interest⁷. Meta-analyses have reported RSE training can substantially improve fitness despite much shorter total exercise duration (one to several minutes)⁸. There is no current data describing the cTn response to RSE.

Experimental studies, mainly in animals, have demonstrated rapid cardioprotective effects (e.g., smaller infarct size) evoked by exercise, termed “exercise preconditioning”, which may be present after a single episode or a few episodes of exercise⁹. These findings raised an interesting question as to whether a few episodes of exercise may rapidly affect cTn response to acute exercise, but there have been few previous studies addressing this. In an animal study¹⁰, eight days of continuous endurance swimming in rats significantly blunted the post-continuous exercise cTnT response. Whether these results can be translated into humans exposing to interval exercise is not known.

Data related to the impact of long-term training upon the cTn response to an acute exercise stimulus is currently limited, contradictory, and has mainly employed moderate-intensity continuous training (MICT) interventions³. Recently, we demonstrated a 12-week MICT or HIE training program largely abolished the post-continuous exercise elevation of cTnT at the same absolute intensity but had no effects on the post-continuous exercise appearance of cTnT at the same relative intensity³. To date, however, no study had directly determined the effects of multiple episodes of interval exercise on the appearance of acute interval exercise-induced cTn.

Consequently, the aims of the present study were (1) to compare cTnT appearance following acute HIE and SIE, when matched for total work and to determine the appearance of cTnT after RSE with short exercise duration (four minutes); and (2) to investigate the effects of 5, 19, and 43 sessions of training of HIE, SIE, and RES on cTnT responses to acute respective exercise. This study recruited young, sedentary, obese females who were completing a 12-week training program targeted at a health-related fitness changes in an at-risk group. This provided the opportunity to work in an ecologically valid training program and target an under-researched group (females generally, untrained). There is limited data evaluating sex-based differences in the cTn response to acute and chronic exercise but our knowledge of potential genetic^{11,12}, metabolic¹³ and health¹⁴ related differences in men and women undertaking training programs allied to the fact that that obesity is associated with higher resting cTn concentration¹⁵, and training status alters post-exercise cTn level¹⁶, suggest that sedentary, young, obese females might show marked adaptation of the exercise-related cTnT response with training.

Methods

Participants

Two hundred and ninety-eight volunteers were recruited publicly through local advertisements to participate in the study (Figure1). In total, 54 females were eligible according to the following inclusion criteria: 1) age range of 18–25 years; 2) body mass index (BMI) $\geq 25 \text{ kg.m}^{-2}$, which is the obesity cut-off for Asian adults¹⁷; 3) body weight remained constant ($\pm 2 \text{ kg}$) during the past three months; 4) no regular physical activities or exercise training; 5) no history of smoking; and 6) no history of hormonal, orthopedic, or cardiovascular diseases, diabetes, hyperlipidemia, hypertension, and polycystic ovary syndrome; and no current use of prescribed medication (including contraceptive pills). Eighteen eligible participants declined to enter the

study for personal reasons; the remaining 36 participants were randomly assigned to one of three groups: HIE (n = 12), SIE (n = 12), and RSE (n = 12). One participant in the SIE group (discontinued intervention) was not included in the final analysis. At the completion of the study, 12 participants from the HIE group, 11 participants from the SIE, and 12 participants from the RSE group were included in the final analysis. After receiving a thorough briefing, the participants gave their written informed consent to participate. The experiment was approved by the regional ethics committee for the use of human and animal subjects in research.

Insert Figure 1 here

Experimental design and procedures

Briefly, on the first and second visits to the laboratory, two respective exercise (HIE, SIE or RSE) sessions were performed to acclimate the participants to cycling and pacing exercise intensity on a cycle ergometer. At least three days later, maximal oxygen uptake ($\dot{V}O_{2\max}$) was completed. Five days after pre-intervention assessments, the HIE, SIE, and RSE groups commenced their respective training. The training period consisted of 44 training sessions carried out over a time span of 12 weeks for all three groups. The 1st (PRE), 6th (EARLY), 20th (MID), and 44th (END) training sessions were selected for observing the cTnT response to acute interval exercise. For each observation, after having refrained from strenuous exercise for 48 h, subsequent to a general warm-up, HIE, SIE, and RSE groups performed their respective scheduled training session on a cycle ergometer. Heart rate (HR) was recorded continuously via a portable HR monitor (Zephyr BioHarness 3.0, Zephyr Technology, Auckland, New Zealand). Immediately afterward, the participants rated the test for perceived exertion (RPE, Borg scale 6–20). Venous blood samples were drawn before exercise (Pre-exe), immediately after (0HR) as well as 3 h (3HR) and 4 h (4HR) after the training session to assess serum cTnT. The timing for the post-exercise blood samples were in accordance with our previous work that demonstrated that blood cTnT concentrations peaked 3 or 4 h after exercise in a laboratory-based study¹⁸. All exercise tests started at 11:00 a.m. and were performed in an air-conditioned laboratory (20 °C and 50% relative humidity). All participants were asked to maintain their daily activity and avoid altering their eating habits during the experimental period.

