



## RESEARCH ARTICLE

## Possible interconnection between irrational doping, veterinary medication, and pathomorphological changes in the iliac artery segment in population of cyclists who have infected and recovered from Covid-19 disease

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## PUBLISHED

30 September 2024

## CITATION

Solakovic, S., Serhatlic, H., et al., 2024. Possible interconnection between irrational doping, veterinary medication, and pathomorphological changes in the iliac artery segment in population of cyclists who have infected and recovered from Covid-19 disease. Medical Research Archives, [online] 12(9).

<https://doi.org/10.18103/mra.v12i9.5680>

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## DOI

<https://doi.org/10.18103/mra.v12i9.5680>

## ISSN

2375-1924

## ABSTRACT

**Introduction:** Doping which includes veterinary drugs as irrational human medicine after the infection with COVID 19 still leaves the field open from the aspect of vascular surgery and angiology of the iliac segment. Reflection of the effect of the COVID 19 virus on the sports performance of athletes in various sports after the corona virus is still present. Some athletes have had a hard time individually coping with the clinical consequences after a long illness of the COVID 19 virus. Even though covert doping is part of the everyday life of an elite athlete, it still remains an unresolved topic in the form of a solution for post-COVID 19 symptoms or switching to or taking some other masked substances that are impossible to detect in the blood, as well as a potential reflection on the morphological changes of the arteries. Although consequences of the corona virus for the cardiorespiratory system have been reported, a question arises as to the connection between the development of iliac syndrome and pathomorphological arterial iliac changes in athletes with suspicion of potential correlation with underground doping substances of pharmacologically untested origin in the Balkan population. Widespread global COVID 19 pandemic and the isolation factor have forced numerous athletes to switch their normal training routine and protocols to alternatives such as cycling with or without abusing illegal substance. Increased intima-media thickness, the first structural change detected in atherosclerosis, is an important surrogate marker in atherosclerosis can be connected with high intensity endurance cyclists, running and triathlon competitive athletes affecting their poor performance status and professional doping levels. In some cases, amateur and recreational athletes are also affected especially if they were exposed to COVID 19 infection and doping. **Goals:** The primary focus of the present study is to determine the initial progression of the disease during and after the COVID 19 pandemic, starting from morphological changes and obstructive arteriopathy of the external iliac artery on account of measuring intima media thickness and the possibility of outset of kinking and obstructive arterial disease of the external iliac artery after 3 years. The secondary focus of the study is to examine the influence of doping on the pathomorphological changes of the external iliac artery during 3 years of research.

**Subjects and Methods:** two groups of were observed (recreational and amateur cyclist). In total 63 selected subjects in the demographic area of former Yugoslavia without cardiovascular disease were observed during the January 2021 and January 2024 period (3 years).

**Results:** Changes in intima-media thickness of iliac artery from baseline 3 years were observed between the standard exercise amateur group and recreational control group. However, intensity exercise under 9000km per year were no significant developing progression of intima-media thickness of iliac artery during 3 years in recreational control group, but minimal progression of intima-media thickness of iliac artery were significant in amateur cycling group due to the potential effect of doping.

**Conclusion:** The application of doping itself is indisputable, but the missing link that would confirm this claim is scientifically limited. We cannot confirm with certainty what is the trigger for the progression of pathomorphological changes and whether the consequences of overcoming the COVID 19 infection or doping. But there are many scientific facts and studies that confirm the connection between progressive atherosclerosis and illegal underground doping substances of pharmacologically untested origin. The consequences may result with a tendency for a futuristic vascular invasive patch or bypass surgical treatment.

**Keywords:** Anabolic steroids, Veterinary drugs, Intima Media Thickness, External iliac artery, Arteriopathy, Doping.

## Introduction

In general, the scientific question is how doping affects individual arterial segments specifically on the iliac arteries in recreational cyclists and amateurs, especially after the infection of COVID 19 is still unknown. Influence of the social media has facilitated the distribution and availability of anabolic steroid consumption as well as of illicit pharmacological recovery substances at any level of sports, whether amateur, professional or recreational. Although available data are limited when it comes to the connection between the recent COVID 19 infection and the abuse of anabolic steroids (pharmaceutical black market and underground products of a questionable character) and the connection of accelerated pathomorphological changes in the arterial segment and development of the iliac syndrome and progression of the iliac artery segment atherosclerosis in athletes, that still remains a topic of discussion on the potential risk worldwide<sup>1,2</sup>.

Numerous massive epidemiological safety measures during COVID 19 pandemic and closure of fitness clubs throughout the world have forced a large number of athletes to remodel their training process (from anaerobic to aerobic) and resort to alternative sports that had not been their first choice (such as cycling) in order to maintain the substance and quality of a training process. Arteriopathy of the external iliac artery, or a more comprehensive term Cyclist's Iliac Syndrome, stands in correlation with intensive professional sports trainings and aerobic activities such as cycling, triathlon, endurance running (marathon), and even biathlon.

All professional sports supra-performances outside of the scope of a normal and usual range of human fitness abilities and beyond the supreme sports professional norms have been linked to doping or suspicion of doping. Doping as a Ex Yugoslavian unofficial underground black-market cult of applicative use tend to be more commonly reported in amateur as well as in recreational sports that are not subject to rigorous doping controls,

which means it thus finds an easier way in such activities, while in professional sports it is under supervision with more or less control<sup>3,4</sup>.

