



## BIOMEDICAL SCIENCES

# Kidney functions adaptations of professional soccer players in response to an entire game season

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**Abstract:** This study investigated the renal function of soccer players after an entire game-season. Thirty-five athletes recruited to play for the Macaé Futebol Clube were invited for this study, of which 18 athletes completed the entire game season. Blood and 24-hour urine were collected at the beginning (Pre-Season) and the end of the game season (Post-Season). Kidney functions were assessed by calculating the urinary excretion, clearance, and fractional excretion of the selected solutes. Plasma creatinine, sodium, total protein, and osmolality were lower in the Post-Season. In contrast, plasma urea was higher in the Post-Season period. Urinary excretion of urea was reduced while albumin excretion was higher in comparison to Pre-Season. The clearances of creatinine, total proteins, and albumin were higher in the Post-Season period. In accordance, the fractional excretion of albumin increased. On the other hand, the clearance and fractional excretion of urea was lower in the Post-Season period. These results show that soccer-associated exercise throughout the entire game-season induces kidney functions adaptations that may prevent dehydration in these athletes through increased urea reabsorption to conserve water. In addition, this data corroborates to increased glomerular permeability to plasma proteins, such as albumin, that soccer players may experience.

**Key words:** kidney functions, soccer, soccer players, urea reabsorption.

## INTRODUCTION

To improve soccer players performance, an important area of sports medicine and physiology have turned to comprehend the physiological adaptations presented by soccer players both during and after a soccer match or a game season (Stølen et al. 2005). Both laboratory and physical performance tests are used to monitor athletes' physiological changes and needs (Svensson & Drust 2005). These information may contribute to the development of directed training strategies to improve overall

performance (Chamari et al. 2005, Hoff 2005, McMillan et al. 2005).

The magnitude of physiological changes presented by soccer players depends on several factors, including athletes' fitness level, training protocols during pre-season and game-season, the positional role in the team, and environmental conditions where the game occurs (Stølen et al. 2005). In addition, individuals who participate in physical exercise experience both acute and long-term physiological adaptations

as a response to such stimuli (Poortmans et al. 1988, Durmic et al. 2015, D'Andrea et al. 2017).

Since the cardiovascular, respiratory, and muscle-skeletal systems are directly related to the physical performance of athletes, such as aerobic and anaerobic capacities, physiological changes of these systems have been extensively investigated in soccer players (Al-Hazzaa et al. 2001, Di Paci et al. 2014, Churchill et al. 2021). Although the renal system plays important role in the maintenance of electrolyte balance and hydration status (Bankir et al. 1989), which are essential for the athletes' overall performance (Von Duvillard et al. 2004), renal adaptations of soccer players have been less investigated (Poortmans 1984, Colombini et al. 2014).

Considering that at rest the kidneys receive about 20% of the cardiac output and during physical exercises a major portion of the cardiac output is shunted to supply cardiorespiratory and skeletal muscles demands, the renal system must adapt to function under these circumstances (Poortmans & Vanderstraeten 1994, McAllister 1998). Indeed, renal function analysis in athletes of different sports including runners (Tian et al. 2011), cyclists (Neumayr et al. 2005), soccer players (Colombini et al. 2014) have reported exercise-induced changes of renal function as evidenced by serum creatinine (SCr) analysis and estimated glomerular filtration rate (eGFR). In addition, proteinuria, another marker of renal function, has been reported to occur both in athletes and non-athletes individuals after intense exercise and strenuous physical efforts (Poortmans 1984, Poortmans & Vanderstraeten 1994).

While many works have addressed acute post-exercise-induced physiological changes presented by these athletes in response to a soccer match (Coelho et al. 2012, Colombini et al. 2014), few others have focused on the long-term physiological adaptations sustained for

longer periods, such as afterwards an entire game season (Nowakowska et al. 2019). In view of this scenario, the aim of this study was to investigate long-term renal function changes of professional soccer players in response to a five-month game season.

## MATERIALS AND METHODS

### Subjects

The participants of this study were professional soccer players from the Macae Futebol Clube, Macae, RJ, Brazil. During the 2018-2019 season, this team competed in the second division of the Rio de Janeiro state championship organized by the Brazilian Confederation of Soccer (CBF). All of the study participants were males, with an average body weight and an average height of  $76.08 \pm 7.74$  Kg and  $179 \pm 5.88$  cm, respectively. After being adequately informed about the goals of the study, each player agreed to provide urine and blood samples for biochemical analysis.