Exercise training

In each training session, the HIE group participants repeated 4-min exercise bouts on a cycle ergometer (Monark, 839E, Sweden) at an intensity of 90% $\dot{V}O_{2\max}$, followed by a 3-min passive recovery until the targeted 200 kJ of work was achieved. By contrast, the SIE group participants repeated 1-min exercise bouts on a cycle ergometer (Monark, 839E, Sweden) at an intensity of 120% $\dot{V}O_{2\max}$, followed by a 1.5-min passive recovery until the targeted 200 kJ of work was achieved. In both groups, participants were instructed to cycle as fast as possible at the beginning of each bout so as to get to the goal cadence of 60 rpm within 2 s, and then were required to keep their cadence at 60 rpm for the entire exercise bout time. The participants in the RSE group repeated 6-s “all-out” sprints interspersed with 9-s passive recovery on a cycle ergometer (Monark, 894E, Sweden) until the targeted 40 repetitions were achieved. At the beginning of the RSE training period, participants started with a resistance of 1.0 kg and worked as hard as they could during the sprinting phase. Once the participant’s fitness level was improved as indicated by reduced HR and perceived exertion (RPE, Borg scale 6–20), resistance was increased by increments of 0.5 kg until arriving at 5% of participant’s body weight. In each training session, three groups completed an identical 10-min warm-up and 5-min cool down at 50–60% of HR_{\max} . For the first four weeks all participants completed one session per day, three days per week. During the fifth through twelfth weeks, the training frequency was increased to four days per week in all three groups. All participants exercised with close supervision, and exercise HR and RPE were monitored at every training session. At the end of the fourth and eighth weeks, the $\dot{V}O_{2\max}$ of all participants was determined to readjust the workload corresponding to the pre-set intensity in HIE and SIE groups. All training sessions were supervised by a researcher, who provided verbal encouragement during the exercise bouts and ensure that the participants trained at the intended intensity. The training adherence of the participants was calculated as the percentage of the actual number of training sessions completed in compliance with the targeted intensity and duration, relative to the total number of training sessions prescribed.

Insert Table 1 here

Graded exercise test

$\dot{V}O_{2\max}$ was determined using a graded cycling exercise protocol that has been described previously³. The participants began at 50 W with a pedal frequency of 60 rpm on a cycle ergometer (Monark, 839E, Sweden); power output was increased by 30 W every 3 min until volitional

exhaustion. Oxygen consumption during the exercise test was measured using a Cosmed breath-by-breath metabolic analyzer (Quark-PFT-ergo, Cosmed, Rome, Italy). $\dot{V}O_{2\max}$ was calculated as the highest 30-s average value. Following the graded exercise test, a power output that elicited approximately 90% and 120% $\dot{V}O_{2\max}$ in the HIE and SIE groups, respectively, was selected from the linear relationship of steady-state $\dot{V}O_2$ versus power output.

Body composition measurement

The participants were instructed to refrain from exercise and alcohol consumption for 24 h. Before each test, participants underwent a 12-hour overnight food and fluid fast. After voiding, barefoot height was determined using a stadiometer and body mass and composition (fat mass, percent fat, and lean body mass) were assessed using multi-frequency bioelectrical impedance with eight tactile electrodes (InBody 720, Biospace Co., Seoul, Korea)¹⁹.

Blood sampling procedures

For each sample, 5 ml of venous blood was drawn from the antecubital vein by venipuncture with the subjects in a seated position. To separate serum, the blood was allowed to clot at room temperature and then centrifuged at 3500 g for 20 min. The serum was drawn off and stored at -80 °C for later analysis of cTnT. cTnT was measured quantitatively with a new high-sensitivity immunoassay based on electrochemiluminescence technology using a Cobas E 601 analyzer (Roche Diagnostics, Penzberg, Germany). This assay has a lower detection limit of 3 ng.l⁻¹ with a upper limit of 10,000 ng.l⁻¹. Serum cTnT concentrations that were below the limit of detection are reported as 1.5 ng.l⁻¹¹⁸. The coefficient of variation at a mean cTnT concentration of 13.5 ng.l⁻¹ is 5.2%. The upper reference limit (URL) for cTnT, defined as the 99th percentile of healthy participants, was 14 ng.l⁻¹²⁰.

Statistical analysis.

The Kolmogorov–Smirnov test was used to evaluate the normality of the data. Non-parametric Friedman's test was used to compare the cTnT across the time points (Pre-exe, 0HR, 3HR, and 4HR) and training sessions (PRE, EARLY, MID, and END) because of the skewed distribution of the cTnT data. Wilcoxon signed ranks tests were completed for pairwise comparisons where appropriate. Moreover, cTnT in the HIE, SIE, and RSE groups were compared using the Kruskal–Wallis test, and the Mann–Whitney U test was completed for pairwise comparisons where

appropriate. The percentages of subjects with cTnT exceeding the limit of detection of 3 ng.l⁻¹ (cTnT positive rate) and the URL of 14 ng.l⁻¹ at each assessment point were compared using Fisher's exact test.

A two-way ANOVA with repeated measures on time was used to examine the changes in work, power, exercise time, exercise mean HR, %HR_{max}, RPE and $\dot{V}O_{2\max}$ across the three groups (HIE, SIE, and RSE) and training period. *Post-hoc* analyses using Newman-Keuls were performed for cases in which the main effect was significant. Statistical significance was assumed at a level of $P < 0.05$. Data analysis was performed using the statistical software package SPSS 20.0 (IBM Corp., Armonk, NY, USA).

Results

No adverse events were reported during testing or training in all three groups. Among the participants who completed the study compliance with the exercise intervention was $99.6 \pm 1.3\%$, $99.0 \pm 2.1\%$, and $99.4 \pm 1.0\%$ in the HIE, SIE, and RSE groups, respectively. Training led to a gradual decrease in exercise time (only in HIE and SIE groups) and mean exercise HR as well as an increase in power (all $P < 0.05$) in a single training session of all groups (Table 1).

Participant characteristics at PRE, MID, and END are presented in Table 2. Training led to a similar decrease in body mass, BMI, body fat mass, and percent fat as well as a similar increase in $\dot{V}O_{2\max}$ (all $P < 0.05$) in all groups. Further, training led to an increase ($P < 0.05$) in Power_{exe} and decrease in HR_{mean} and %HR_{max} in all three groups (Table 3).

Insert Table 2 and Table 3 here

The acute exercise cTnT data for all three groups across the training period are presented as cohort data in Table 4 and as individual data points for pre-exercise (Pre-exe) and peak post-exercise (Post-exe) values in Figure 2. The cTnT increased after acute exercise ($P < 0.05$) at the PRE and EARLY assessments in all three groups with no between-group differences for HIE and SIE although the response after RSE was smaller. Accordingly, acute interval exercise also led to an increase ($P < 0.05$) in cTnT positive rates in the HIE (PRE, EARLY, and MID), SIE (PRE and MID), and RSE (PRE and EARLY). Finally, at the MID and END assessments acute HIE had no significant effect on cohort post-exercise cTnT (all $P > 0.05$) in all groups with a reduced frequency of positive individual cTnT responses.

