



LJMU Research Online

Legaz-Arrese, A, Lopez-Laval, I, George, KP, Jose Puente-Lanzarote, J, Moliner-Urdiales, D, Javier Ayala-Tajuelo, V, Mayolas-Pi, C and Reverter-Masia, J

Individual variability in cardiac biomarker release after 30 min of high-intensity rowing in elite and amateur athletes

<http://researchonline.ljmu.ac.uk/3169/>

Article

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

Legaz-Arrese, A, Lopez-Laval, I, George, KP, Jose Puente-Lanzarote, J, Moliner-Urdiales, D, Javier Ayala-Tajuelo, V, Mayolas-Pi, C and Reverter-Masia, J (2015) Individual variability in cardiac biomarker release after 30 min of high-intensity rowing in elite and amateur athletes. APPLIED

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/>



Applied Physiology, Nutrition, and Metabolism
Physiologie appliquée, nutrition et métabolisme

Individual variability in cardiac biomarker release after 30 min high intensity rowing in elite and amateur athletes

Journal:	<i>Applied Physiology, Nutrition, and Metabolism</i>
Manuscript ID:	apnm-2015-0055.R1
Manuscript Type:	Article
Date Submitted by the Author:	n/a
Complete List of Authors:	Legaz-Arrese, Alejandro; University of Zaragoza, Section of Physical Education and Sports López-Laval, Isaac; University of Zaragoza, George, Keith; John Moores University Puente-Lanzarote, Juan José; Lozano Blesa University Hospital, Moliner-Urdiales, Diego; University Jaume I, Ayala-Tajuelo, Vicente; Consorcio Hospitalario Provincial de Castellón, Mayolas-Pi, Carmen; University of Zaragoza, Reverter-Masià, Joaquín; University of Lleida
Keyword:	athlete performance, elite athlete performance < athlete performance, exercise intensity < exercise, exercise performance < exercise, exercise physiology < exercise

SCHOLARONE™
Manuscripts

1 *Individual variability in cardiac biomarker release after 30 min high intensity rowing in*
2 *elite and amateur athletes*

3

4 Legaz-Arrese A, López-Laval I, George K, Puente-Lanzarote JJ, Moliner-Urdiales D, Ayala-
5 Tajuelo VJ, Mayolas-Pi C, Reverter-Masià J

6

7 *Alejandro Legaz-Arrese. Section of Physical Education and Sports, University of Zaragoza. C/Domingo Miral
8 S/N, 50009 Zaragoza, Spain. Phone: 0034676226874. Fax: 0034976761720. E-mail: alegaz@unizar.es.

9 Isaac López-Laval. Section of Physical Education and Sports, University of Zaragoza. C/Domingo Miral S/N,
10 50009 Zaragoza, Spain. Phone: 0034666434773. E-mail: ilopezlaval@hotmail.com.

11 Keith George. Resarch Institute for Sport and Exercise Sciences, Liverpool John Moores University, Byron
12 Street L3 3AF, Liverpool, UK. Phone: +44(0)1519046228. K.George@ljmu.ac.uk.

13 Juan José Puente-Lanzarote. Service of Biochemistry, Lozano Blesa University Hospital, C/Domingo Miral
14 S/N, 30009 Zaragoza, Spain. Phone: 0034976765700. jjpuente@salud.aragon.es.

15 Diego Moliner-Urdiales. Department of Education, University Jaume I, Avda Sos Baynat s/n, 12071 Castellón,
16 Spain. Phone: 0034964728000. E-mail: moliner18891@hotmail.com.

17 Vicente Ayala-Tajuelo. Consorcio Hospitalario Provincial de Castellón, Avinguda del Doctor Clarà, 19, 12002
18 Castellón, Spain. Phone: 0034964359700. E-mail: informacion@dipc.es.

19 Carmen Mayolas-Pi. Section of Physical Education and Sports, University of Zaragoza. C/Domingo Miral S/N,
20 50009 Zaragoza, Spain. Phone: 0034976761000. E-mail: carmayo@unizar.es.

21 Joaquín Reverter-Masià. Research Group Human Movement, University of Lleida, C/Partida Caparrella S/N,
22 25192 LLeida, Spain. Phone: 0034625375734. E-mail: reverter@didesp.udl.cat.

23

24 *Corresponding author.

25

26

27

28

29

30

31 **Abstract**

32 This study had two specific objectives; 1) to examine the individual variation in the pattern of
33 cardiac troponin I (cTnI) and N-terminal pro-brain natriuretic peptide (NT-proBNP) response
34 to high intensity rowing exercise, and 2) to establish if individual heterogeneity in biomarker
35 appearance was influenced by athletic status (elite vs. amateur). We examined cTnI and NT-
36 proBNP in 18 elite and 14 amateur rowers before and 5 min, 1, 3, 6, 12, and 24 h after a 30
37 min maximal rowing test. Peak post-exercise cTnI (pre: 0.014 ± 0.030 , peak post: $0.058 \pm$
38 $0.091 \mu\text{g.L}^{-1}$, $p = 0.000$) and NT-proBNP (pre: 15 ± 11 , peak post: $31 \pm 19 \text{ ng.L}^{-1}$, $p = 0.000$)
39 were elevated. Substantial individual heterogeneity in peak and time course data noted for
40 cTnI. Peak cTnI exceeded the upper reference limit (URL) in 9 elite and 3 amateur rowers.
41 No rower exceeding the URL for NT-proBNP. Elite rowers had higher baseline ($0.019 \pm$
42 0.038 vs. $0.008 \pm 0.015 \mu\text{g.L}^{-1}$; $p = 0.003$) and peak post-exercise cTnI (0.080 ± 0.115 vs.
43 $0.030 \pm 0.029 \mu\text{g.L}^{-1}$; $p = 0.022$) than amateur rowers but the change with exercise was
44 similar between groups. There were no significant differences in baseline and peak post-
45 exercise NT-proBNP between groups. In summary, marked individuality in cTnI response
46 was noted to a short but high intensity rowing bout. Athlete status did not seem to mediate
47 the change in cardiac biomarkers to high intensity exercise.

48

49 **Keywords:** exercise; cTnI; NT-proBNP; athletic status; rowing, elite athletes, amateur athlete

50

51

52

53

54

55

56 ***Introduction***

57 An increasing number of studies have described the elevation of cardiac troponin I (cTnI), a
58 biomarker of cardiac cell necrosis, and N-terminal pro-brain natriuretic peptide (NT-proBNP),
59 a biomarker of cardiac dysfunction, after prolonged and strenuous exercise (Scharhag et al.
60 2008; Shave et al. 2010a). The cardiac biomarker response to short-duration, high-intensity
61 exercise is largely unknown although some have suggested that within the endurance exercise
62 domain cTnI increased with exercise intensity (Legaz-Arrese et al. 2011; Serrano-Ostáriz et
63 al. 2011). Shave et al. (2010b) are one of the few groups to have studied the cTnI response
64 shorter, high-intensity bouts of exercise. In spite of the limited volume of exercise (30 min
65 all-out treadmill run) cTnI was elevated during recovery in 75% of athletes (Shave et al.
66 2010b).