Since a lot of time and lot of clinical and laboratory tests may pass from the start of camouflaged symptomatology of exhaustion from the beginning of lactate measurement, the overtraining syndrome, and a usual loss of electrolytes and leg pain, before one suspects and confirms the diagnosis, this phenomenon constitutes a noticeable health and professional issue in progression, by way of reducing physical and fitness performances in sports professionalism, for which an individual bears health and professional consequences<sup>5</sup>. The decade professional cycling still most commonly accompanies further progression of arterial diseases with elongation and external iliac artery kinking, and thus attracts most attention to the development of the very symptomatology of obstruction of external iliac artery hemodynamic, where a lot of questions still remain unresolved, and the responses thereto remain based on a good theoretical structuring<sup>5,6,7</sup>.

Studies contain proven histopathological data that do not determine the signs of atheromatosis but subendothelial fibrosis with a loss of longitudinal elasticity with of collagen fiber replacement, which is suspected to have originated due to a possible chronic pathology of hyper-hemodynamic trauma maximization in relation to endothelium<sup>8-13</sup>. Progression of the external iliac artery arteriopathy develops an anatomical angulation of the artery position, with a possibility of psoas muscle hypertrophy, with a circumference exceeding 3cm, as well as of the very dorsal forces of repetitive action of hip muscle flexions. The potential theory of a sharp individual position between anatomical artery bypass caused by variable angle position as well as variable seats of variable bicycle frames as one of the possible potential risk factors, even a potential threat of arterial wall dissection<sup>14-17</sup>.

This atherosclerotic pathological process is significantly associated disease was linked to a professional sports cycling by the Chevalier et al. in

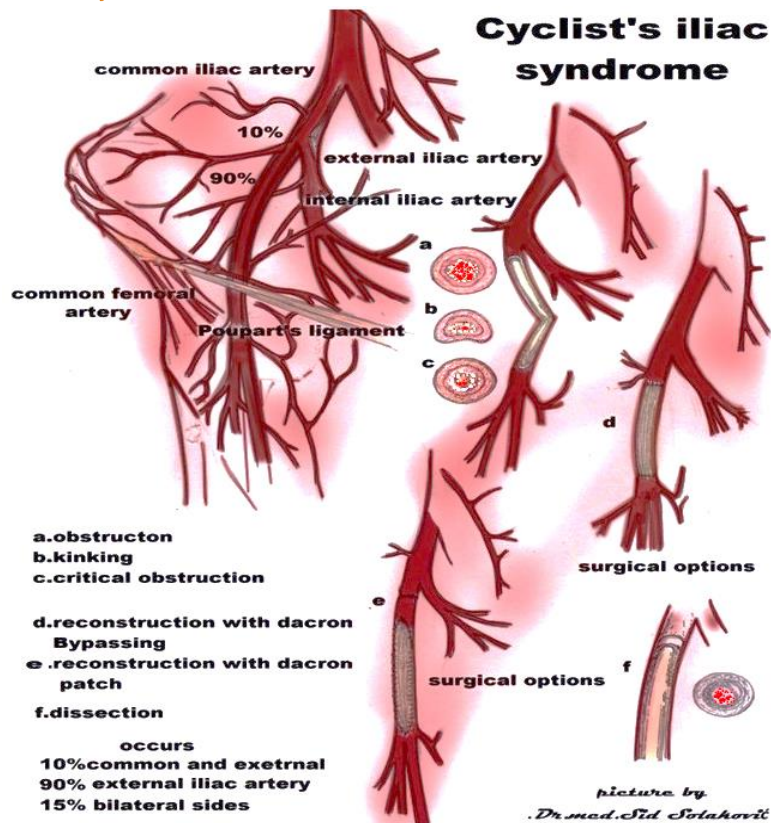
the mid-1980's<sup>11</sup>. Although the entire iliac segment is exposed to the effect of muscular mechanization and shear stress. In 90% of the cases it affects the sitting-induced anatomic angulation of artery iliac external distance of 2-6 cm, while in only 10% of the cases there is an isolated or combined thickness of the common iliac artery and the external iliac artery, while the internal iliac artery, due to its anatomic position, is not prone to professional sports cycling disease given its anatomic localization. A harmful effect of doping on the iliac segment endothelium still remains unknown. External iliac artery arteriopathy is transferred from the external iliac artery to the common femoral artery under the inguinal ligament, creating compressive ligament effect for a potential onset of kinking and vascular obstruction, with the already present pathological angulation<sup>1,3,7</sup>.

Unlike common and the external iliac artery atherosclerosis that may affect both extremities, it usually affects the less dominant lower extremity in monocyclic muscular dynamics, but the symptoms may also be bilateral in 15% of the cases<sup>18-23</sup>. The disease is predominantly associated with sports professionalism where the demands of sports performances prevail over the forces of physiological hemodynamics, and put them on a higher and prolonged level at which the action of bloodstream impacting force or shear stress is exposed to a maximum and long-term durability, as well as the enormous forces of elasticity affecting the artery on account of a strong cardiac output, with a loss of longitudinal elasticity due to possible chronic pathology of sports trauma hyper-hemodynamics on the initial thickness of the iliac endothelium media even all the way to adventitia without calcium deposit in the arterial wall of the iliac artery<sup>20-21</sup>. Although all pathological matters have been more or less mentioned here, there are numerous other effects on the action of the very disease of genetic or anabolic steroid-induced effect of undetected masked doping. Illegal and legal recovery agents of all forms and shapes, especially synthetic forms of testosterone

propionate/ cypionate and insulin as adenosine triphosphate (ATP) imitate muscular application with the effect of EPO erythropoietin and pre-competition autotransfusion as one of the favorite doping agents in professional sports cycling. Hematocrit and erythropoiesis are increased to the point where blood acts as an inhomogeneous mass, thus potentiating the effect on the blood wall endothelium and increasing the effect of shear stress.