Insert Table 4 and Figure 2 here

Discussion

To our knowledge, this study is the first to characterize cTnT responses to different forms of acute high intensity, intermittent exercise and to determine the impact of training progression in these forms of exercise on the cTnT response to acute interval exercise. The main findings of this study are that, for sedentary obese young women, 1) equal-work (200 kJ) HIE and SIE induced similar cTnT elevations after acute exercise before any significant training accumulation, 2) the cTnT response to an acute bout of RSE was elevated, but to a lesser extent than after HIE and SIE, 3) five sessions of training (HIE, SIE, or RSE) did not blunt the cTnT response to acute exercise, and 4) at the MID and END assessments acute HIE had no significant effect on cohort post-exercise cTnT in all groups with a reduced frequency of positive individual cTnT responses.

cTnT responses to three forms of acute high intensity interval exercise.

When all three groups were combined, we observed most of our participants (89%, 31 of 35) demonstrated an increase in cTnT after exercise at the PRE-assessment, but only 11% (four of 35) of them exceeded the URL (14 ng.l^{-1}). The prevalence (11%) is lower than that (83%) from a meta-analysis on continuous endurance exercise²¹ that used the same high-sensitivity assays. Given that a higher cardiac load is likely to result in a greater cTnT elevation⁶, the findings are not surprising, as the total mechanical work performed in the present study was very low (200kJ or ~ 50kJ) when compared with previous studies that used continuous endurance tasks over many hours, days and even weeks^{21,22}.

Our current data show that, when identical total mechanical work is being completed during the cycling trials, HIE and SIE elicited similar cTnT elevations despite employing different exercise intensities. Our group⁶ and Stewart et al²³ have demonstrated that continuous aerobic exercise performed above the gas exchange threshold can induce cTn elevation. The present study extends this to higher intensity and interval type exercise. We can conclude that equal-work interval exercise may induce similar cTnT elevation when intensity varies but is above the gas exchange threshold. Nevertheless, additional studies are still warranted to clarify whether, provided that total work accomplished are similar, variables of interval exercise such as intensity and duration of work and relief intervals can be manipulated without impacting cTnT response.

The similar cTnT elevation between HIE and SIE could be attributed to similar myocardial work, as reflected by relative HRs during exercise trials (HIE vs. SIE, %HR_{max}: 85 ± 4 vs. 85 ± 4). This must be approached with some caution considering that HR lag and inertia at exercise onset and cessation occurred during interval exercise⁷.

While previously thought to be a phenomenon exclusive to ultra-endurance exercise, cTnT elevation has also recently been found to be present after high-intensity exercise of relatively short duration such as half-marathon race²⁴. Our recent study suggests that the exercise-induced elevation of cTnT might occur even after a typical bout of physical activity recommended by public health guidelines³. In the present study, we complement our recent findings by showing the “all-out” sprints in RSE with very short duration also resulted in substantial cTnT elevation in most participants, but the increase was somewhat less than that in HIE or SIE, likely due to a much lower total mechanical work of RSE (RSE vs. HIE or SIE: ~ 50 vs. 200 kJ). To our knowledge, so far, the shortest exercise that elicited cTnT elevation only had a duration of 12 min (exercise session: two series of 12×30 -second sprints)²⁵. The current results with RSE further shorten the duration to 4 min and suggest that a surprisingly small amount of high-intensity interval exercise may lead to a small but detectable cTnT elevation. This is also the first study to demonstrate detectable cTnT elevation may be observed as short as 10 min following the start of the interval-type exercise (i.e., cTnT increase immediately after RSE), which indicates the exercise-induced cTnT elevation may occur rapidly. Considering shorter protocols are nowadays becoming a trend in health-related research²⁶ and interval type exercise is common in daily life, especially in children, it is important for future studies to identify how a short duration of exercise is still sufficient to cause high levels of cTnT in a range of different populations.

Impact of training progression on the cTnT response to acute interval exercise

Chen et al¹⁰ noted that eight days of continuous endurance swimming in rats significantly blunted the post-exercise cTnT response. This supports the concept that rapid cardioprotective effects may be evoked after a few episodes of exercise, termed “exercise preconditioning”⁹. In the present human study, we observed that similar cTnT responses to exercise between the first and sixth training sessions in all three regimes. These human data seem to indicate that cardioprotective effects after the five interval exercise sessions does not include a blunting of the cTnT response to acute exercise, and the reason(s) remains unclear. The standardized use of laboratory-based

settings in the current study largely excludes the possibility that the effects of environment influenced the exercise preconditioning in HIE and SIE. Considering the efficacy of classic preconditioning is attenuated in the presence of risk factors for cardiovascular disease (CVD), such as obesity⁹, we can speculate the fact that the female participants were obese may have impaired or delayed the exercise preconditioning. This speculation is supported by a field-based study showing, in subjects with CVD risk factors, moderate-intensity long-distance exercise-induced increase in cTnI levels was comparable across four consecutive exercise days²⁷. Nevertheless, to further support such an assertion, future studies in laboratory-based settings, which take risk factors of CVD into account, will need to be undertaken.

We recently assessed the effects of a 12-week training (~ 44 total sessions) program of interval exercise on cTnT response to continuous exercise³. Thus, the present study complements our prior work. In the current study, we observed that all forms of acute interval exercise at the last (the 44th) training session had no effect on the cohort cTnT concentration with almost no positive individual cTnT responses to acute interval exercise. The reduced myocardial work, as reflected by lower mean exercise HR and reduced exercise duration is likely, at least partially, to explain the blunting of the cTnT response. This speculation is supported by our recent observation that 12 weeks of high-intensity interval training largely abolished the post-continuous exercise elevation of cTnT at the same absolute intensity but had no effects on the post-continuous exercise appearance of cTnT at the same relative intensity³. In fact, exercise training *per se* may not abolish the post-exercise cTnT elevation but increases the absolute exercise intensity threshold for the cTnT elevations, by improving participants' cardiorespiratory fitness. Changes in fitness may explain contradictory results. For example, our current findings may seem to be at odds with Legaz-Arrese et al.²⁸ who noted that endurance training resulted in higher post-continuous exercise cTnT. Legaz-Arrese et al.²⁸ employed an all-out time trial as the acute exercise bout before and after training, and thus higher relative and absolute exercise intensities post-training can be assumed due to improved fitness levels. The higher post-exercise values of cTnT after training might be attributable to the higher exercise intensity post-training. Any training-induced changes in post-exercise cTnT must take into account absolute and relative intensity of the exercise provocation.