67 Importantly Shave et al. (2010b) observed that the cTnI appearance during recovery was
68 markedly heterogeneous and confirmed similar individuality of response noted in field based
69 studies of prolonged exercise (Shave et al. 2010a) as well as an observation from a meta-
70 analysis (Shave et al. 2007). The percentage of individuals with post-exercise cTnI or cTnT
71 levels above the upper reference limit (URL) has varied from 0% (Roth et al. 2007) to 100%
72 (Middleton et al. 2008) in individual studies but this may partially represent the “lottery” of a
73 single post-exercise blood test. It is important that in on-going cardiac biomarker research
74 that multiple post-exercise blood draws occur to fully understand any heterogeneity in cTnI
75 or NTpro-BNP peak concentrations as well as recovery kinetics (Middleton et al. 2008).

76 The influence of exercise intensity on NT-proBNP release is less well known. Within the
77 endurance exercise domain data suggests that NT-proBNP increase may be more influenced
78 by exercise duration (Serrano-Ostáriz et al. 2009) but studies involving shorter bouts of high
79 intensity exercise in well-trained athletes are limited.

80 Individual variability in biomarker response in the extant literature has been speculated to be,
81 at least partially, related to training or “athletic” status. It has been suggested that highly-
82 trained individuals have lower post-exercise cTnI and NT-proBNP release (Mehta et al. 2012;
83 Neilan et al. 2006). Indeed, the only two previous studies on elite athletes reported normal
84 post-exercise cardiac biomarker levels (Bonetti et al. 1996; König et al. 2003). Contrary, we
85 have recently observed in untrained subjects that a controlled endurance training intervention
86 resulted in higher pre- and post-exercise values of cTn with no changes in NT-proBNP
87 (Legaz-Arrese et al., 2015). Currently, the influence of training level on cardiac biomarker
88 release has not yet been evaluated in a controlled study with disparate groups in terms of
89 training or athletic status completing a similar (relative) high intensity exercise bout. Finally,
90 it has been postulated that increases in both biomarkers may be dependent on their respective
91 resting values (Legaz Arrese et al. 2005; Serrano-Ostáriz et al. 2011) although this construct
92 has not been studied in different athlete groups.

93 Consequently, the purpose of the present study was to determine the cardiac biomarker
94 response to a short duration, high intensity bout of rowing with specific emphasis on detailing
95 individual responses across multiple assessment points during a 24 hr recovery period. A
96 secondary purpose was to determine the influence of athlete status on cTnI and NT-proBNP
97 release by comparing two cohorts; amateur and elite rowers.

98

99 ***Material and Methods***

100

101 *Participants*

102 Thirty-two male rowers were recruited from a large Rowing Club in Spain through an open
103 invitation to all of its members. Volunteers included elite rowers ($n = 18$) who had at least 3
104 yr of competitive history at the national or international level (1 world champion, 1 under-23

105 world champion, 1 Olympic competitor, 2 Spanish champions, and 3 Spanish sub-
106 champions) and were training ≥ 5 days per week and non-competitive amateur rowers ($n =$
107 14) who trained ≤ 3 days per week. All rowers provided informed written consent. The study
108 followed the ethical guidelines of the Declaration of Helsinki and was approved by the
109 Research Ethics Committee of the Government of Aragón (CEICA; Spain).

110

111 *Research Design and Protocols*

112 All rowers attended a preliminary testing session 1 week before the main study was
113 performed. At this initial testing body height was measured to the nearest 0.1 cm (SECA 225
114 SECA, Hamburg, Germany). Body mass was determined to the nearest 0.05 kg (SECA 861,
115 SECA, Hamburg, Germany). A questionnaire was completed to obtain personal data,
116 performance level, training history, and history of any cardiac symptoms. Exclusion criteria
117 were a significant personal or early family history of cardiovascular disease and/or abnormal
118 ECG at baseline examination.

119 The rowers then performed a progressive incremental test to exhaustion on a Concept II
120 rowing ergometer (Model C, Morrisville, VT, USA) to determine the maximal heart rate
121 (HR) (Polar Electro Oy, Kempele, Finland). Prior to the test, the rowers completed a self-
122 paced 5-min warm-up ($HR < 130 \text{ beats} \cdot \text{min}^{-1}$). The test began at a workload of 150 W (elite
123 rowers) or 75 W (amateur rowers) with workload increments of 50 W every 3 min until
124 exhaustion. Strong verbal encouragement was provided to all participants.

125 After a minimum of 7 days all participants returned to the laboratory to complete the 30 min
126 rowing test. All participants were fully habituated to the 30 min all-out rowing test protocol
127 and were asked to abstain from strength training and strenuous exercise for 48 h before
128 testing. All high-intensity testing sessions occurred at 11:00 am in a sports hall at a
129 temperature of 18-21 °C and a relative humidity of 50-60%. The rowers completed a self-

130 paced 5-min warm-up (HR <130 beats.min⁻¹) followed by a 30-min “all-out” rowing test.
131 Pairs of rowers competed side-by-side to mimic a regular competition and again strong verbal
132 encouragement was provided. During the test HR was recorded continuously via a Polar HR
133 monitor (Polar Electro Oy, Kempele, Finland) and downloaded using Polar Precision
134 Performance software (v. 3.0). The mean power output (W) and distance covered were
135 recorded every 5 min from the rowing ergometer screen. Immediately after the test was
136 completed, the participants rated the test for perceived exertion (RPE) (Borg and Kaijser
137 2006). Venous blood samples were taken before, immediately after (5 min), as well as 1, 3, 6,
138 12, and 24 h after exercise to assess serum cardiac-specific biomarkers.

139

140 *Blood Sampling and Analysis*

141 Blood samples were drawn by repetitive venipuncture from an antecubital vein and quickly
142 centrifuged. The serum and plasma were drawn off and stored at -80 °C for later analysis.
143 cTnI was analyzed from samples of EDTA (ethylenediaminetetraacetic acid) plasma with the
144 Access AccuTnI assay (Beckman Coulter, Fullerton, CA, USA). The imprecision profile of
145 839 duplicate samples showed 10% and 20% coefficients of variation values of 0.014 and
146 0.008 $\mu\text{g.L}^{-1}$, respectively. The URL for cTnI, defined as the 99th percentile of healthy
147 participants, was 0.04 $\mu\text{g.L}^{-1}$ (Eggers et al. 2007). NT-proBNP was analyzed in the serum
148 with an Elecsys proBNP electrochemiluminescent immunoassay on the Roche Elecsys 1010
149 (Roche Diagnostics, Lewes, United Kingdom) with an analytical range of 5 – $35,000$ ng.L^{-1}
150 and intra- and interassay imprecisions of 0.7 – 1.6% and 5.3 – 6.6% , respectively. The URL for
151 NT-proBNP was considered to be 125 ng.L^{-1} (Silver et al. 2004).