Study participation required each player to obtain a medical release to practice physical exercises, and they had to have trained during the pre-season. Based on these inclusion criteria, 35 athletes were selected. Of those, 24 athletes accepted to participate in the study. Six athletes were discharged from the team during the game season based on technical and administrative reasons. These athletes were excluded from the study. Eighteen athletes completed the entire game season. The 24-hour urine and fasting blood samples were collected from each player in two distinct phases: one day before the training period started (Pre-Season) and five days after the end of the game season (Post-Season). The experimental protocol was designed to assess kidney functions that are maintained after a significant recovery period in which athletes were not submitted to any training schedule. For sample collection the

players were instructed to fast for at least 8 hours prior to blood collection and to start urine collection early in the morning 24 hours prior to laboratory visit. The players were also instructed to collect all the urine produced over a full 24-hour period in a special container provided by the laboratory.

The levels of sodium, urea, glucose, total protein, creatinine, albumin, and osmolality were measured in all of the samples. The kidney function profile was determined using the solute clearance method.

All of the experimental procedures were approved by the Research Ethics Committee of the Federal University of Rio de Janeiro – Clementino Fraga Filho University Hospital (protocol number: 047/01) and complied with all the rules established by REC 047/01 involving research with human subjects. A free and informed consent form was obtained from each volunteer for participation in the study after clarification of all doubts arising from their respective reading.

### **Pre-Season and Post-Season training protocol**

The experimental protocol lasted a total of 20 weeks (five months) and was split into Pre-Season (four weeks) and Season periods (16 weeks). The athletes performed four training sessions per week during the Pre-Season period and six training sessions per week thereafter. Four weeks after the end of the Pre-Season period, one official game was added each week. The team participated in 11 official games in the Rio de Janeiro state championship throughout this period.

The training protocol for the regular season period that consisted of six sessions per week involved recovery training (e.g., continuous running with an intensity between 55-65% of the maximum heart rate); aerobic training (e.g., 70-85% of maximum heart rate); soccer-specific

training (e.g., activities performed according to the athlete's position); specific speed training (e.g., full speed running with and without a ball for 15-35 m); tactical training (e.g., activities performed according to the team's tactical scheme); technical training (e.g., offense vs. defense on small fields); collective training (e.g., practice match consisting of two 30 minute halves); and recreational training (e.g., athletes performing different functions than usual during the collective).

### **Urine and blood sampling**

Subjects provided blood samples in a seated position in the morning after a 8-hour fasting period. Blood was collected from the antecubital vein (5 mL) using a vacuum tube containing Ethylenediamine-Tetra-Acetic Acid (EDTA). Then the plasma was obtained by centrifuging the blood at  $3000 \times g$  for 5 minutes. The fractionated plasma samples were stored at  $-20^{\circ}\text{C}$  until the time of analysis. The 24-hour urine was collected and an aliquote of 40 mL was stored in a 50 mL conic bottom tube at  $-20^{\circ}\text{C}$  until the time of analysis. To avoid the acquisition of incomplete 24-hour urine samples, the athletes received the instructions for an adequate 24-hour urine collection and storage before taking it to the laboratory. All the athletes stated that they had a complete 24-hour urine collection.

### **Parameters used and determination of urinary and plasma solutes concentration**

The concentrations of creatinine (plasma and urine), urea (plasma and urine), total protein (plasma), glucose (plasma and urine) and albumin (plasma) were determined using the Creatinine PP, Urea PP, Total Protein PP, Glucose PP, Albumin PP Kits respectively (Analisa Diagnostica Ltda, Brazil). Proteinuria (urine) and albuminuria (urine) were assessed with the Proteinuria PP Kit (Analisa Diagnostica

Ltda) and Microalbumin Kit (InVitro Diagnostica, Brazil). The concentration of sodium (plasma and urine) was determined using the Sodium Rapid Kit (InVitro Diagnostica, Brasil). All procedures were performed according to the instructions provided by the manufacturers. All measurements were performed using a Thermoplate Basic biochemical analyzer.

### Determination of osmolality urinary and plasma

The osmolality (Osm), which represents the number of osmotically active particles per kilogram of solution, of the plasma and urine were measured using a vapor pressure methodology with a WESCOR Vapro 5600 Osmometer. All recordings were made according to the instructions of the manufacturer.