In addition, we also noted a gradual decrease in training HR during the progression of high-intensity interval training. This phenomenon also has been noted in our prior³ and another study²⁹. Of note, it has been suggested that the use of intermittent effort instead of continuous could have independent physiological effects such as metabolic fluctuations, which *per se* induces a greater activation of mitochondrial biogenesis³⁰. Whether this is related to a gradual decrease in exercise HR during the progression of interval training or an alternative explanation of the gradual blunting of the cTnT response to acute interval exercise in the present study is unclear but worth exploring in further research.

Individual variability in cTnT response to acute interval exercise

This study confirmed the findings of previous studies that considerable inter-individual variation exists in cTnT response to acute exercise^{24,31-34}. The novel aspect of our study is that we examined the effects of training progression on individual variability in response to three forms of interval exercise. The finding demonstrated a similar trend in changes in inter-subject variability from the 1st to 44th training session, and the largest inter-individual variability occurred on the 6th session (Figure 2). The factors that influence the marked inter-subject variability in the exercise-associated cTnT response are not fully understood but could not be explained in our data by power output and/or peak HR during exercise, exercise form, time of day, or environment. Moreover, there were no significant differences in age, body mass, $\dot{V}O_{2max}$, and percentage fat of subjects between high and low responders on the 1st, 6th or 20th training session, indicating that the variability could not be attributed to subject characteristics we assessed. Further determination of factors mediating this heterogeneity was constrained by our relatively small and homogeneous cohort. Of note, addressing a principal limitation of other studies^{16,32,33,35} that typically focused on single factors, Eijssvogels et al. assessed the influence of multiple parameters on post-exercise cTnI levels in a large and heterogeneous cohort, and noted a large portion (> 90%) of the post-exercise cTnI levels cannot be explained³⁶. Therefore, one may suggest that cTn increases seem to be random and be irrespective of subject and exercise characteristics.

Limitations

There are a few limitations that should be considered. The data in the current study pertain only to young female participants with obesity and, as such, generalizability of the data is limited. Further, although we attempted to control for menstrual cycle health (no oral contraceptive users

and no one with menstrual dysfunction) in the female participants, we could not constrain testing to specific phases of the menstrual cycle on each exercise session observed. This could have some influence upon post-exercise cTnT concentrations and a specific menstrual cycle phase study would be useful. In addition, although we made a great effort to control exercise intensity, the relatively exercise intensity performed in all trials of each training mode was not exactly the same, as the four assessments in the HIE and SIE occurred at different timepoints after applying the corresponding updated exercise power output, and the “all-out” nature of RSE. Nonetheless, given the ecological validity, we believe that our design is clinically relevant as this represents the *real* situation of interval training exposures. Finally, the logistical issues induced by doubling the number of tests in extremely short time windows (1st, 6th, 20th, and 44th training session) prevented the inclusion of control groups primarily due to our study design of a three-regime comparison.

In conclusion, in previously sedentary young obese females, equal-work HIE and SIE induced similar cTnT elevation in response to acute high intensity, intermittent exercise. A smaller cTnT increase also occurred after a smaller exercise volume associated with RSE. In all three training regimes, an elevated post-exercise cTnT could be expected in the early stages of training but this response was gradually abolished with increased exposure to interval exercise in real training settings. Clinicians should be aware that an elevated cTnT can be observed even after an extremely short duration of high-intensity interval exercise, and the progression of interval training can largely affect cTnT response to acute interval exercise.

Perspectives

In the current study, almost all participants presented with an increase in cTnT following interval exercise that suggests that an exercise-induced cTnT elevation is largely obligatory and thus likely physiological in nature. This argument is supported by our recent animal studies, which demonstrated that the elevation of cTnT post-exercise was not associated with any histological evidence of irreversible cardiomyocyte injury, suggesting a cytosolic release of the biomarker rather than a breakdown of bound contractile proteins³⁷. Based on our current data, clinicians should be aware that an elevated cTnT may occur rapidly following extremely short duration high-intensity interval exercise. Our study also provides some additional clinical insight, as we found that cTnT responses to interval exercise are dependent on training period. Specifically, an elevated cTnT can be expected in the early stages of interval training, but cTnT positive rates would reduce

with increased exposure to interval exercise in *real* training settings, e.g. the appearance of a large increase in cTnT (above the URL of 14 ng. l⁻¹) in interval training experienced participants with a recent history of acute interval exercise should raise a potential red flag for further clinical investigation. Such information is relevant for clinicians as it could improve medical decision-making.

Acknowledgement

This work was supported by the National Natural Science Foundation of China (Grant No. 31771319). The authors would like to express their appreciation to Mr. Ziwei Zheng and Mr. Xiangui Zhu for their support and assistance, and to the participants for their co-operation.