152

153 *Statistical analysis*

154 Statistical analyses were performed using the IBM Statistical Package for the Social Sciences
155 (IBM SPSS Statistics, v. 20.0 for WINDOWS). Cohort data are presented as the mean \pm
156 standard deviation unless otherwise stated. Kolmogorov-Smirnov tests were used to check for
157 normal distribution and data for cTnI and NT-proBNP were log-transformed prior to
158 statistical testing. To measure the impact of sampling time during recovery (pre, 5 min, 1, 3,
159 6, 12, and 24 h post-exercise) as well as athletes status (elite and amateur) upon cTnI and NT-
160 proBNP mixed model 2-way ANOVAs were performed with post-hoc Bonferroni tests
161 employed when appropriate. The association between the exercise increase in both
162 biomarkers and other relevant variables (e.g., baseline biomarker concentration, mean and
163 max exercise HR) were assessed using bivariate Pearson's product-moment correlation
164 coefficients. The values were considered to be significant if $p < 0.05$.

165

166 **Results**

167 The characteristics of the elite and amateur rowers are shown in Table 1. The elite rowers had
168 more years of training, greater weekly training frequency, and higher weekly training volume
169 (all $p < 0.05$). Performance during the grade rowing test was greater in the elite rowers ($294 \pm$
170 18 W vs. 211 ± 44 W; $p = 0.000$) whereas maximum HR was similar between groups (elite:
171 196 ± 7 beats.min⁻¹; amateur 193 ± 9 beats.min⁻¹; $p = 0.372$).

172

173 *Maximal 30-min rowing test*

174 All of the subjects completed the maximal 30-min rowing test and every blood draw.
175 Performance during the 30 min all out test was substantially greater in the elite athlete (Table
176 2). Whilst mean HR was higher in the elite (180 ± 7 beats.min⁻¹) compared to the amateur
177 rowers (171 ± 12 beats.min⁻¹; $p = 0.023$) there was no difference in the maximum HR (elite

178 rowers: 195 ± 7 beats.min⁻¹, amateur rowers: 188 ± 11 beats.min⁻¹; $p = 0.061$) or RPE (elite
179 rowers: 8.7 ± 0.5 , amateur rowers: 8.6 ± 0.5 ; $p = 0.536$).

180

181 *cTnI release*

182 A significant main effect of sampling time was observed for cTnI with an elevation at 3-, 6-,
183 and 12-h post-exercise compared to baseline ($p = 0.000$) (Table 3). All participants presented
184 with an increase in cTnI post-exercise with the URL for cTnI exceeded by 2 rowers at all
185 measurements points and another 10 rowers (8 elite and 2 amateur) having sporadic data
186 points above the URL during recovery (Fig. 1). The maximum post-exercise cTnI was
187 observed at 3 h in 11 individuals, 6 h in 19 individuals, and 12 h of recovery in 2 individuals.
188 A significant main effect for athlete status was observed with cTnI data higher in elite rowers
189 including pre-exercise values (amateur: 0.008 ± 0.015 $\mu\text{g.L}^{-1}$; elite: 0.019 ± 0.038 $\mu\text{g.L}^{-1}$; $p =$
190 0.003). There was no significant interaction of test time and athlete status with respect to
191 cTnI ($p = 0.311$). In support of this the maximal increase in cTnI (peak-baseline) was not
192 significantly different between groups (elite: 0.062 ± 0.083 $\mu\text{g.L}^{-1}$; amateur: 0.023 ± 0.021
193 $\mu\text{g.L}^{-1}$; $p = 0.145$). The absolute post-exercise cTnI values were significantly correlated with
194 the basal values ($r = 0.88$, $p = 0.000$) as well as mean exercise HR ($r = 0.35$, $p = 0.048$)

195

196 *NT-proBNP release*

197 There was a main effect of time with an increase in NT-proBNP from pre-exercise at 5 min,
198 1-, 3-, 6-, 12-, and 24-h post-exercise ($p = 0.001$; Table 3). There was a rise in NT-proBNP
199 post exercise in all subjects but the URL was not exceeded by any subject (Fig. 2). The
200 maximum post-exercise NT-proBNP values were observed at 5 min in 10 individuals, 1 h for
201 4 individuals, 6 h for 7 individuals, 12 h for 4 individuals, and 24 h for 11 individuals. There
202 was no significant main effect of athlete status on NT-proBNP data and there was no time by

203 athlete status interaction effect. In support of this latter point there was no difference between
204 the elite and amateur rowers with respect to the peak NT-proBNP increase (14 ± 11 vs. $18 \pm$
205 13 ng.L^{-1} , respectively; $p = 0.470$). Basal NT-proBNP values were significantly correlated
206 with the maximum post-effort values ($r = 0.83$, $p = 0.000$) but there was no correlation
207 between change in NT-proBNP and cTnI data.

208

209 ***Discussion***

210 The main findings of this study were; (1) a single 30-min bout of “all-out” rowing exercise
211 resulted in a significant increase in the cTnI and NT-proBNP in both elite and amateur
212 rowers, (2) significant individual heterogeneity in peak cTnI during recovery was noted with
213 the URL for cTnI exceeded in 12/32, (3) less individual variability was apparent in peak NT-
214 proBNP response with no data point exceeded the URL, (4) baseline and post-exercise cTnI
215 data were higher in elite rowers, but (5) the rowing-induced changes in cTnI and NT-proBNP
216 were independent of athlete status.

217

218 *Post-exercise cTnI peak and kinetics in elite and amateur rowers*

219 Our results in rowers extend the findings of Shave et al. (2010b) who employed a 30 min
220 high intensity run and demonstrate that cTnI is elevated following short-duration, high-
221 intensity exercise in non-elite athletes. An elevation in cTnI occurred in all participants
222 despite the relatively short duration and limited exercise volume. In prolonged exercise there
223 is some evidence to suggest that cTnI release is positively associated with exercise intensity
224 (Fu et al. 2009; Serrano-Ostáriz et al. 2011; Shave et al. 2007). Whilst the current study does
225 not compare exercise intensities it adds to the extant data that different types and intensities
226 of exercise can stimulate an increase in circulating cTnI. According to the results of Shave et
227 al. (2010b) cTnI release following short-duration intense exercise may be as common as

228 when prolonged exercise trials are studied and the current study supports this contention.
229 This also underscores the necessity to complete blood draws during recovery (Middleton et
230 al. 2008).

231 To our knowledge, this study is the first to demonstrate cTnI release with exercise in elite
232 athletes with values that exceed the URL in some, but not all, participants. Previously, only
233 two studies had evaluated cTnI release in elite athletes. Bonetti et al. (1996) analyzed 25
234 cyclists participating in the Giro d'Italia and reported detectable cTnT values in only 5
235 athletes; moreover, these values were below the cut-offs considered to be indicative of
236 myocardial insult. Similarly, König et al. (König et al. 2003) reported normal post-exercise
237 cTnT levels in 11 professional road cyclists. Both studies were constrained by limited blood
238 sampling (pre- and post-exercise design) and by less-sensitive measurement equipment.