Due to limitations of these studies, the segment remains a matter of scientific debate and potential connection of the success of masking illegal substances and the very effect of the previous COVID 19 infection<sup>24-27</sup>. The affected population group are, on average, athletes aged between 22 and 25, with the average distance covered annually ranging from 8000-35000 kilometers, or more than 150000 kilometers as a career average. By way of hip muscles provocative maneuvers the arterial duplex spectrum may be diagnosed in more than 80% of the patients with confirmed disease. Surgical options vary in relation to the clinical picture and dislocation as well as elongation of endofibrotic lesions and obstruction of the external iliac artery from the saphenous vein interposition as well as endarterectomy with an external patch / patch plasty.

Since all the research has been predominantly related to the already presented symptomatology and asymptotology of professional athletes, while data are limited concerning the use of bicycles for free, recreational and amateur purposes, one should compare whether the increase of intima media thickness is related to the intensity, mileage, kilowatts, cadences as well as decade use of the bicycle and the effect of doping for various sports purposes, and try to find a nexus and the missing link between the illegal agents in the development of the very initial capsule of the disease progression kinking with a view of the effect of underground pharmaceutical industry and sports science and a potential outcome of surgical treatment.



Picture 1 Shows the potential possibility of classic surgical therapy as well as the most common predilection sites of iliac artery segment disease. Surgical options of iliac-femoral reconstruction with bypass technique or Patch Angioplasty

#### AIM OF STUDY

The primary aim of the present study is to determine the initial progression of the disease during and after the COVID 19 pandemic, starting from morphological changes and obstructive arteriopathy of the external iliac artery on account of measuring intima media thickness and the possibility of onset of kinking and obstructive arterial disease of the external iliac artery after 3 years (36 months). Although the arterial disease covers all three arterial layers of the iliac artery anatomy, the research will not be done concerning the priority of predilection values and various aberrations of iliac artery magistral segment pathology. Secondary aims include measurements that will be in correlation of subjects with various intensities and units of amateur and recreational training, the distance covered, and the effect of intensity, distance and duration of training with the connection between the progression of intima media thickness of the external iliac artery in various forms of cycling, and a self-initiated application of doping (stacking of illicit doping substances of testosterone hormone as well as anabolic steroids).

#### ETHICAL RESEARCH CONSIDERATION

In the interest of sports and health of the athletes and recreational cyclists, it is necessary to effectively reduce the abuse of doping and prevent its very application, and thus limit the undesired effects of the doping substances. On account of the previous COVID 19 infection and a decline in performances, the very self-initiated concept of doping as well as alternative measures of applying illegal substances for recovery in the form of ethical principles of medical and sports profession, multiple multi-disciplinary talks were held with each of the individual self-initiated subjects of this study concerning the consequences of the harm caused to the health by the self-initiated application of anabolic steroids with and without indications and medical consultation and supervision as to where such road leads. Also try to ban the very application of anabolic steroids as well as similar doping substances as well as influence the avoidance of the same substances in order to impair mental and physical health. The potential of individual shortcomings in fields (medicine, sports sciences, vascular surgery) through a multidisciplinary study

with a focus on the pathology of arterial iliac disease should be emphasized.

## Material and Methods

### PARTICIPANTS AND EXPERIMENTAL DESIGN

The study was conducted in the demographic areas of the countries of former Yugoslavia, as well as in individual healthcare institutions in those countries. The investigation was finally done as a double-blind prospective 36-month study between early January 2021 and January 2024, whose data were in limited number and statistically processed at the BiH Faculty of Sports and Physical Education, Universities of Sarajevo, East Sarajevo and partly also at the Special Hospital Dr. Solaković.

The study observed a group of 63 participants, 27 of whom were amateur and 36 recreational subjects, who were only engaged in cycling and who were using anonymous doping in their amateur or recreational training and training recovery process. The task was to examine the effect of mileage on the intima media thickness of the external iliac artery with medium average which have values before performing data analysis of amateur participants' right ( $0.46 \pm 0.03$ ) and left ( $0.48 \pm 0.03$ ), and the values before performing data analysis recreational participants' right ( $0.45 \pm 0.02$ ) and left ( $0.44 \pm 0.03$ ), and to try and draw a parallel between mileage, kilowatts and intensity in relation to the progression of inflammatory intima media thickness of the external iliac artery in amateurs and recreational subjects, as well as the outset of potential kinking with using vascular ultrasound method. The possibility of the most common potential pathomorphological changes occurs on the external iliac artery, that is why the primary focus of this study will be the external iliac artery.

Before the study began, all the subjects were examined by an entire medical team, led by a vascular surgeon and a sports medicine team of international experts in sports medicine and recreational sports at the BiH Faculty of Sports and Physical Education, Universities of Sarajevo. Their

examination also took place on completion of the study. All patients have completed the study successfully. There were no lost-to-follow-up subjects. The progression of intima-media thickness will be measured by abdominal ultrasound probe 2.5 MHz or vascular linear probe 7-15 MHz while limiting possible minimal departures. Professional cyclists will not be included in the 3-year study. Out of the 63 participants,  $63 \pm 2$  of them had COVID 19 infection during the study,  $14 \pm 4$  more than once; also, the 63 participants confirmed a subjective negative effect of Covid 19 infection on their current performance, and confirmed their use in order to enhance their performance and achieve the previous level. Due to the very multidisciplinary complexity of the approach to the topic itself, as well as the scientific limitations of the compactness of data from the fields of medicine, sports science, illegal underground doping substances, post-COVID symptoms, as well as outdated veterinary withdrawn drugs, a mixed method research of scientific research methodologies was conducted, which leaves the scientific field open for more detailed scientific and more specific analysis of individual research areas.