### Determination of the Glomerular Filtration Rate, solutes clearance and fractional excretion

The Glomerular Filtration Rate (GFR) reflects the first stage of urine formation. Herein, the GFR based on creatinine clearance was determined using the following equation:

$$\text{GFR (mL/min)} = [(UF \times U_{\text{Crea}}) / P_{\text{Crea}}]$$

Where: UF = urinary flow (mL/min),  $U_{\text{Crea}}$  = Urine creatinine concentration (mg/dL),  $P_{\text{Crea}}$  = Plasma creatinine concentration (mg/dL).

The clearance of other solutes was determined using the same equation, replacing GFR with Clearance<sub>x</sub>,  $P_{\text{Crea}}$  with  $P_{x'}$  and  $U_{\text{Crea}}$  with  $U_{x'}$ , where the subscripted X represents the selected solute.

Additionally, the fractional excretion (FE) of the solutes was determined using the following equation:  $FE = (C_x / GFR) \times 100$ . Where: FE = Fractional Excretion (%),  $C_x$  = solute clearance, GFR = Glomerular Filtration Rate.

### Urinary flow

Urinary flow is a simple methodology for evaluating the 24 hour urinary output per unit of time. It is expressed in mL/min and represents a direct relationship with the ability of the kidneys to dilute and/or concentrate the urine. The urinary flow was calculated using following the equation:  $UF \text{ (mL/min)} = V \text{ (mL)} / T \text{ (min)}$ . Where: UF= urinary flow, V= 24 hours volume of urine and T= time of urine collection.

### Evaluation of Osmolar Clearance

Osmolar Clearance is the theoretical volume of urine with the same osmolality as the plasma eliminated per unit time. It is calculated using the following equation:

$$\text{Osmolar Clearance} = (\text{Urine flow} \times \text{Osmolality urine}) / \text{Osmolality plasma} = \text{mL/min}$$

### Statistical analysis

Data are expressed as means  $\pm$  SEM. The Shapiro–Wilk normality test was performed to prove the Gaussian distribution of the data. Once the normality condition was satisfied, the data were analyzed with the unpaired Student's t-test using the GraphPad Prism 8.0 software (GraphPad, San Diego, CA, USA). Differences with p values of less than 0.05 were considered significant.

## RESULTS

### Plasma solute concentrations and osmolality

The plasmatic concentrations of creatinine, urea, sodium, glucose, total protein, albumin, and plasma osmolality of soccer players were analyzed. The plasma solutes concentrations and osmolality are presented in Table I. The plasmatic concentration of creatinine, sodium, total protein, and plasmatic osmolality were lower in the Post-Season period ( $0.63 \pm 0.05$  mg/dL,  $p < 0.05$ ;  $136.00 \pm 1.96$  mmol/L,  $p < 0.05$ ;  $3.26 \pm 0.21$

**Table I. Plasma solute concentration (Mean  $\pm$  SEM).**

Plasma Concentration	Pre-Season	Post-Season
Creatinine (mg/dL)	1.27 $\pm$ 0.02	0.63 $\pm$ 0.05*
Urea (mg/dL)	28.81 $\pm$ 1.68	33.27 $\pm$ 1.28*
Sodium (mmol/L)	145.30 $\pm$ 3.42	136.00 $\pm$ 1.96*
Glucose (mmol/L)	102.30 $\pm$ 2.57	104.8 $\pm$ 3.30
Total protein (g/dL)	5.91 $\pm$ 0.17	3.26 $\pm$ 0.21*
Albumin (mg/dL)	4.88 $\pm$ 0.15	5.06 $\pm$ 0.30
Osmolality (mOsm/kg)	297.40 $\pm$ 6.07	275.5 $\pm$ 2.63*

**p<0.05 \*.**

g/dL,  $p<0.05$ ; and  $275.5 \pm 2.63$  mOsm/Kg,  $p<0.05$ ) in comparison to the Pre-Season period ( $1.27 \pm 0.02$  mg/dL,  $145.30 \pm 3.42$  mmol/L,  $5.91 \pm 0.17$  g/dL, and  $297.40 \pm 6.07$  mOsm/Kg, respectively). In contrast, the plasma concentration of urea was higher in the Post-Season period ( $33.27 \pm 1.28$  mg/dL,  $p<0.05$ ) than in the Pre-Season period ( $28.81 \pm 1.68$  mg/dL).