239 Despite the fact that all participants experienced a rise in cTnI post-exercise the magnitude of
240 peak post-exercise levels was variable, which also supports the data from Shave et al.
241 (2010b). Recent studies have also demonstrated “positive” high sensitivity cTnT (hs-cTnT)
242 values after prolonged exercise in most subjects (86-94%) (Mingel et al. 2009; Saravia et al.
243 2010; Scherr et al. 2011; Tian et al. 2012), but with marked heterogeneity in peak hs-cTnT
244 (Scherr et al. 2011; Tian et al. 2012). It is not known what personal, environmental or
245 exercise-related factors mediate the heterogeneity and this requires on-going study. Whilst
246 we observed variability in the peak cTnI values recorded 94% of participants recorded their
247 peak cTnI between 3 or 6 h which suggests some consistency in cTnI kinetics and agrees
248 with previous data gathered after a treadmill run (Tian et al. 2012).

249 As in previous studies (Legaz-Arrese et al. 2011; Serrano-Ostáriz et al. 2011), it is interesting
250 that the main factor that significantly predicted post-exercise values of cTnI was their
251 respective pre-exercise values. In a broad range of pathologies and patient groups baseline
252 cTn values are repeatedly and robustly associated with adverse cardiovascular prognosis and

253 mortality (deFilippi et al. 2010). In healthy population little attention has been focused to the
254 variability of baseline cTn values and whether this variability may have clinical significance.
255 On this matter, our results provide that the athletic status may be one of the factors that
256 determine the heterogeneity in baseline cTnI. Further research into the factors associated with
257 the inter-subject variability in the baseline values of cTn are required.

258 Certain authors suggest that the post-exercise cTnI release is greater in less well-trained
259 individuals (Fortescue et al. 2007; Mehta et al. 2012; Mingels et al. 2009; Neilan et al. 2006).
260 However, other studies did not observe any relationship between training level and cTnI
261 release (Eijsvogels et al. 2015; Hubble et al. 2009; Jassal et al. 2009; Scherr et al. 2011;
262 Serrano-Ostáriz et al. 2009). Our results demonstrating greater pre- and post-exercise values
263 of cTn in elite rowers than in amateur rowers. These data are consistent with our recent
264 controlled endurance training intervention (Legaz-Arrese et al. 2015) and a field based study
265 with marathoners (Saravia et al. 2010). Contradiction with previous studies may relate to
266 differences in exercise regime, training status as well as the limited by the number of blood
267 samples taken during the recovery period, in past work.

268 There has been some descriptive association between peak post-exercise cTnI and mean
269 exercise HR (Fu et al. 2009; Legaz-Arrese et al. 2011; Serrano-Ostáriz et al. 2009).
270 Conversely, the higher absolute and relative work performed by the elite rowers in the 30 min
271 exercise bout did not result in a greater change in cTnI during recovery when compared to
272 amateur rowers. Overall there is no convincing evidence that exercise intensity mediated the
273 cTnI response within the current research design.

274 We do not know the reasons behind the higher cTnI baseline levels in elite vs. amateur
275 rowers. A previous study also showed that runners with detectable hs-cTnT were
276 significantly better trained than runners in whom hs-cTnT was non-detectable (Saravia et al.
277 2010). Also, we observed that a controlled endurance training intervention resulted in higher

278 pre-exercise values of hs-cTnT (Legaz-Arrese et al. 2015). One hypothesis is that this effect
279 is due to the successive training sessions with limited recuperation time for elite athletes.
280 However, this seems unlikely to be a factor in this study because subjects were required to
281 abstain from vigorous athletic activity for 48 h before each exercise test. Furthermore, if the
282 greater baseline cTnI values were a consequence of incomplete recuperation, they ought to
283 have similarly increased baseline levels of NT-proBNP, based on the results observed in this
284 study. In a previous study, a significantly higher baseline hs-cTnT concentration was
285 obtained in males compared to females (Mingels et al. 2009). Given that the mean heart size
286 is larger for male and elite athletes than for female and amateur athletes (Legaz-Arrese et al.
287 2006; Legaz Arrese et al. 2005), it is reasonable to expect different cTn reference values
288 between these groups. Future research may wish to address this issue.

289

290 *Post-exercise NT-proBNP peak and kinetics in elite and amateur rowers*

291 This investigation is, to our knowledge, the first study that demonstrates NT-proBNP release
292 as a consequence of a short-duration, high-intensity exercise in elite athletes. Increased NT-
293 proBNP has been reported in multiple prolonged endurance exercise studies (Legaz-Arrese et
294 al. 2011; Neilan et al. 2006; Sahlén et al. 2008; Serrano-Ostáriz et al. 2009), and the current
295 data extend this phenomenon to short-duration, high-intensity exercise. The observed
296 increase are somewhat smaller than previous (ultra) endurance exercise studies (Neilan et al.
297 2006; Serrano-Ostáriz et al. 2009) which may not be surprising when one considers that BNP
298 is elevated in response to volume overload and myocyte stretch (Shave et al. 2007) and this is
299 likely to be stressed to a much greater extent in endurance exercise.

300 Our results demonstrate that like to cTnI, NT-proBNP values post exercise, as well as overall
301 kinetic of appearance, is subject to a degree of heterogeneity. In agreement with the above
302 mentioned study of Tian et al. (2012), levels of NT-proBNP increased immediately after

303 exercise and were still elevated at 24 h. The elevation in NT-proBNP at 24 h reflects an
304 increase beyond the kinetics of NT-proBNP and its half-life (Silver et al. 2004). Other factors
305 associated with strenuous exercise, such as a temporary reduction in kidney function and
306 changes in cardiac function and hemodynamics, have been suggested to contribute to a
307 sustained elevation in NT-proBNP (Tian et al. 2012), but this requires further study.

308 Our results show that although peak NT-proBNP data was heterogeneous the URL was not
309 exceeded by any subject. Contrary to the data for cTnI there was no apparent difference in
310 NT-proBNP between subject groups. In previous studies the influence of training level or
311 athletic status on NT-proBNP release has been controversial (Herrmann et al. 2003; Legaz-
312 Arrese et al. 2011, 2015; Neilan et al. 2006; Scharhag et al. 2006; Serrano-Ostáriz et al.
313 2009), likely because of the inability to precisely control for several variables, such as effort
314 duration. Specifically, our study confirms previous results showing that the baseline NT-
315 proBNP is a key factor related to exercise-induced NT-proBNP increase (Carranza-García et
316 al. 2011; Legaz-Arrese et al. 2011, 2015; Sahlén et al. 2008; Serrano-Ostáriz et al. 2011).

317 Interestingly, we observed greater individual variability in time to peak NT-proBNP than for
318 cTnI, and consequently, previous studies may significantly underestimate NT-proBNP
319 release if a single post-exercise sample is taken. Future studies should be performed to
320 determine NT-proBNP kinetics differences among individuals after different types of
321 exertion.