## Results

The results of the study are contained in the continuation of the text. Typical POST COVID 19 Symptomatology in both groups ACG vs. RCG ( $n=63$  participants)  $p>0.005$ ).

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Sleep problems (transient and persistent symptoms)	5±3
Headache (occasional)	1±3
Dizziness when standing up (light headedness)	2±1
Pins-and-needles feelings (transient symptoms)	4
Change in smell or taste (transient symptoms)	2
Depression or anxiety (transient and persistent symptoms)	2
Anxiety (occasional)	13 ±3
Tiredness or fatigue that interferes with daily life (occasional)	14±3
Joint or muscle pain in calf (occasional)	8
Joint or muscle pain in thigh (occasional)	4
Joint or muscle pain in lower back (occasional)	1
Difficulty breathing or shortness of breath	0
Chest pain (with no evidence of Heart Disease)	0

The results of study above are specific to our demographic area and provide a wide range of multidisciplinary information for both amateur and recreational cycling. The results of the analysis of the study showed that of the 19 post-COVID symptoms in both groups (amateur and recreational), joint or muscle pain (calf, thigh, lower back) occur in 13 participants (or 20.63%)

participants and Tiredness or Fatigue in 14 (or 22.21%) participants and Anxiety in 13±3 (20,63%) participants (were statistically most common (p>0.005). There was statistically confirmed no cardiac chest pain and Difficulty breathing or shortness of breath (in connection with cardiac diseases) in any of the examined participants (p>0.005).

**Table 1.** Resulting average for Amateur Cyclists Group (ACG=27), after 12, 24, 36 months (p>0.005)

	12 months	24 months	36 months
Average of Human height	174cm±0.3cm	174cm±0.3cm	174cm±0.3cm
Average of Human weight	65±2,1kg	63±2,1kg	64 ± 2.9kg
Average age male in years	31 ±0.2	30 ±1.2	32±0.5
Amateur career in years	9.5±2.1	10.5±2.1	3±2.1
Average of Activity Calories after one year	449.233 C	519.239 C	499.389 C
Average distance in one year	8.055.1 km	8.258.8 km	8.393.4 km±21km
Average of Total Activity Time on bike in year	361h 53m	316h 17m	317h±18m
Rides count	218±0.6	190 ±0.6	232± 17
Average Elevation Gain	129.493(m)	96.995 m (m)	71.488 (m)
Average Speed (kph)	22.2(kph)	26.1 (kph)	26.4±0.9 (kph)
Average Heart Rate	156 ±0.9(bpm)	155 ±0.3(bpm)	155 ±0.4 (bpm)
Average Run Cadence	79±0.58	79±0.58	79±0.58
Abuse of Anabolic androgenic. steroids (orals /i.m) and EPO	13±1	16±1	16±.1
Abuse Testosterone propionate 100 mg/ml	16 ±1	14	14
Abuse Testosterone enanthate 250 mg/ml	0	0	3
Abuse Testomix (Sustanon 250/300 mg/ml)	0	1	1

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	12 months	24 months	36 months
Abuse Human growth hormone (HGH)	23	25	4±2
Tribulus terrestris (TT) supplementation (testoboosters)	0	0	7
Corticosteroids	24	20	20±2
Painkiller (Tramadol or Vicodin)	17	21	19±4
Suspect subjects on other illegal drugs	3	23±2	20
Erythropoietin	22±2	22±1	20.34
Abuse of Boldenone undecylenate	5	3	1±.1
Kinking left EIA (or other iliac artery anatomy part)	0	0	0
Kinking right EIA (or other iliac artery anatomy part)	0	0	0
Lost to follow up	0	0	0

The Table 1 and 2 indicates the monitored changes of different multidisciplinary parameters in amateur cyclists who were infected with the COVID 19 virus during the pandemic in a period of 12 months, 24

months and 36 months, and the impact of the abuse of various substances and potential as a reflection on the performance as well as the Patho morphology of the iliac arteries.

Table 2. Resulting average for Recreational Cyclists Group (RCG =36) after 12. 24. 36 months (p>0.005)

	12 months	24 months	36 months
Average of Human height	183 ±2.3cm	183 ±2.3cm	183 ±2.3cm
Average of Human weight	87±2.9	86±2.9	83±3.1
Average age male in years	29 ±1.2	30 ±1.2	30 ±1.2
Amateur career in years	0	0	0
Average of Activity Calories after one year	299.319 C	269.559 C	319.219 C
Average distance in one year	3.296.3 km ±21km	4.926.3 km ±11km	4.129.3 km ±15km
Average of Total Activity Time on bike in year	155h 47m	103h 37m	133h 37m
Rides count	99±11	204±0.7	119±0.9
Average Elevation Gain	16.902 m (m)	28.041 m (m)	29.280 m (m)
Average Speed (kph)	21.2±0.4 (kph)	23.3±0.4 (kph)	23.2±0.3 (kph)
Average Heart Rate	136 ±0.6 (bpm)	132 ±0.6 (bpm)	133 ±0.6 (bpm)
Average Run Cadence	79±0.52	67±0.59	79±0.18
Abuse of Anabolic androgenic. steroids (orals /i.m) and EPO	0	0	0
Abuse Testosterone propionate 100 mg/ml	0	0	0
Abuse Testosterone enanthate 250 mg/ml	0	0	0
Abuse Testomix (Sustanon 250/300 mg/ml)	0	0	0
Abuse Human growth hormone (HGH)	0	0	0
Tribulus terrestris (TT) supplementation (testoboosters)	24	22±1	23±1