There were no significant differences in the plasma concentrations of glucose and albumin in the Post-Season ( $104.8 \pm 3.30$  mg/dL and  $5.06 \pm 0.30$  mg/dL, respectively) in comparison to the Pre-Season ( $102.30 \pm 2.57$  and  $4.88 \pm 0.15$  mg/dL).

These data suggest that over the course of the Rio de Janeiro State Championship, the soccer players might be undergoing systemic modifications involved in the control of these plasma solutes concentrations. In association to the lower plasma osmolality, it is possible to point that these systemic modifications might be also related to the control of plasma volume, osmolality and protein metabolism of these athletes.

### Urinary solute excretion and urine osmolality

To verify whether the observed changes in the concentrations of plasma creatinine, urea, sodium, protein and plasma osmolality were modulated by kidney functions, particularly

by the excretion capacity of the kidneys, we evaluated the amount of excreted solutes in the urine (Table II).

The urinary excretion of urea was lower in the Post-Season period ( $15.87 \pm 1.14$  g/24 h,  $p<0.05$ ) when compared to the Pre-Season period ( $23.76 \pm 1.88$  mg/24 h). In contrast, it was observed a higher urinary excretion of albumin in the Post-Season ( $19.35 \pm 3.92$  mg/24 h,  $p<0.05$ ) in comparison to the Pre-Season ( $2.46 \pm 0.41$  mg/24 h). There were no significant differences on the urinary excretion of sodium, glucose, total protein, and creatinine and on the urinary osmolality when comparing the Post-Season and Pre-Season results (Table II). Based on these results, it is possible to suggest that the kidneys are functioning to retain more urea. This response may have been triggered to increase water reabsorption by the kidneys of soccer players during training sessions and soccer matches, in which overall water depletion may occur. Regarding the increased urinary excretion of albumin observed in the Post-Season period, it might be related both to increased glomerular permeability to albumin or decreased proximal tubule reabsorption of albumin.

**Table II. Urinary solutes excretion (Mean  $\pm$  SEM).**

	<b>Pre-Season</b>	<b>Post-Season</b>
Creatinine (mg/24h)	1698.62 $\pm$ 148.20	1336.79 $\pm$ 148.40
Urea (g/24h)	23.76 $\pm$ 1.88	15.87 $\pm$ 1.14*
Sodium (mmol/24h)	109.00 $\pm$ 11.89	118.70 $\pm$ 7.66
Glucose (mmol/24h)	39.52 $\pm$ 5.39	48.63 $\pm$ 7.72
Total protein (g/24h)	0.1596 $\pm$ 0.036	0.1597 $\pm$ 0.012
Albumin (mg/24h)	2.46 $\pm$ 0.41	19.35 $\pm$ 3.92*
Osmolytes (mOsm/24h)	497.60 $\pm$ 42.93	457.50 $\pm$ 53.51
Osmolality (mOsm/kg)	520.10 $\pm$ 60.31	532.80 $\pm$ 78.50

**p<0.05 \*.**

### Urinary Flow, GFR and clearance of solutes

To better understand if the renal excretion of solutes previously reported were not related to urinary output per se, the 24h urine volume of each athlete was collected. Next, the renal clearances of creatinine, urea, sodium, glucose, total protein, and albumin were determined based on the plasma and urinary concentrations of these selected solutes.

As shown in Table III, there was no significant change on the 24 h urinary volume and urinary flow (ml/min) of the athletes in the Post-Season in comparison to the Pre-Season period. The clearance of creatinine was higher in the Post-Season (140.50  $\pm$  21.18 ml/min, p<0.05) than in the Pre-Season analysis (93.93  $\pm$  6.58 ml/min). Similarly, it was observed that the clearances of total proteins and albumin was higher in the Post-Season period (0.0035  $\pm$  0,0003 ml/min, p<0.05 and 0.000246  $\pm$  0.000044 ml/min, p<0.05, respectively) in comparison to the Pre-Season (0.0018  $\pm$  0.0003 ml/min and 0.000039  $\pm$  0.000006, respectively). On the other hand, the clearance of urea was lower in the Post-Season (29.48  $\pm$  2.71 ml/min, p<0.05) when compared to the Pre-Season period (48.43  $\pm$  4.03 ml/min). The clearances of sodium, glucose, and osmolytes

(ml/min) from the Pre-Season to Post-Season period showed no changes.

Overall, we can estimate that the renal system of these athletes undergoes adaptations to physiologically maintain body homeostasis in response to the training protocol and game's season when the players are most required. This suggestion is specially evidenced by the increased clearance of creatinine and decreased clearance of urea, indicating both glomerular and tubular adaptations, respectively.