322

323 *Implications*

324 The fact that cTnI elevation was observed in all, in the absence of any other signs or
325 symptoms of cardiovascular disease as well as with a rapid onset of accumulation and
326 recovery within the study period would add to the suggestion that this phenomenon is a
327 normal physiological process. Clinicians should be aware regardless of athletic status, it is

328 possible to observe cTnI but not NT-proBNP values exceeding the URL in the first hours of
329 recovery after a short-duration, high-intensity exercise period in a high percentage of
330 individuals. Since cTnI is recommended as a sensitive and specific marker for cardiac
331 damage in the diagnosis of acute myocardial infarction, caution should be taken when
332 interpreting post-exercise cTnI levels. The results of this study are relevant for clinicians as it
333 could improve medical decision making.

334

335 *Strengths and limitations*

336 Strengths of the present study include the controlled exercise regimen, matched elite and
337 amateur rowers, serial blood sampling, and the inclusion of cTnI and NT-proBNP values.
338 However, several limitations should be considered. Two of the rowers had cTnI above the
339 URL pre-exercise. The study is limited by only having analyzed associations between
340 biomarkers and athletic status in young male rowers. The impact of age and sex should be
341 studied as factors that may partially mediate the release of cardiac biomarkers with exercise
342 (Scharhag et al. 2008; Shave et al. 2010). The observed differences in the values of cTnI and
343 NT-proBNP between elite and amateur rowers may have resulted from differences in the
344 level of training but could also be associated with other factors, such as genetic differences.
345 To resolve this issue, because of the difficulty of establishing a control group with athletes, it
346 would be also interesting to observe in previously untrained subjects, the effect of training
347 programs on exercise-induced cardiac biomarker release.

348

349 *Conclusions*

350 In conclusion, our results show that 30 min of high-intensity rowing results in the elevation
351 of both cTnI and NT-proBNP across a 24 h recovery period. Whilst a rise in cTnI and NT-
352 proBNP was observed in all rowers, the peak values recorded were highly variable with some

353 cTnI data above URL. Kinetic data for cTnI were more consistent and there does not appear
354 to be an important role for athlete or training status in mediating exercise biomarker
355 responses beyond the impact of potential group differences in baseline data.

356

357 *Acknowledgments*

358 We gratefully acknowledge the participation and collaboration of all elite and amateur rowers
359 from Club Nautic Amposta (Spain). This study was supported by the DEP 2010-16767 grants
360 from the National Plan for Research, Development and Innovation (R + D + i) MICINN.

361

362 *References*

363 Bonetti, A., Tirelli, F., Albertini, R., Monica, C., Monica, M., and Tredici, G. 1996. Serum
364 cardiac troponin T after repeated endurance exercise events. *Int. J. Sports Med.* 17: 259–262.
365 PMID:8814506.

366 Borg, E., and Kaijser, L. 2006. A comparison between three rating scales for perceived
367 exertion and two different work tests. *Scand. J. Med. Sci. Sports* 16: 57–69. PMID:16430682.

368 Carranza-García, L.E., George, K., Serrano-Ostáriz, E., Casado-Arroyo, R., Caballero-
369 Navarro, A.L., and Legaz-Arrese, A. 2011. Cardiac biomarker response to intermittent
370 exercise bouts. *Int. J. Sports Med.* 32: 327–331. doi:10.1055/s-0030-1263138.
371 PMID:21547864.

372 deFilippi, C.R., de Lemos, J.A., Christenson, R.H., Gottdiener, J.S., Kop, W.J., Zhan, M., et
373 al. 2010. Association of serial measures of cardiac troponin T using a sensitive assay with
374 incident heart failure and cardiovascular mortality in older adults. *JAMA* 304: 2494–2502.
375 doi:10.1001/jama.2010.1708. PMID:21078811.

- 376 Eggers, K.M., Lagerqvist, B., Venge, P., Wallentin, L., and Lindahl, B. 2007. Persistent
377 cardiac troponin I elevation in stabilized patients after an episode of acute coronary syndrome
378 predicts long-term mortality. *Circulation* 116: 1907–1914. PMID:17909103.
- 379 Eijsvogels, T.M., Hoogerwerf, M.D., Maessen, M.F., Seeger, J.P., George, K.P., Hopman,
380 M.T., et al. 2015. Predictors of cardiac troponin release after a marathon. *J. Sci. Med. Sport.*
381 18: 88-92. doi:10.1016/j.jsams.2013.12.002. PMID:24440407.
- 382 Fortescue, E.B., Shin, A.Y., Greenes, D.S., Mannix, R.C., Agarwal, S., Feldman, B.J., et al.
383 2007. Cardiac troponin increases among runners in the Boston Marathon. *Ann. Emerg. Med.*
384 49: 137–143. PMID:17145114.
- 385 Fu, F., Nie, J., and Tong, T.K. 2009. Serum cardiac troponin T in adolescent runners: effects
386 of exercise intensity and duration. *Int. J. Sports Med.* 30: 168–172. doi:10.1055/s-0028-
387 1104586. PMID:19199217.
- 388 Herrmann, M., Scharhag, J., Miclea, M., Urhausen, A., Herrmann, W., and Kindermann, W.
389 2003. Post-race kinetics of cardiac troponin T and I and N-terminal pro-brain natriuretic
390 peptide in marathon runners. *Clin. Chem.* 49: 831–834. PMID:12709384.
- 391 Hubble, K.M., Fatovich, D.M., Grasko, J.M., and Vasikaran, S.D. 2009. Cardiac troponin
392 increases among marathon runners in the Perth Marathon: the Troponin in Marathons
393 (TRIM) study. *Med. J. Aust.* 190: 91–93. PMID:19236297.
- 394 Jassal, D.S., Moffat, D., Krahn, J., Ahmadie, R., Fang, T., Eschun, G., et al. 2009. Cardiac
395 injury markers in non-elite marathon runners. *Int. J. Sports Med.* 30: 75–79. doi:10.1055/s-
396 0028-1104572. PMID:19177312.
- 397 Klinkenberg, L.J., Res, P.T., van Loon, L.J., van Dieijen-Visser, M.P., and Meex, S.J. 2012.
398 Strong link between basal and exercise-induced cardiac troponin T levels: Do both reflect
399 risk? *Int. J. Cardiol.* 158: 129–131. doi:10.1016/j.ijcard.2012.04.050. PMID:22560936.