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	12 months	24 months	36 months
Corticosteroids	0	0	0
Painkiller (Tramadol or Vicodin)	0	0	0
Erythropoietin	0	0	0
Suspect subjects on other illegal drugs	0	0	0
Abuse of Boldenone undecylenate	1	2	2
Kinking left EIA (or other iliac artery anatomy part)	0	0	0
Kinking right EIA (or other iliac artery anatomy part)	0	0	0
Lost to follow up	0	0	0

The Table 3. shows the progression of intima medial thickness in recreational cyclists' group (RGC) and amateur cyclists' group (ACG) who were infected with the COVID 19 virus during the pandemic over a period of 12 months, 24 months and 36 months which the values of the data analysis were done by ultrasound. According to the data

results of the conducted study for after 3 years of research among the amateur group of cyclists, the average of age was  $29 \pm 1.2$  years and average of height was  $174 \pm 0.3$ cm. While interesting data indicate on the average active career was  $9.5 \pm 2.1$  years.

**Table 3.** Intima Media Thickness (IMT) in Amateur Cyclists Group (ACG) vs. Recreational Cyclists Group (RCG); ( $p > 0.005$ )

	IMT ACG	IMT RCG
Average IMT of Left EIA after 12 months	$0.48 \pm 0.03$	$0.45 \pm 0.03$
Average IMT of Right EIA after 12 months	$0.46 \pm 0.03$	$0.45 \pm 0.03$
Average IMT of Left EIA after 24 months	$0.58 \pm 0.03$	$0.45 \pm 0.03$
Average IMT of Right EIA after 24 months	$0.56 \pm 0.03$	$0.46 \pm 0.03$
Average IMT of Left EIA after 36 months	$0.57 \pm 0.03$	$0.46 \pm 0.03$
Average IMT of Right EIA after 36 months	$0.56 \pm 0.03$	$0.46 \pm 0.03$

Also, the Average of Wattmeter after 36 months in the group of amateurs statistically recorded the higher number of Watts ( $318 \pm 72$ ) compared to the average data in the recreational group of ( $202 \pm 27$ ) Watts ( $p > 0.005$ ). It is a statistical fact indicate that enormous numbers of amateur individuals when comparing the supplementation between the two groups, the amateur group statistically preferred abuse of human growth hormone (HGH) (on average for three years in (25.21 or 92.59%) subjects, while the recreational group was more focused on using Test boosters in 23.11 subjects on average ( $p > 0.005$ ).

Also, the benefits are only reflected in the reduced maximum heart rate of amateur cyclists after three

years of  $155 \pm 0.03$  beats per minute on average. Statistically exceeding the maximum heart rate of recreational athletes of  $134 \pm 0.03$  beats per minute on average. ( $p > 0.005$ ). The results of riding the distance on average of  $8.393.4 \text{ km} \pm 21 \text{ km}$  among amateur cyclists is statistically significantly higher than the average distance traveled by the recreational group of cyclists  $4.129.3 \text{ km} \pm 15 \text{ km}$  ( $p > 0.005$ ). Also, the average weight was statistically significantly lower in the amateur group of participants of  $64 \pm 2.9 \text{ kg}$  on average with a difference after 36 months from the group of recreational participants of  $83 \pm 3.1$  kilograms on average which is statistically more significant for the characteristics of this group ( $p > 0.005$ ).



The focus was on the measurement of the intima media thickness over a period of three years in both groups (amateur and recreational). It showed different and interesting results (Table 3). The Results were in amateur statistically higher  $0.56 \pm 0.03$  (mm) on the right external iliac artery and also on the left external iliac artery  $0.57 \pm 0.03$  (mm) in comparison to recreational group in which the indicative benchmarks were much lower ( $0.46 \pm 0.03$ ) on left and ( $0.46 \pm 0.03$ ) on the right side on external iliac artery. ( $p > 0.005$ ).

Regarding information and data about the testosterone esters, Testosterone propionate 100 mg/ml (of unknown dosage) was most frequently used in the amateur population group with a peak from the first year of testing in  $16 \pm 1$  subjects or 22.85% with a slight drop after three years in 14 subjects or 17.41 % ( $p > 0.005$ ). We were not able to collect results and information on the cycle itself because most of the subjects kept it as a private secret (especially dose adjustments). Further research in doping topic after 36 months revealed that the most popular ester of testosterone in the amateur group was propionate while other esters such as enanthate or testomix / Sustanon (4 types of testosterone: 1 fast-releasing ester, the second medium medium-releasing ester and 4 slow-releasing esters) were not popular, probably because of the very duration of doping detection in blood which is also statistically significant ( $p > 0.005$ ).