### Fractional excretion of solutes

By analysing the Fractional Excretion (FE) of renal solutes, we sought to better estimate the reabsorptive capacity of renal tubules. Since this analysis represents the percentage of a particular solute excreted in the urine after the glomerular filtration process, it is possible to estimate this tubular function.

We observed lower FE (%) of urea in the Post-Season period (21.40  $\pm$  2.63, p<0.05) than in the Pre-Season period (52.68  $\pm$  3.96). Conversely, the FE (%) of albumin was higher in Post-Season (0.000176  $\pm$  0.000031, p<0.05) in comparison to Pre-Season (0.000044  $\pm$  0.000009). The FE (%) of sodium, glucose, and total protein remained



**Table III. Renal solute clearances and urinary flow (Mean  $\pm$  SEM).**

	<b>Pre-Season</b>	<b>Post-Season</b>
Urinary Volume (ml/24h)	1207.00 $\pm$ 202.80	991.10 $\pm$ 91.23
Urinary Flow (ml/min)	0.838 $\pm$ 0.14	0.688 $\pm$ 0.06
Creatinine (ml/min)	93.93 $\pm$ 6.58	140.50 $\pm$ 21.18*
Urea (ml/min)	48.43 $\pm$ 4.03	29.48 $\pm$ 2.71*
Sodium (ml/min)	0.5165 $\pm$ 0.055	0.6098 $\pm$ 0.051
Glucose (ml/min)	0.0275 $\pm$ 0.004	0.02819 $\pm$ 0.005
Total protein (ml/min)	0.0018 $\pm$ 0.0003	0.0035 $\pm$ 0.0003*
Albumin (ml/min)	0.000039 $\pm$ 0.000006	0.000246 $\pm$ 0.000044*
Osmolytes (ml/min)	1.155 $\pm$ 0.09	1.156 $\pm$ 0.13

**p<0.05 \*.**

unchanged between both periods (Table IV). This data, in conjunction with renal solute clearances analysis, indicates that the renal tubules increased its urea reabsorptive capacity. It is possible to suggest that this adaptation might be necessary to improve water reabsorption by the kidneys in an attempt to maintain adequate body fluid volumes in conditions of water loss, such as during a soccer match on a tropical environment. The increased urinary excretion of albumin, as evidenced by higher FE (%) of albumin, indicates either an increased glomerular filtration barrier permeability to albumin or a reduced reabsorption of albumin by the renal proximal tubules.

## DISCUSSION

The present study assessed biochemical and functional markers of renal function of soccer players in response to a five-month game season. The Post-Season analysis revealed that these athletes present renal function adaptations that

persists even after a five-day resting period, such as increased urea reabsorption and creatinine clearance. In addition, it was also observed an increased urinary excretion of albumin (albuminuria) in the Post-Season analysis.

As part of an initial renal function analysis, the plasma creatinine and urea concentrations were assessed. The plasma creatinine concentration of soccer players has been reported to be slightly increased in relation to the normal range of general population (Banfi & Del Fabbro 2006, Banfi et al. 2011). This finding has been attributed to the higher muscle mass of athletes from different sport modalities and shows direct correlation to their body mass index (BMI) (Banfi et al. 2006). In accordance, the Pre-Season plasma creatinine of the soccer players enrolled in our study was indeed close to the higher limit of serum creatinine range as reported by other authors (Banfi et al. 2009, Meyer & Meister 2011).

On the other hand, these athletes presented lower plasma creatinine concentration in the

**Table IV. Fractional excretion of urinary solutes (Mean  $\pm$  SEM).**

Fractional Excretion (%)	Pre-Season	Post-Season
Urea (%)	52.68 $\pm$ 3.96	21.40 $\pm$ 2.63*
Sodium (%)	0.59 $\pm$ 0.06	0.46 $\pm$ 0.06
Glucose (%)	0.027 $\pm$ 0.0048	0.018 $\pm$ 0.0048
Total protein (%)	0.0021 $\pm$ 0.0005	0.0031 $\pm$ 0.0004
Albumin (%)	0.000044 $\pm$ 0.000009	0.000176 $\pm$ 0.000031*
Osmolytes (%)	1.27 $\pm$ 0.08	0.82 $\pm$ 0.10*

**p<0.05 \*.**

Post-Season analysis. While acute increases of plasma creatinine have been reported by following a soccer match (Colombini et al. 2014), long-term modifications of plasma creatinine was not observed in elite soccer players throughout a game season (Meyer & Meister 2011). Although it is tempting to suggest that the reduced plasma creatinine concentration observed in our study might result from an unbalance between creatinine elimination and production, there was no changes on the urinary excretion creatinine. Therefore, an extra-renal component might be contributing to the observed reduced levels of plasma creatinine.