- 400 König, D., Schumacher, Y.O., Heinrich, L., Schmid, A., Berg, A., and Dickhuth, H.H. 2003.
401 Myocardial stress after competitive exercise in professional road cyclists. *Med. Sci. Sports*
402 *Exerc.* 35: 1679–1683. PMID:14523304.
- 403 Legaz Arrese, A., Serrano Ostáriz, E., González Carretero, M., and Lacambra Blasco, I.
404 2005. Echocardiography to measure fitness of elite runners. *J. Am. Soc. Echocardiogr.* 18:
405 419–426. PMID:15891751.
- 406 Legaz-Arrese, A., González-Carretero, M., and Lacambra-Blasco, I. 2006. Adaptation of left
407 ventricular morphology to long-term training in sprint- and endurance-trained elite runners.
408 *Eur. J. Appl. Physiol.* 96: 740–746. PMID:16283369.
- 409 Legaz-Arrese, A., George, K., Carranza-García, L.E., Munguía-Izquierdo, D., Moros-García,
410 T., and Serrano-Ostáriz, E. 2011. The impact of exercise intensity on the release of cardiac
411 biomarkers in marathon runners. *Eur. J. Appl. Physiol.* 111: 2961–2967. doi:10.1007/s00421-
412 011-1922-3. PMID:21442162.
- 413 Legaz-Arrese, A., López-Laval, I., George, K., Puente-Lanzarote, J. J., Mayolas-Pi, C.,
414 Serrano-Ostáriz, E., Revilla-Martí, P., Moliner-Urdiales, D., & Reverter-Masià J. 2015. The
415 impact of an endurance training programme on exercise-induced cardiac biomarker release.
416 *American Journal of Physiology. Heart and Circulatory Physiology.* *In press.*
- 417 Mehta, R., Gaze, D., Mohan, S., Williams, K.L., Sprung, V., George, K., et al. 2012. Post-
418 exercise cardiac troponin release is related to exercise training history. *Int. J. Sports Med.* 33:
419 333–337. doi:10.1055/s-0031-1301322. PMID:22377942.
- 420 Middleton, N., George, K., Whyte, G., Gaze, D., Collinson, P., and Shave, R. 2008. Cardiac
421 troponin T release is stimulated by endurance exercise in healthy humans. *J. Am. Coll.*
422 *Cardiol.* 52: 1813–1814. doi:10.1016/j.jacc.2008.03.069. PMID:19022162.
- 423 Mingels, A., Jacobs, L., Michielsen, E., Swaanenburg, J., Wodzig, W., and van Dieijen-
424 Visser, M. 2009. Reference population and marathon runner sera assessed by highly sensitive

- 425 cardiac troponin T and commercial cardiac troponin T and I assays. *Clin. Chem.* 55: 101–
426 108. doi:10.1373/clinchem.2008.106427. PMID:18988757.
- 427 Neilan, T.G., Januzzi, J.L., Lee-Lewandrowski, E., Ton-Nu, T.T., Yoerger, D.M., Jassal,
428 D.S., et al. 2006. Myocardial injury and ventricular dysfunction related to training levels
429 among nonelite participants in the Boston marathon. *Circulation* 114: 2325–2333.
430 PMID:17101848.
- 431 Roth, H.J., Leithäuser, R.M., Doppelmayr, H., Doppelmayr, M., Finkernagel, H., von
432 Duvillard, S.P., et al. 2007. Cardiospecificity of the 3rd generation cardiac troponin T assay
433 during and after a 216 km ultra-endurance marathon run in Death Valley. *Clin. Res. Cardiol.*
434 96: 359–364. PMID:17453141.
- 435 Sahlén, A., Winter, R., Lind, B., Jacobsen, P.H., Ståhlberg, M., Marklund, T., et al. 2008.
436 Magnitude, reproducibility, and association with baseline cardiac function of cardiac
437 biomarker release in long-distance runners aged \geq 55 years. *Am. J. Cardiol.* 102: 218–
438 222. doi:10.1016/j.amjcard.2008.03.042. PMID:18602525.
- 439 Saravia, S.G., Knebel, F., Schroeckh, S., Ziebig, R., Lun, A., Weimann, A., et al. 2010.
440 Cardiac troponin T release and inflammation demonstrated in marathon runners. *Clin. Lab.*
441 56: 51–58. PMID:20380359.
- 442 Scharhag, J., Urhausen, A., Schneider, G., Herrmann, M., Schumacher, K., Haschke, M., et
443 al. 2006. Reproducibility and clinical significance of exercise-induced increases in cardiac
444 troponins and N-terminal pro brain natriuretic peptide in endurance athletes. *Eur. J.*
445 *Cardiovasc. Prev. Rehabil.* 13: 388–397. PMID:16926669.
- 446 Scharhag, J., George, K., Shave, R., Urhausen, A., and Kindermann, W. 2008. Exercise-
447 associated increases in cardiac biomarkers. *Med. Sci. Sports Exerc.* 40: 1408–1415.
448 doi:10.1249/MSS.0b013e318172cf22. PMID:18614952.

- 449 Scherr, J., Braun, S., Schuster, T., Hartmann, C., Moehlenkamp, S., Wolfarth, B., et al. 2011.
450 72-h kinetics of high-sensitive troponin T and inflammatory markers after marathon. *Med.*
451 *Sci. Sports Exerc.* 43: 1819–1827. doi:10.1249/MSS.0b013e31821b12eb. PMID:21448080.
- 452 Serrano-Ostáriz, E., Legaz-Arrese, A., Terreros-Blanco, J.L., López-Ramón, M., Cremades-
453 Arroyos, D., Carranza-García, L.E., et al. 2009. Cardiac biomarkers and exercise duration
454 and intensity during a cycle-touring event. *Clin. J. Sport Med.* 19: 293–299.
455 doi:10.1097/JSM.0b013e3181ab3c9d. PMID:19638823.
- 456 Serrano-Ostáriz, E., Terreros-Blanco, J.L., Legaz-Arrese, A., George, K., Shave, R., Bocos-
457 Terraz, P., et al. 2011. The impact of exercise duration and intensity on the release of cardiac
458 biomarkers. *Scand. J. Med. Sci. Sports* 21: 244–249. doi:10.1111/j.1600-0838.2009.01042.x.
459 PMID:19919634.
- 460 Shave, R., George, K.P., Atkinson, G., Hart, E., Middleton, N., Whyte, G., et al. 2007.
461 Exercise-induced cardiac troponin T release: a meta-analysis. *Med. Sci. Sports Exerc.* 39:
462 2099–2106. PMID:18046180.
- 463 Shave, R., Baggish, A., George, K., Wood, M., Scharhag, J., Whyte, G., et al. 2010a.
464 Exercise-induced cardiac troponin elevation: evidence, mechanisms, and implications. *J. Am.*
465 *Coll. Cardiol.* 56: 169–176. doi:10.1016/j.jacc.2010.03.037. PMID:20620736.
- 466 Shave, R., Ross, P., Low, D., George, K., and Gaze, D. 2010b. Cardiac troponin I is released
467 following high-intensity short-duration exercise in healthy humans. *Int. J. Cardiol.* 145: 337–
468 339. doi:10.1016/j.ijcard.2009.12.001. PMID:20079546.
- 469 Silver, M.A., Maisel, A., Yancy, C.W., McCullough, P.A., Burnett, J.C., Francis, G.S., et al;
470 BNP Consensus Panel. 2004. BNP Consensus Panel 2004: A clinical approach for the
471 diagnostic, prognostic, screening, treatment monitoring, and therapeutic roles of natriuretic
472 peptides in cardiovascular diseases. *Congest. Heart Fail.* 10: 1–30. PMID:15604859.