Also stunning is that the use of Tribulus terrestris (TT) (as a testosterone booster supplementation) confirmed in both groups, statistically with a lot a higher representation of consume in recreational group in 23,1 subjects (63,88%) after 36 months and lesser in amateurs 7 subjects or 19,44% ( $p > 0.005$ ). The amateur group had subjective benefits from its use due to the application of the testosterone hormone while in the recreational group the data indicate that no one abused injectable testosterone hormone of any kind of his esters. ( $p > 0.005$ ). The study indicated a statistically significant use of prohibited substances of

erythropoietin EPO in amateur cyclists (likely to stimulate growth and to raise the level of red blood cell count, hemoglobin and hematocrit in the blood). Changes in EPO abuse are more dominant with an average of 20.34 subjects or (70.07%), which is more than a half of the examined group in a period of 36 months, in contrast to recreational cyclists, of which only one subject used it for the entire 36 months ( $p > 0.005$ ).

The entire results of the conducted study indicate and confirm the presence of high level of doping in the amateur sport of cycling with the abuse of highly effective substances raising certain cycling performance to a higher level ( $p > 0.005$ ). An interesting fact is also the application of veterinary drugs such as Boldenone undecylenate which is present in both groups but only a few, insignificantly small number of amateur cyclists used it ( $p > 0.005$ ).

Also significant scientific representation after 36 months of study is abuse of corticosteroids in 21 subjects or (58,33%) and painkillers (Tramadol or Vicodin, for example) were confirmed in 19 subjects or (52,77%). More convincingly dominant in the group of amateur cyclists unlike the recreational group which indicates that half of amateur cyclists abuse these drugs during period of 36 months ( $p > 0.005$ ). We are not sure with other scientific data and studies why especially Boldenone undecylenate and is abused in cycling. Assumptions on account of the data are that there is a strong probability of using prohibited pharmacological means of recovery that are easily detected in a doping test due to the poor and limited economic status of individuals after COVID 19 pandemic, especially in the Balkan region.

## Discussion

The hidden risk of abuse of steroids or similar illicit agents for recovery at any level of sports continues to represent a Russian roulette where the price of performances is an irreparable deterioration of health. The possibility of irrational cycles of numerous oral as well as intramuscular applications

of testosterone derivatives as well as synthetic unverified testosterone esters that directly affect cytokine secretion as well as by COVID-19 in the end causing arterial occlusion on the iliac arterial segment is not excluded. Considering that the iliac segment is well compensated by the arterial collateral network, the clinical symptomatology of ischemia may be completely absent, especially in the case of provoked physical effort for specific sports performances<sup>28, 29</sup>.

The problem of interaction of COVID 19 virus with doping and symptoms related to the diseased condition will continue to be an unsolved secret for a long time, although some facts are evident. We assume that the use of veterinary drugs such as Boldenone undecylenate in cycling would have an eventual application in connection with low values of erythrocytes, hemoglobin or hematocrit and possibly because of its collagen synthesis and benefit of preservation and regeneration of joints. Although these substances of long esters can be detected for a long time in the blood, there is still enough medical unexplained abuse of veterinary drugs such as Boldenone undecylenate in sports use. A part of the professional and amateur cycling sport is a part of a global business, which is in constant cat-and-mouse game synergy (hiding from doping detection) where one can achieve success but through continual and quality training aimed at enhancing weak performances and strengthening own superiority, by hook or by crook, in any legal or illegal manner, regardless of potential health damage that goes hand in hand with the sports profession.

A lot of questions regarding this disease are partly clear, but still remaining masked and unresolved is the connection and interaction of doping agents, which leaves open the question of potential risk factors of suspected doping in recreational subjects who have been exposed to the clinical picture and confirmed diagnosis of the external iliac artery endofibrosis. As for the very etiology of predisposition and connection of the effect of doping in professional or any other form of cycling,

one thing is for sure, that the mere connection of disease progression and the well-hidden (masked) anabolic preparations contributes to the endothelium inflammation progression and a potential onset of disease during major physical exertions in professional, amateur, and recreational sports. Even though most suitable for the progression of thickness with a progression of disease symptomatology in excess of 14,500 km covered annually with a strong clinical picture of critical lumen stenosis of the external iliac artery over 75% is the surgical concept of interposing Dacron graft or patch angioplasty for manifesting further continuity at either amateur, recreational or professional levels with extraordinary results for the success of primary patency of 90% in professionals, whereas endovascular procedure (Stent /PTA) is not a method of choice during progression on account of the very etiology of potential treatment of the disease, so they still remain a subject of debate and potential endovascular solution that has a limited application in dealing with this disease or the ability to resume the professional cycling career<sup>7,9,30,31,32</sup>.

Potential application of stent in arteriopathy of arterial lumen obstruction is not recommended from the surgical point of view, nor is the endovascular PTA angioplasty of iliac artery section, so that the treatment method of surgical bypass application still remains primary solution, and in case of involvement of infrainguinal arteriopathy on the femoralis communis artery, then distal reconnection would be on the healthy femoral segment (Fig.1). The ignored and well-hidden problem of doping and genetic predisposition still leaves a multitude of open and unresolved theories and issues. The study has shown a progression of intima media thickness, and a potential progression of endofibrotic lesions in doped amateur cyclists who have covered an average annual mileage of over  $9,776.24 \pm 23.8$  km. As for the conservative therapeutic option in a progression of narrowed hemodynamics of more than 50% without a clinical picture of the very

symptomatology in case of amateur or recreational cyclists, one of the possible solutions would be adequate remodulation of physical activity, in which the inflammatory atheromatous part would be spared further maximization of bloodstream impact hemodynamics on the already damaged iliac artery endothelium (shear stress reduction), avoiding the previous cycling position if one were to exclude the very effect of the illegal substances for recovery<sup>23,24</sup>.