Additional information that might point to a reduced creatinine production in these athletes should be further explored in future studies.

In the present study it was observed that soccer players presented higher plasma urea concentration in the Post-Season period. Manna et al. (2010) also found increased plasma urea concentration in soccer players after an 8-week training protocol followed by a 4-week competitive phase when compared to baseline data (Manna et al. 2010). The mechanisms contributing to this rise of serum urea, although not fully elucidated, are related to the rate of

urea production and elimination (Weiner et al. 2015).

Some authors have suggested that elevated serum urea results from increased muscle catabolism and protein turnover in conditions where athletes are submitted to physical exhaustion, as in reduced recovery intervals or intense training loads (Hartmann & Mester 2000, Coutts et al. 2007). While this hypothesis may not be ruled out in the present study, we suggest that kidneys also play an important role to the rise of plasma urea of soccer players in the Post-Season period, as evidenced by a significant reduction of 24-h urinary excretion of urea.

Besides, the renal reabsorption of urea may indicate a physiological response to conserve water by increasing urea concentration in the inner medullary interstitium, which enhances renal water reabsorption (Bankir & Trinh-Trang-Tan 2000, Sands 2007). This is an expected response since soccer players commonly experience periods of hypohydration due to significant water losses during a match (Kurdak et al. 2010, Silva et al. 2011). The exercise-associated water depletion is even more pronounced in hot environments, such as those



in a tropical country like Brazil (Shirreffs et al. 2005). Thus, it is reasonable to point that the renal system of these athletes have adapted to converse water.

Exercise-associated hyponatremia is a condition in which athletes present a decrease of serum sodium to levels below 135 mmol/L after an intense physical activity (Rosner & Kirven 2007, Hew-Butler et al. 2017). In the present study, although the athletes did not present hyponatremia, plasma sodium levels were decreased to the lower limit in the Post-Season period. The first possible explanation for such observation might be related to electrolyte losses through sweating that soccer players experience during a match (Maughan 1991, Maughan et al 2004). Therefore, the significant depletion of sodium that is experienced by soccer players in response to successive sweating periods (Maughan et al. 2005, Shirreffs et al. 2005), such as during a game season, may result on the plasma sodium decrease.

The intake of electrolyte-free drinks also contribute to the decrease of sodium plasma levels since hypotonic fluids may lead to plasma dilution (Maughan 1991, Monteiro et al. 2003). As a response, these athletes also present reduced plasma osmolality due to the role of sodium chloride in the control of plasma osmolality (Ackerman 1990). Therefore, the observation that the soccer players of our study also presented reduced plasma osmolality in the Post-Season period, is an expected condition.

The balance of sodium in the human organism is also dependent on the renal capacity to retain or excrete filtered sodium (Feehally et al. 2018). Considering that the athletes showed no change on the renal clearance and FE (%) of sodium, these results indicate that the extrarenal components of sodium balance contributed more to the reduced plasma sodium

levels observed in the Post-Season period than the renal components.

In association with the plasma concentration of the selected solutes used in the present study, the urinary concentrations and mass excretion of these solutes, as well as solute clearances, may indicate how the renal system of the soccer players adapt in response to the whole game season.

Interestingly, the clearance of creatinine, which is commonly be used to estimate the GFR (eGFR), showed to be higher in the Post-Season period. It has been long known that several factors may contribute to the control of GFR (Hall & Hall 2020). These factors act mostly through the modulation of renal blood flow (RBF) and the net ultrafiltration pressure inside the glomerular capillaries (Hall & Hall 2020). Consequently, an increase on the RBF or changes in afferent and efferent arteriolar resistance, which may result in an elevated net ultrafiltration pressure, could lead to an increase of creatinine clearance (Hall & Hall 2020).