References

1. Wu AH, Apple FS, Gibler WB, Jesse RL, Warshaw MM, Valdes R, Jr. National Academy of Clinical Biochemistry Standards of Laboratory Practice: recommendations for the use of cardiac markers in coronary artery diseases. *Clin Chem*. 1999;45(7):1104-1121.
2. Shave R, Baggish A, George K, et al. Exercise-induced cardiac troponin elevation: evidence, mechanisms, and implications. *J Am Coll Cardiol*. 2010;56(3):169-176.
3. Nie J, Zhang H, Kong Z, et al. Impact of high-intensity interval training and moderate-intensity continuous training on resting and postexercise cardiac troponin T concentration. *Experimental physiology*. 2018;First published: 16 January 2018. DOI: 2010.1113/EP086767.
4. MacInnis MJ, Gibala MJ. Physiological adaptations to interval training and the role of exercise intensity. *The Journal of physiology*. 2017;595(9):2915-2930.
5. Gaesser GA, Angadi SS. High-intensity interval training for health and fitness: can less be more? *Journal of applied physiology (Bethesda, Md : 1985)*. 2011;111(6):1540-1541.
6. Fu F, Nie J, Tong T. Serum Cardiac Troponin T in Adolescent Runners: Effects of Exercise Intensity and Duration. *International Journal of Sports Medicine*. 2009;30(3):168-172.
7. Buchheit M, Laursen PB. High-intensity interval training, solutions to the programming puzzle: Part I: cardiopulmonary emphasis. *Sports medicine (Auckland, NZ)*. 2013;43(5):313-338.
8. Taylor J, Macpherson T, Spears I, Weston M. The effects of repeated-sprint training on field-based fitness measures: a meta-analysis of controlled and non-controlled trials. *Sports medicine (Auckland, NZ)*. 2015;45(6):881-891.
9. Thijssen DHJ, Redington A, George KP, Hopman MTE, Jones H. Association of Exercise Preconditioning With Immediate Cardioprotection: A Review. *JAMA Cardiol*. 2018;3(2):169-176.
10. Chen Y, Serfass RC, Mackey-Bojack SM, Kelly KL, Titus JL, Apple FS. Cardiac troponin T alterations in myocardium and serum of rats after stressful, prolonged intense exercise. *Journal of applied physiology (Bethesda, Md : 1985)*. 2000;88(5):1749-1755.
11. Semenas E, Nozari A, Wiklund L. Sex differences in cardiac injury after severe haemorrhage and ventricular fibrillation in pigs. *Resuscitation*. 2010;81(12):1718-1722.

- 12.Spolarics Z. The X-files of inflammation: cellular mosaicism of X-linked polymorphic genes and the female advantage in the host response to injury and infection. *Shock (Augusta, Ga)*. 2007;27(6):597-604.
- 13.Foryst-Ludwig A, Kintscher U. Sex differences in exercise-induced cardiac hypertrophy. *Pflugers Archiv : European journal of physiology*. 2013;465(5):731-737.
- 14.Genovesi S, Zaccaria D, Rossi E, Valsecchi MG, Stella A, Stramba-Badiale M. Effects of exercise training on heart rate and QT interval in healthy young individuals: are there gender differences? *Europace*. 2007;9(1):55-60.
- 15.Daniels LB. The enemy of good?: making the most of highly sensitive troponin assays. *J Am Coll Cardiol*. 2013;61(18):1914-1916.
- 16.Mehta R, Gaze D, Mohan S, et al. Post-exercise cardiac troponin release is related to exercise training history. *Int J Sports Med*. 2012;33(5):333-337.
- 17.World Health Organization. The Asia-Pacific perspective: redefining obesity and its treatment. In: Sydney: Health Communications Australia; 2000.
- 18.Tian Y, Nie J, Huang C, George KP. The kinetics of highly sensitive cardiac troponin T release after prolonged treadmill exercise in adolescent and adult athletes. *Journal of Applied Physiology*. 2012;113(3):418-425.
- 19.Kyle UG, Bosaeus I, De Lorenzo AD, et al. Bioelectrical impedance analysis-part II: utilization in clinical practice. *Clinical nutrition (Edinburgh, Scotland)*. 2004;23(6):1430-1453.
- 20.Giannitsis E, Kurz K, Hallermayer K, Jarausch J, Jaffe AS, Katus HA. Analytical validation of a high-sensitivity cardiac troponin T assay. *Clin Chem*. 2010;56(2):254-261.
- 21.Sedaghat-Hamedani F, Kayvanpour E, Frankenstein L, et al. Biomarker changes after strenuous exercise can mimic pulmonary embolism and cardiac injury--a metaanalysis of 45 studies. *Clin Chem*. 2015;61(10):1246-1255.
- 22.Gresslien T, Agewall S. Troponin and exercise. *Int J Cardiol*. 2016;221:609-621.
- 23.Stewart GM, Yamada A, Haseler LJ, et al. Influence of exercise intensity and duration on functional and biochemical perturbations in the human heart. *The Journal of physiology*. 2016;594(11):3031-3044.
- 24.Nie J, George KP, Tong TK, et al. The Influence of a Half-Marathon Race Upon Cardiac Troponin T Release in Adolescent Runners. *Current Medicinal Chemistry*. 2011;18(23):3452-3456.
- 25.Weippert M, Divchev D, Schmidt P, et al. Cardiac troponin T and echocardiographic dimensions after repeated sprint vs. moderate intensity continuous exercise in healthy young males. *Scientific reports*. 2016;6:24614.
- 26.Vollaard NBJ, Metcalfe RS. Research into the Health Benefits of Sprint Interval Training Should Focus on Protocols with Fewer and Shorter Sprints. *Sports medicine (Auckland, NZ)*. 2017;47(12):2443-2451.
- 27.Eijssvogels T, George K, Shave R, et al. Effect of prolonged walking on cardiac troponin levels. *Am J Cardiol*. 2010;105(2):267-272.
- 28.Legaz-Arrese A, Lopez-Laval I, George K, et al. Impact of an endurance training program on exercise-induced cardiac biomarker release. *American journal of physiology Heart and circulatory physiology*. 2015;308(8):H913-920.
- 29.Zhang H, Tong TK, Qiu W, et al. Comparable Effects of High-Intensity Interval Training and Prolonged Continuous Exercise Training on Abdominal Visceral Fat Reduction in Obese Young Women. *Journal of diabetes research*. 2017;2017:5071740.