473 Tian, Y., Nie, J., Huang, C., and George, K.P. 2012. The kinetics of highly sensitive cardiac
474 troponin T release after prolonged treadmill exercise in adolescent and adult athletes. *J. Appl.*
475 *Physiol.* (1985) 113: 418–425. doi:10.1152/jappphysiol.00247.2012. PMID:22653984.

476

477 **Figure Legends**

Fig. 1. Individual data points for cTnI ($\mu\text{g}\cdot\text{L}^{-1}$) in elite ($n = 18$) (a) and amateur ($n = 14$) (b) rowers at pre-exercise (PRE), as well as 0, 1, 3, 6, 12, and 24 h (0HR, 1HR, 3HR, 6HR, 12HR, 24HR, respectively) after a 30 min maximal rowing test. The horizontal dotted line is the upper reference limit (99th percentile) at $0.04 \mu\text{g}\cdot\text{L}^{-1}$.

Fig. 2. Individual data points for NT-proBNP ($\text{ng}\cdot\text{L}^{-1}$) in elite ($n = 18$) (a) and amateur ($n = 14$) (b) rowers at pre-exercise (PRE), as well as 0, 1, 3, 6, 12, and 24 h (0HR, 1HR, 3HR, 6HR, 12HR, 24HR, respectively) after a 30 min maximal rowing test. All values were lower than the URL ($125 \text{ng}\cdot\text{L}^{-1}$).

Table 1. Participant characteristics by athletic status.

	Age (years)	Weight (kg)	Height (cm)	Rowing training history (years)	Rowing training frequency (sessions/week)	Rowing training volume (hours/week)
Elite rowers	21.0 ± 4.1	77.9 ± 6.0	181.4 ± 6.0	8.2 ± 5.4*	6.9 ± 0.3*	22.1 ± 6.6*
Amateur rowers	21.2 ± 2.0	76.6 ± 8.7	177.0 ± 9.0	3.7 ± 1.5	1.6 ± 0.5	2.9 ± 0.8

Note: Values are means ± standard deviations (elite rowers: $n = 18$; amateur rowers: $n = 14$). * Significant differences between elite and amateur rowers.

Table 2. Performance during the maximal 30-min rowing test.

	0-5 min power (W)	5-15 min power (W)	15-25 min power (W)	25-30 min power (W)	Mean power (W)	Percentage of max power (%)
Elite rowers	260 ± 23*	254 ± 22*	251 ± 23*	286 ± 27*	259 ± 23*	88 ± 3*
Amateur rowers	165 ± 48	156 ± 37	157 ± 33	179 ± 37	161 ± 36	76 ± 5

Note: Values are means ± standard deviations (elite rowers: $n = 18$; amateur rowers: $n = 14$). * Significant differences between elite and amateur rowers. Similar pacing strategy was observed in both groups, with a significant increase in rowing performance in the last 5 min.

Table 3. cTnI ($\mu\text{g.L}^{-1}$) and NT-proBNP (ng.L^{-1}) before and after 30 min of high-intensity rowing exercise.

		Pre-exercise	5 min post	1 h post	3 h post	6 h post	12 h post	24 h post	<i>p</i> value		
									Time	Group	Time x Group
cTnI	Elite rowers	0.019 ±	0.022 ±	0.030 ±	0.069 ±	0.079 ±	0.045 ±	0.023 ±	0.000	0.010	0.311
		0.038	0.048	0.051	0.095	0.116	0.073	0.046			
		(6)	(6)	(17)	(44)	(50)	(28)	(6)			
	Amateur rowers	0.008 ±	0.008 ±	0.011 ±	0.025 ±	0.028 ±	0.020 ±	0.007 ±			
		0.015	0.013	0.018	0.028	0.029	0.019	0.007			
		(7)	(7)	(7)	(14)	(21)	(21)	(7)			
NT-proBNP	Elite rowers	14 ± 11	25 ± 18	21 ± 16	19 ± 14	18 ± 12	18 ± 11	19 ± 14	0.001	0.322	0.171
		(0)	(0)	(0)	(0)	(0)	(0)	(0)			
		(0)	(0)	(0)	(0)	(0)	(0)	(0)			
	Amateur rowers	17 ± 12	25 ± 19	25 ± 17	26 ± 18	26 ± 18	28 ± 18	27 ± 17			
		(0)	(0)	(0)	(0)	(0)	(0)	(0)			
		(0)	(0)	(0)	(0)	(0)	(0)	(0)			

Note: Values are means ± standard deviations (elite rowers: $n = 18$; amateur rowers: $n = 14$). In brackets the percentage of subjects with serum

cardiac biomarkers exceeding the URL.