Professional cyclists could only prosper from surgery in terms of improving their professional performances, even concerning the symptomatology of less than 50% iliac lumen obstruction in the form of meeting the competition criteria and fulfilling the competition norms. Although connected in synergy to atheromatous disease of the external iliac artery, the intensity, professionalism, duration of an athlete's career and illegal pharmacological agents for recovery are indications for surgical disease, there are still provocative maneuvers and load tests introduced. Although according to Chevalier<sup>11</sup>, apart from symptomatology atheromatous disease of the external iliac artery also found in decade professional cyclists with an average of between 14,500 and 20000 km covered annually are connections between metabolism in amino acids containing sulphur and general metabolic diseases. Although it is a rare disease predominantly located on the external iliac artery or common iliac artery, it also may appear on the iliac femoral bypass below ligamentum inguinale (Poupart's ligament), representing a locus minoris for the development and growth of progression of further disease that involves different options of surgical treatment (Picture 1). Aubel, et al.<sup>7</sup> underline a potential skill in hiding and masking illegal substances during the 11-year generation career 2005-2016 with the most probable possibility of avoiding the very detection of illegal pharmacological agents, which raises doubts as to erythropoietin EPO/ as various fast-acting forms of synthetic testosterone, as well as its derivatives<sup>2</sup>.

Also rising with the application of erythropoietin is erythropoiesis as well as blood viscosity, which results in a high risk of thrombosis, increased intensity of endothelial reflex (shear stress) due to the increase in hematocrit as well as the "sludge phenomenon," and poor blood flow to distal parts of extremities, affecting the destruction of the tissue ad individual organs, which results in individual psychological subjective phenomena, which in turn induces individual cyclists to use pulsometer due to deep sleep phases when they would find themselves in a certain phase of bradycardia so the pulsometer acts as a thrombophylactic due to waking up. Although, on the one hand, in professional cycling everything revolves around the elevation of the hematocrit and the effect of endurance training and due to its promising enormous effect on the physiological adaptation of endurance and cardiac output unlike potential arteriovenous difference in the very transport of oxygen, there are strong factors affecting the improvement of human performances in endurance training, which raises hope in the quality and success of the professional career and the very benefit of monetary profit with the potential risk of development of iliac syndrome in cyclists<sup>33</sup>.

Whatever the explanation that science may have concerning further relationship between interactions of various doping substances (illegal pharmacological substances for recovery), there are still gaps in the very nexus and interaction between the inflammation of iliac artery endothelium and potential thrombosis, cerebrovascular insult, cardiovascular arrest and the effect of interaction between factors of pharmacological agents and an individual's mental status<sup>34-39</sup>. Although some scientific studies<sup>40</sup> point to an ineffectiveness of sports manipulation with erythropoietin without clear data on the training process intensity, the subject's weight, the level of years of doing cycling, as well as combination of use of other substances, while many other studies reported effects and significant improvement of blood doping performances without combinations

with other illegal substances in professional cyclists with an increase of hematocrit following application) erythropoietin (5-7%) with a significant increase of endurance intensity with 346-340 Watts and a decline in the maximum frequency on average from 177 to 168, which explains the very role of viscosity in cycling, as well as objective improvement of anaerobic force by 10% after only 26 days without any muscle mass increase, which goes in favor of achieving better endurance performances and maintaining the intensity<sup>41,42,43</sup>.

It is believed that an additional masked application of synthetic testosterone and anabolic steroids with a combination of erythropoietin increases blood viscosity with borderline hematocrit and enormous intensity a cyclist produces increases repetitive shear stress with endothelial dysfunction, with an initial atheromatosis, which is an important predictor in the further progression and pathology of atherosclerosis by the destruction of elastic material within the vascular wall, with an expansion of the subendothelial space, and a degradation of elastin on the level of the aorta and iliac arteries, which begins to show after 10 weekly applications of synthetic testosterone derivatives. Also, the femoral artery in animal models shows that the intracellular area of the arterial wall is filled with cellular detritus without any effect of repetitive trauma on the application of synthetic testosterone derivatives. Most of the negative connotations attributed to the effects of androgens on the cardiovascular system stem from the observational link established between sudden death and androgen abuse in athletes. To the best of our knowledge, there is no study in the scientific literature presenting statistically significant data to support a causative role for anabolic androgens in cardiovascular adverse events in athletes. In this context, perhaps the chronic administration of anabolic androgens at supraphysiological rather than physiological levels leads to toxicity and death, though robust studies are needed to substantiate this. Testosterone is seldom affiliated with the circulatory system, if at all. Its role as a

promoter of erythropoiesis has not been discussed extensively. In fact, an elevated hematocrit is a side effect associated with the administration of acute supraphysiological concentrations of testosterone. The testosterone concentration utilized differed from study to study, as well as vascular exposure time to testosterone. It is logical to propose that, depending on whether exposure to testosterone is acute or chronic, vasoconstriction or vasodilatation may be elicited to maintain vasomotor tone and hemodynamic homeostasis.