30. Combes A, Dekerle J, Webbourn N, Watt P, Bougault V, Daussin FN. Exercise-induced metabolic fluctuations influence AMPK, p38-MAPK and CaMKII phosphorylation in human skeletal muscle. *Physiol Rep*. 2015;3(9).
31. Nie J, George KP, Tong TK, Tian Y, Shi Q. Effect of Repeated Endurance Runs on Cardiac Biomarkers and Function in Adolescents. *Medicine and Science in Sports and Exercise*. 2011;43(11):2081-2088.
32. Legaz-Arrese A, Lopez-Laval I, George K, et al. Individual variability in cardiac biomarker release after 30 min of high-intensity rowing in elite and amateur athletes. *Appl Physiol Nutr Metab*. 2015;40(9):951-958.
33. Legaz-Arrese A, Lopez-Laval I, George K, et al. Individual variability of high-sensitivity cardiac troponin levels after aerobic exercise is not mediated by exercise mode. *Biomarkers*. 2015;20(4):219-224.
34. Nie J, Tong TK, George K, Fu FH, Lin H, Shi Q. Resting and post-exercise serum biomarkers of cardiac and skeletal muscle damage in adolescent runners. *Scandinavian Journal of Medicine & Science in Sports*. 2011;21(5):625-629.
35. Lopez-Laval I, Legaz-Arrese A, George K, et al. Cardiac troponin I release after a basketball match in elite, amateur and junior players. *Clin Chem Lab Med*. 2016;54(2):333-338.
36. Eijssvogels TM, Hoogerwerf MD, Maessen MF, et al. Predictors of cardiac troponin release after a marathon. *J Sci Med Sport*. 2015;18(1):88-92.
37. Nie J, George K, Duan F, Tong TK, Tian Y. Histological evidence for reversible cardiomyocyte changes and serum cardiac troponin T elevation after exercise in rats. *Physiol Rep*. 2016;4(24):e13083.

Table 1. The work, power, exercise time, mean heart rate (HR) and rating of perceived exertion (RPE) of training sessions during the 12-week intervention consisted of 44 training sessions. (Data are mean \pm SD)

	HIE (n=12)			SIE (n=11)			RSE (n=12)		
	Session 1-12	Session 13-28	Session 29-44	Session 1-12	Session 13-28	Session 29-44	Session 1-12	Session 13-28	Session 29-44
Work (kJ)	200	200	200	200	200	200	48 \pm 4	57 \pm 4*	64 \pm 6* [†]
Power (Watt)	119 \pm 12	132 \pm 14*	146 \pm 15* [†]	161 \pm 18	191 \pm 19*	205 \pm 21* [†]	202 \pm 16	238 \pm 16*	269 \pm 24* [†]
Exercise time (min)	28.3 \pm 2.8	25.5 \pm 2.8*	23.1 \pm 2.5* [†]	21.0 \pm 2.2	17.6 \pm 1.8*	16.4 \pm 1.8* [†]	4 \pm 0	4 \pm 0	4 \pm 0
HR (beats.min ⁻¹)	174 \pm 7	174 \pm 11	168 \pm 7*	168 \pm 9	164 \pm 7	162 \pm 7*	175 \pm 8	168 \pm 7*	165 \pm 8* [†]
RPE	16 \pm 1	17 \pm 1*	17 \pm 1*	16 \pm 1	17 \pm 1*	17 \pm 1*	15 \pm 1	16 \pm 1	16 \pm 1

HIE, high-intensity interval exercise training; SIE, sprint interval exercise training; RSE, repeated sprint exercise training

* Significantly different from corresponding value of Session 1-12, $P < 0.05$

[†] Significantly different from corresponding value of Session 13-28, $P < 0.05$

Table 2. Participant characteristics during the 12-week intervention consisted of 44 training sessions. (Data are mean \pm SD)

	HIE (n=12)			SIE (n=11)			RSE (n=12)		
	PRE	MID	END	PRE	MID	END	PRE	MID	END
Age (yr)	20.0 \pm 1.0			20.5 \pm 1.6			21.2 \pm 2.0		
Height (cm)	161.0 \pm 6.7			163.4 \pm 2.7			162.3 \pm 5.6		
Weight (kg)	70.0 \pm 7.5	68.4 \pm 6.3*	65.7 \pm 6.7*†	74.4 \pm 11.3	72.5 \pm 10.5*	71.1 \pm 10.9*†	69.5 \pm 6.8	67.4 \pm 6.7*	64.9 \pm 6.2*†
Body mass index (kg.m ⁻²)	27.0 \pm 2.8	26.2 \pm 2.8*	25.5 \pm 3.0*†	27.9 \pm 4.3	27.2 \pm 4.0*	26.6 \pm 4.2*†	26.4 \pm 1.9	25.6 \pm 2.0*	24.6 \pm 1.8*†
Body fat (%)	33.4 \pm 2.8	31.5 \pm 3.3*	30.0 \pm 3.5*†	33.4 \pm 3.7	31.3 \pm 3.7*	31.5 \pm 4.4*	32.5 \pm 2.3	30.2 \pm 2.7*	28.9 \pm 2.5*†
Fat mass (Kg)	24.3 \pm 3.8	21.6 \pm 3.9*	19.9 \pm 4.1*†	25.2 \pm 6.7	23.3 \pm 6.5*	22.9 \pm 6.8*	22.4 \pm 3.7	20.5 \pm 3.4*	18.8 \pm 2.9*†
$\dot{V}O_{2max}$ (ml.kg ⁻¹ .min ⁻¹)	28.5 \pm 2.2	32.2 \pm 2.1*	36.7 \pm 4.2*†	26.2 \pm 4.4	29.9 \pm 3.7*	35.2 \pm 5.8*†	27.6 \pm 3.3	30.4 \pm 2.4*	33.6 \pm 2.9*†
$\dot{V}O_{2max}$ (ml.kg _{FFM} ⁻¹ .min ⁻¹)	44.0 \pm 3.2	47.6 \pm 3.7*	52.5 \pm 6.9*†	39.2 \pm 5.4	43.6 \pm 3.7*	51.5 \pm 7.5*†	40.7 \pm 5.4	43.7 \pm 3.6	47.2 \pm 4.0*†

HIE, high-intensity interval exercise training; SIE, sprint interval exercise training; RSE, repeated sprint exercise training; PRE, before the 1st exercise session; MID, after the 12th exercise session; END, after the 44th exercise session.