Draft

Fig. 1

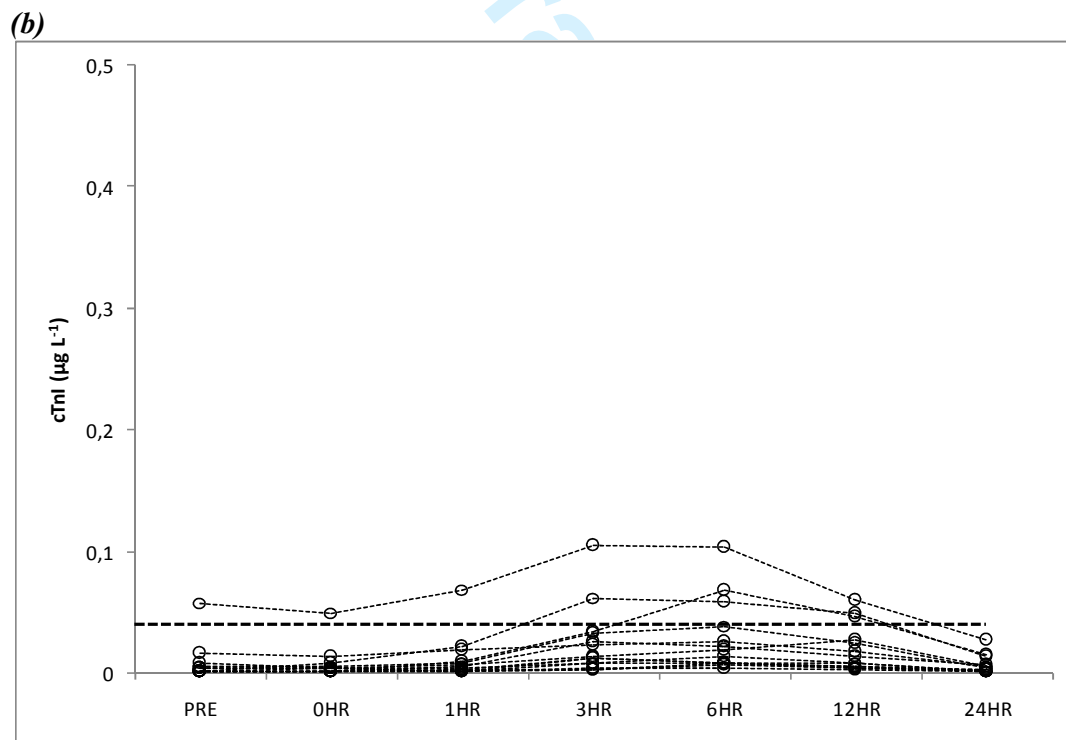
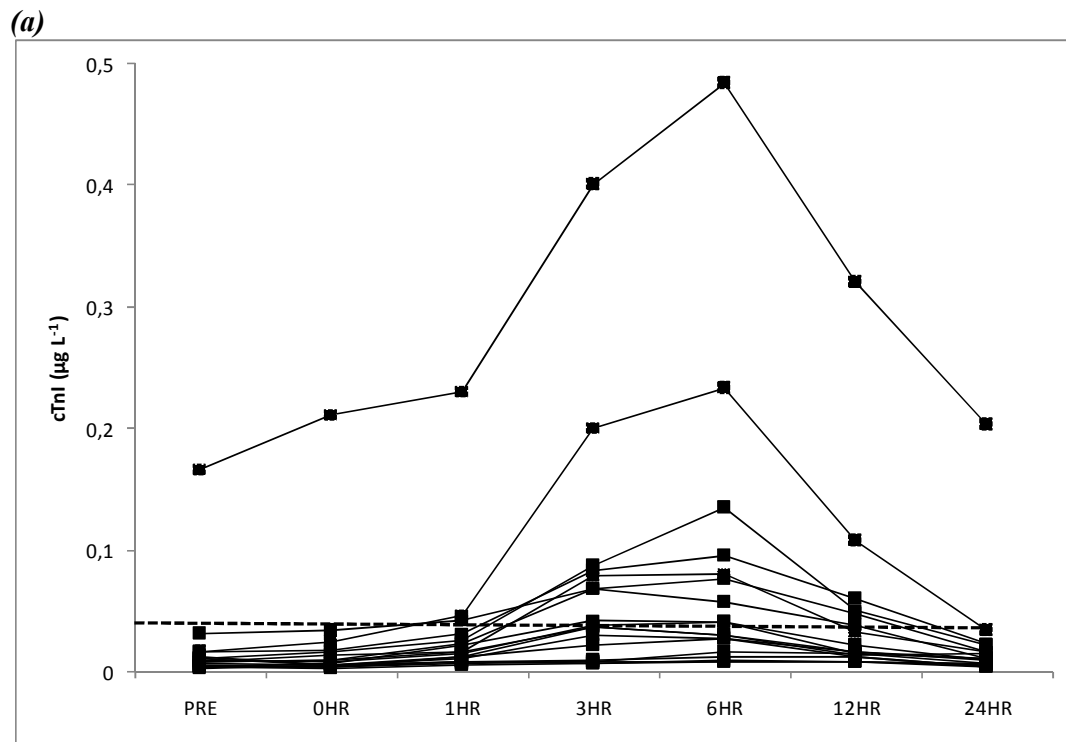
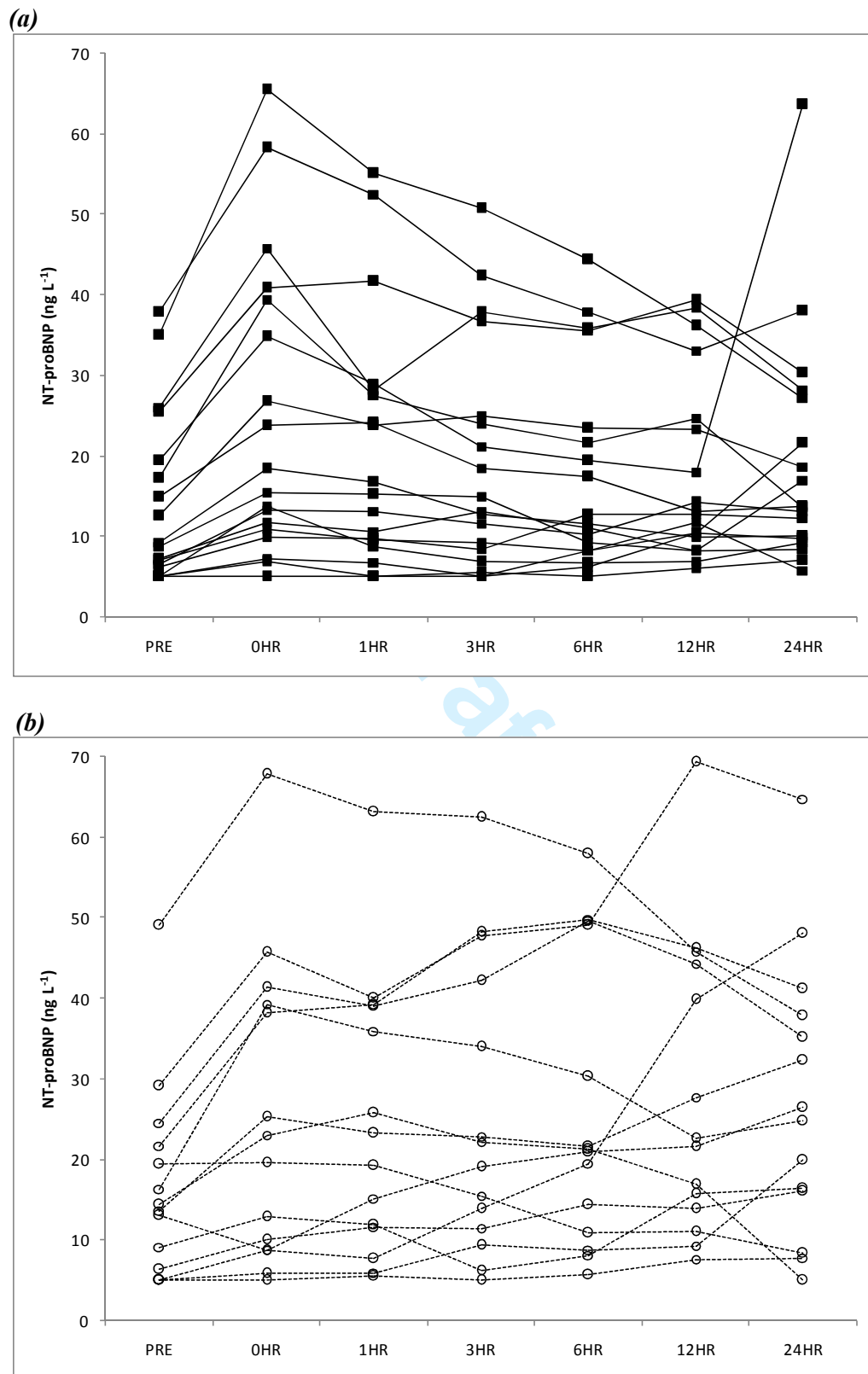


Fig. 2



Draft