On the other hand, the substance used in the cycles is boldenone undecylenate. As a animal anabolic steroid used in the treatment of horses, with the specificity of the regeneration of the musculoskeletal system and performance improvement, it has a very pronounced period of doping detection in human use due to long esters. However, its benefits of improving preforms and the quality of recovery as well as preserving muscle mass and endurance are very tempting. for sports abuse. In case of athletes, we could consider that toxic levels of androgen such as testosterone could lead to Intima-Media thickness due to increase in levels of hematopoietin, modulation of PGI2 synthetasis. Vascular exposure time to testosterone is chronic, hemodynamic of blood stream is in constant change. Therefore, all of these factors should be taken into consideration when it comes to Cyclists Iliac Syndrome. It was shown that endogenous insulin can help to increase testosterone synthesis and inhibit testosterone binding to SHBG, thereby decreasing concentrations of Sex Hormone Binding Globulin (SHBG)-bound testosterone and increasing free circulating testosterone. Although they have brought the process of masking to the level of perfection, despite their partial awareness of the risks and consequences of a potential hypoglycemic shock and brain structures impairment in insulin-taking athletes, which have been scientifically proven and known, and although cycling is based on an anaerobic concept benefitting from the anti-catabolic insulin effect,

numerous athletes have recognized those facts and incorporated them in their daily training programs, so it is still used, proven or partly proven, and there are speculations on direct connection between the combination (stacking) of illegal pharmacological substances for recovery in perfecting and improving daily training performances in the form of increasing the inflow of amino acids into the muscle cell, and a correlation in the Cyclists Iliac Syndrome, all of which results in a potential for further disease progression and a further potential of developing Type II diabetes mellitus<sup>44-47</sup>.

Anyway, although the world has been partly arrogant and self-confident on the issue of doping problems, a hematological paradox and a reliable quality of efficiency of conducting doping controls, we remain convinced that athletes or elite-ranked professional athletes who do not want to be caught have been skillfully, through unknown stacking, continually taking illegal experimental underground pharmacological substances, unknown to the public, which may be a potential trigger for the development of diseases and disease progression to the stage of surgical treatment of iliac vascular segment endofibrosis, which is why we are of the opinion that some elite athletes have been physically fit thanks to the use of pharmacologically illegal or legal substances. This still leaves ample room for open questions and limited answers as to the strictly camouflaged treatments of professional athletes and the training processes hidden from the public, and a synergy of potential development of the very pathology of the disease<sup>48</sup>. Depending on the quality of training, the level of athlete's fitness, as well as the quality of treatment with illegal pharmacological substances and suspended athletes who tested positive, but did not have a disease, may even go towards supporting the quality of training process; however, masking illegal pharmacological substances and a recent COVID 19 infection would have a potential of onset of a pathological condition of external iliac artery or common artery endofibrosis; unless the opposite is scientifically proven, it could be taken

as a possible risk factor for the onset of disease<sup>49-58</sup>. Although there have been some desperate moves after long-term symptoms of COVID 19, the application of doping substances as well as veterinary drugs with an anabolic effect that are specific in raising erythropoiesis, it is still necessary to emphasize the caution that these drugs themselves carry the thrombogenic potential of the arterial and venous system<sup>59-64</sup>.

It is our opinion that the progression of intima media thickness of the external iliac artery may potentially lead to obstructive arteriopathy of the external iliac artery, as well as on application of illegal substances for recovery (doping) and a potential possibility of recent COVID 19 virus does not rule out connection with the very progression of intima-media thickness. The hidden risk of obstructive arteriopathy of the external iliac artery is proportional to the training intensity, mileage and decade hemodynamic load on endothelial external iliac arteries, so there exists a progress of progression of intima media thickness in recreational and amateur athletes who cover more than 12000km annually on average, as well as in recreational athletes who cover lesser distances with the application of illegal substances for recovery (doping) erythropoietin, as well as various testosterone esters of variable sports doses, most likely also the application of other well-masked substances (adrenaline effect) which in a synergy raise the technology of human performances to a higher level. Sports non-competitive cycling of an individual concept (as a type of physical activity in the form of preventive medicine) remains one of the leading therapeutic sports, in terms of free anaerobic and/or aerobic recreation, as well as in terms of cardiovascular protection, vascular rehabilitation and the very training anaerobic and aerobic health concept of monocyclic movement. The possibility of onset of kinking and intima media thickness of iliac segment arteries in the application of the concept of illegal substances for recovery and connection of recent COVID 19 infection still cannot be ruled out, but is the subject of further

research of pathomorphological changes to the iliac artery segment.

## Further Research

Since the hidden race between health and health risks in professional, amateur and now also recreational sport is rather depressing. The practice does not really seem bright given the well-masked doping in the form and shape of improved dynamic performances in all domains of sport and sport branches. So one can even talk about a hidden epidemic of using anabolic synthetic testosterone derivatives. Similar pharmacological substances for recovery or even much more advanced substances (like HGH growth hormone) that are very difficult to detect. Which even includes ordinary amateur and recreational cycling population. As well as the presence of epidemic in all branches and levels of sport. Optimal vascular treatment in such potential patients. Apart from risk factors for the external iliac artery endofibrosis (psoas muscle thickness. repetitive monocyclic trauma of extraluminal and intraluminal type.

incorrect sitting position. length aberrations of common and external iliac arteries). Should be considered as doping as well as exposure to COVID 19 infection as possibly risky option for mere additional progression for the development of a pathological process on the iliac magistral segment. In the future, there is still an open scientific field between individuals who were infected with the COVID 19 virus and the reflection of their performances through the abuse of underground doping, which can potentially cause damage on the iliac artery segment.

## Conflict of Interest:

The authors declare no conflict of interest.

## Funding Statement:

None.

## Acknowledgements:

None.

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