* Significantly different from corresponding value of PRE, $P < 0.05$

† Significantly different from corresponding value of MID, $P < 0.05$

Table 3. Acute exercise data during the 12-week intervention consisted of 44 training sessions. (Data are mean \pm SD)

	Power_{exe} (W)	Time_{exe} (min)	Work_{exe} (KJ)	HR_{mean} (beat.min ⁻¹)	%HR_{max}	RPE
HIE (n=12)						
PRE	119 \pm 12	28 \pm 3	200 \pm 0	157 \pm 9	85 \pm 4	15 \pm 3
EARLY	119 \pm 12	28 \pm 3	200 \pm 0	155 \pm 6	84 \pm 4	16 \pm 3
MID	132 \pm 14* [†]	26 \pm 3* [†]	200 \pm 0	147 \pm 7* [†]	80 \pm 5* [†]	18 \pm 1*
END	146 \pm 15* ^{†‡}	23 \pm 3* ^{†‡}	200 \pm 0	144 \pm 11* [†]	79 \pm 7* [†]	18 \pm 2*
SIE (n=11)						
PRE	160 \pm 18	21 \pm 2	200 \pm 0	148 \pm 11	85 \pm 4	18 \pm 2
EARLY	160 \pm 18	21 \pm 2	200 \pm 0	147 \pm 7	85 \pm 5	17 \pm 3
MID	191 \pm 19* [†]	18 \pm 2* [†]	200 \pm 0	146 \pm 7	84 \pm 5	19 \pm 2
END	205 \pm 21* ^{†‡}	16 \pm 2* ^{†‡}	200 \pm 0	138 \pm 11* ^{†‡}	79 \pm 7* ^{†‡}	18 \pm 2
RSE (n=12)						
PRE	193 \pm 17	4 \pm 0	46 \pm 4	169 \pm 5	94 \pm 7	18 \pm 2
EARLY	204 \pm 15*	4 \pm 0	49 \pm 4*	171 \pm 8	95 \pm 6	18 \pm 1
MID	256 \pm 31* [†]	4 \pm 0	61 \pm 8* [†]	166 \pm 6 [†]	92 \pm 7 [†]	19 \pm 1
END	282 \pm 30* ^{†‡}	4 \pm 0	67 \pm 8* ^{†‡}	156 \pm 9* ^{†‡}	87 \pm 9* ^{†‡}	19 \pm 1

HIE, high-intensity interval exercise training; SIE, sprint interval exercise training; RSE, repeated sprint exercise training; PRE, the 1st training session; EARLY, the 6th training session; MID, the 20th training session; END, the 44th training session (the last training session of the twelfth week); Power_{exe}, power output during exercise; Time_{exe}, total exercise duration; Work_{exe}, work output during exercise; HR_{mean}, mean heart rate during training session; %HR_{max}, percentage of individual maximal heart rate during training session; RPE, rating of perceived exertion at end of exercise

* Significantly different from corresponding value of PRE, $P < 0.05$

[†] Significantly different from corresponding value of EARLY, $P < 0.05$

[‡] Significantly different from corresponding value of MID, $P < 0.05$

Table 4. Serum cardiac troponin T (ng.l⁻¹) before (Pre-exe) and immediately (0HR), 3h (3HR) and 4 h (4HR) after a training session of high-intensity interval exercise (HIE), sprint interval exercise (SIE) and repeated sprint exercise (RSE) during the 12-week intervention.

	Pre-exe	0HR	3HR	4HR
Median (Range)				
HIE (n=12)				
PRE	1.50 (1.50-4.74)	1.50 (1.50-4.65)	5.92 (4.70-35.93)*†	6.10 (3.98-26.88)*†
EARLY	1.50 (1.50-5.15)	2.42 (1.50-5.50)*†	7.24 (1.50-63.78)*†	6.58 (1.50-49.56)*†
MID	1.50 (1.50-1.50)	1.50 (1.50-1.50)	1.50 (1.50-20.07)	1.50 (1.50-20.09)
END ^a	1.50 (1.50-1.50)	1.50 (1.50-3.09)	1.50 (1.50-4.17)	1.50 (1.50-3.59)
SIE (n=11)				
PRE	1.50 (1.50-3.98)	1.50 (1.50-4.20)	6.27 (3.24-37.51)*†	5.34 (1.50-28.25)*†
EARLY	1.50 (1.50-3.91)	1.50 (1.50-7.32)	4.42 (1.50-51.94)*†	4.32 (1.50-47.18)*†
MID	1.50 (1.50-1.50)	1.50 (1.50-1.50)	1.50 (1.50-9.21)	1.50 (1.50-7.20)
END	1.50 (1.50-1.50)	1.50 (1.50-1.50)	1.50 (1.50-7.45)	1.50 (1.50-6.73)
RSE (n=12)				
PRE	1.50 (1.50-3.46)	2.30 (1.50-3.98)*	3.63 (1.50-8.21)*‡	3.41 (1.50-7.29)*
EARLY	1.50 (1.50-3.12)	1.50 (1.50-3.62)	3.03 (1.50-15.49)*	3.68 (1.50-13.42)*
MID	1.50 (1.50-4.27)	1.50 (1.50-5.12)	1.50 (1.50-6.93)	1.50 (1.50-6.56)
END	1.50 (1.50-1.50)	1.50 (1.50-1.50)	1.50 (1.50-4.41)	1.50 (1.50-1.50)
Positive Rate 1 / 2 (%)				
HIE (n=12)				
PRE	8.3 / 0	33.3 / 0	100*† / 16.7	100*† / 16.7
EARLY	41.7 / 0	50.0 / 0	83.3*† / 25.0	91.7*† / 16.7
MID	0 / 0	0 / 0	41.7* / 8.3	41.7* / 8.3
END ^a	0 / 0	8.3 / 0	8.3 / 0	8.3 / 0
SIE (n=11)				
PRE	27.3 / 0	27.3 / 0	100*† / 18.2	81.8*† / 18.2
EARLY	36.4 / 0	45.5 / 0	72.7 / 9.1	72.7 / 9.1
MID	0 / 0	0 / 0	45.5* / 0	36.4* / 0
END	0 / 0	0 / 0	18.2 / 0	18.2 / 0
RSE (n=12)				
PRE	16.7 / 0	50.0 / 0	66.7*†‡ / 0	58.3* / 0
EARLY	8.3 / 0	16.7 / 0	58.3* / 8.3	75.0*† / 0
MID	8.3 / 0	8.3 / 0	25.0 / 0	25.0 / 0
END	0 / 0	0 / 0	8.3 / 0	0 / 0