In this context, we could hypothesize that the increased creatinine clearance presented by the athletes during the Post-Season period might be a renal response to two possible conditions: a) fluid-overload due to excessive hydration during the resting period or b) an activation of the renin-angiotensin-angiotensinogen system (RAAS), both of which could increase GFR. Despite these suggestions, it is important to note that the estimation of GFR by the clearance of creatinine in athletes have been questioned by some authors (Poortmans & Vanderstraeten 1994). Thus, we can not rule out the possibility that the elevation of creatinine clearance was due to altered levels of plasma creatinine in these athletes, leading to an superestimated eGFR.

As discussed earlier, we suggest that the reduced urinary excretion of urea presented

in the Post-Season period may result from enhanced renal reabsorption of urea in an attempt to increase water retention. The observation that soccer players also presented lower clearance and FE (%) of urea in the Post-Season analysis corroborates to the hypothesis that the kidneys of these individuals have increased its urea reabsorption capacity in response to the conditions experienced during the game season.

Of great importance to the renal function analysis, the urinary excretion of total proteins and albumin contribute to the assessment of both glomerular filtration membrane integrity and tubular protein reabsorption capacity (Viswanathan & Upadhyay 2011). Although renal excretion of total proteins and albumin, known as proteinuria and albuminuria, are related to the pathophysiology of many renal diseases, the exercise-induced proteinuria has been described as transient observation presented by athletes after sports exercises (Shephard 2016, Wołyniec et al. 2019).

In the present study it was observed a 7-fold increase on the 24h urinary excretion of albumin in the Post-Season period in comparison to baseline. On the other hand, there was no change on the total protein urinary excretion of these athletes. Similar observation has been reported by Poortmans et al (1988) in a laboratory study with cyclists, in which volunteers presented a 48-fold increase of albumin excretion in comparison to baseline, while total proteins excretion only increased 14-fold. This discrepancy between proteinuria and albuminuria may be related to different origins of post-exercise-induced proteinuria, which might be both related to increased glomerular membrane permeability to albumin and reduced tubular reabsorption of low-molecular weight proteins present in the ultrafiltrate (Poortmans et al. 1988).

The absence of proteinuria in association with an increased renal clearance of total proteins in the Post-Season point to an enhanced reabsorption of low-molecular weight proteins by the proximal tubules. This mechanism may explain the observation that soccer players present spontaneous regression of exercise-induced proteinuria after exercise cessation (Edes et al. 1990). Furthermore, the results presented in this study indicate that the recovery of nephron components involved in the generation of exercise-induced albuminuria may take longer than those related low-molecular weight proteinuria after exercise termination. The association of exercise-induced proteinuria and albuminuria to the progression of chronic kidney diseases remains to be clarified.

In sum, these results suggest that soccer players present renal adaptations in response to soccer-associated exercises that they perform during the entire game season. The prominent renal adaptations are those related to water conservation through increased urea reabsorption. In addition, based on our scheme of sample collection, it is possible to suggest that the kidneys are “trained” to conserve water in response to successive periods of dehydration that soccer players experience throughout an entire game season. This “trained” capacity seems to last longer periods since the post-season analysis were performed five days after exercise cessation.

### **Study Limitations**

Study limitations should be taken into account when generalizing our findings. First, the number of athletes participating in the study was reduced in the end of game season because six soccer players were discharged from the team based on technical and administrative reasons. Consequently, data collected from these athletes at the Pre-Season period were excluded

from our analysis. Second, the assessment of other renal function markers, such as markers of tubular dysfunction (KIM-1 and N-GAL) would provide a better comprehension of the effects of soccer-associated exercises on this nephron segments. At last, based on the variation of plasma creatinine levels that athletes may present (Poortmans & Vanderstraeten 1994), the use of a more accurate method for GFR estimation, such as inulin clearance, would be of great value when analysing this parameter in soccer players.

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RASP: Writing, discussion of the data and data collection. IMB: Scientific review of clinical issues of the datas. IRA: Laboratory analyses of blood and urine solutes. KVP: Laboratory analyses of blood and urine solutes. TBC: Laboratory analyses of blood and urine solutes. VCT: Laboratory analyses of blood and urine solutes. APM: Volunteer recruitment and interview, blood and urine samples collection and sample trial. BGR: Scientific review of the sports issue of the datas. NMF: Scientific review of the manuscript and data analyses. CMB: Scientific review of the manuscript and data analyses. RNF: Scientific review of the manuscript and data analyses. JSM: Project coordinator, writing, discussion of the data, data collection, laboratory analyses of blood and urine solutes, blood and urine samples collection, sample trial, scientific review of the manuscript and data analyses.