PRE, the 1st training session; EARLY, the 6th training session; MID, the 20th training session; END, the 44th training session; Positive Rate 1, percentage of subjects with cTnT exceeding the limit of detection of 3 ng.l⁻¹; Positive Rate 2, percentages of subjects with cTnT exceeding the upper reference limit of 14 ng.l⁻¹; ^a n=11

* Significantly different from corresponding Pre-exe value, P<0.05

† Significantly different from corresponding MID and END value, P<0.05

‡ Significantly different from corresponding HIE and SIE value, P<0.05

Figure legends

Figure 1. The recruitment, retention and group designation participants throughout the trial.

HIE, high-intensity interval exercise training; SIE, sprint interval exercise training; RSE, repeated sprint exercise training

Figure 2. Pre-exercise (Pre-exe) and peak post-exercise (Post-exe) cardiac troponin T (cTnT, ng.l⁻¹) after a training session of high-intensity interval exercise (HIE), sprint interval exercise (SIE) and repeated sprint exercise (RSE) during the 12-week intervention (scale is log plotted because of the data spread). Individual data points are presented by circles with values for the same participant connected by lines for each condition.

Note: PRE, the 1st training session; EARLY, the 6th training session; MID, the 20th training session; END, the 44th training session; The horizontal dotted line is the upper reference limit; The double-arrow line is the median of cTnT values at pre-exercise (Pre-exe) or Post-exercise (Post-exe); ○, single subject; ⁿ●, n subjects;

* Significantly different from corresponding Pre-exe value, $P < 0.05$;

‡ Significantly different from corresponding HIE and SIE value, $P < 0.05$

Figure 1

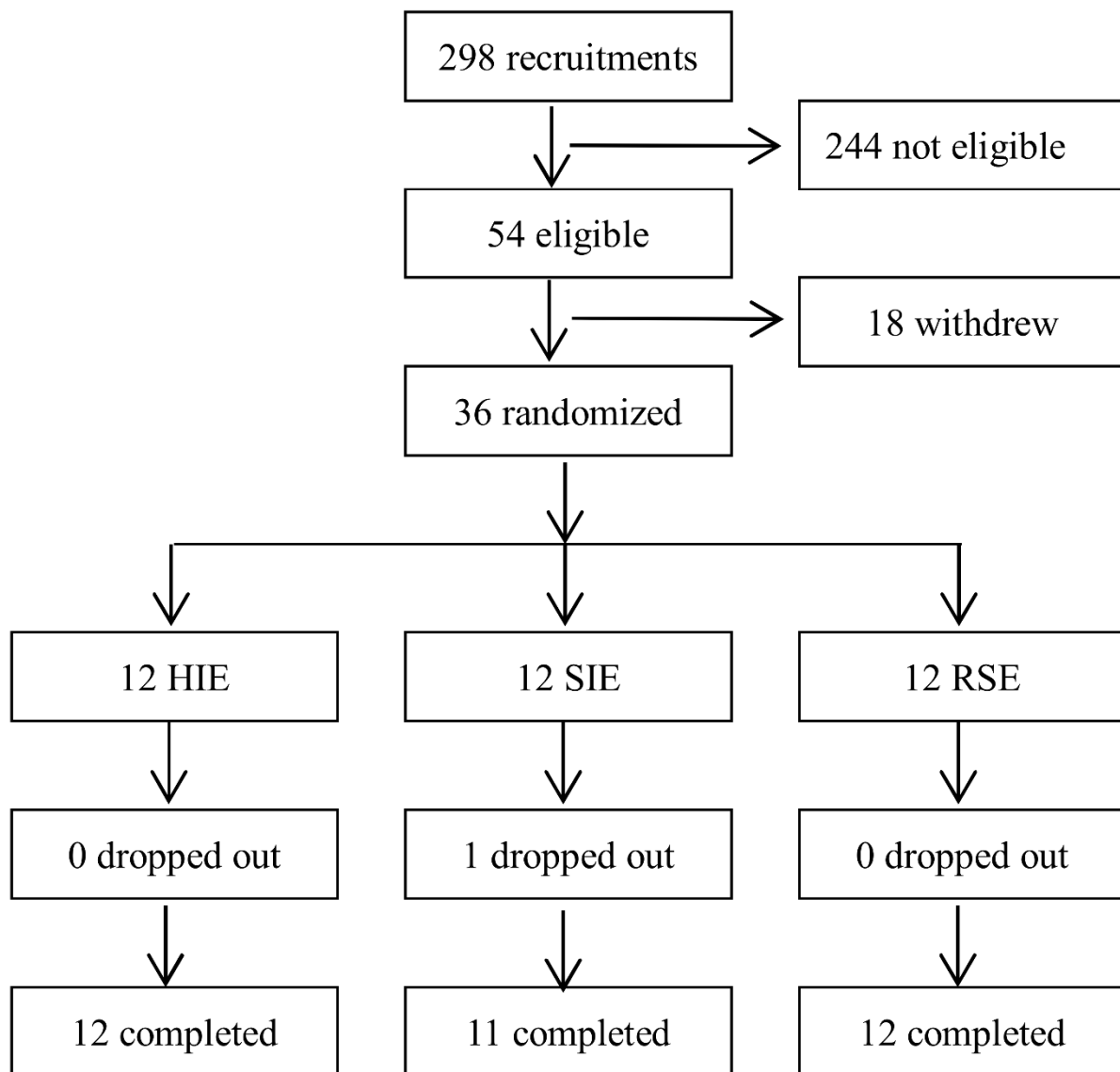


Figure 2

