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Quantitative evaluation of subchondral bone injury of the plantaro-lateral condyles of the third metatarsal bone in Thoroughbred horses identified using nuclear scintigraphy: 48 cases

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Keywords: horse; subchondral bone injury; orthopaedic; nuclear scintigraphy

Summary

Reasons for performing study: **Increased radio-isotope uptake (IRU) in the subchondral bone of the plantaro-lateral condyle of the third metatarsus (MTIII) is a commonly reported scintigraphic finding and potential cause of lameness in UK Thoroughbred racehorses in training and has not been fully documented.**

Objectives: **To characterise lameness attributable to IRU of the subchondral bone of MTIII, compare the scintigraphic findings of these horses with a normal population and evaluate the use of scintigraphy as an indicator of prognosis.**

Hypothesis: **IRU will be in significantly higher in horses with subchondral bone injury and will be related to prognosis and future racing performance.**

Methods: **Data were analysed from 48 horses in which subchondral bone injury of the plantaro-lateral condyle of MTIII had been diagnosed using nuclear scintigraphy and that met the inclusion criteria. Data recorded included age, sex, trainer, racing discipline, lameness assessment, treatment regimes, radiographic and scintigraphic findings, response to diagnostic analgesia where performed and racing performance pre- and post diagnosis. Region of interest (ROI) counts were obtained for the plantar condyle and the mid diaphysis from the latero-medial view, the ratio calculated and then compared with a control group of clinically unaffected horses.**

Results: **The mean condyle mid-diaphysis ROI ratio was significantly ($P<0.001$) higher in the affected population and with positively correlation ($P = 0.024$) with the level of lameness. The presence of radiographic findings had no significant effect on the ROI ratio.**

Conclusion: **Subchondral bone injury of the plantar lateral condyles of MTIII is a significant cause of lameness in UK Thoroughbred racehorses. Nuclear scintigraphy is a useful diagnostic imaging modality in the detection of affected horses but is a poor indicator of prognosis for the condition.**

Potential relevance: **Better understanding of the clinical manifestations, diagnosis of and prognosis for subchondral bone injury will benefit the Thoroughbred industry in the UK.**

Introduction

Increased uptake of radionucleotide (IRU) in the plantaro-lateral condyle of the third metatarsus (MTIII) is found commonly in young horses in race training and in the majority of cases may be considered a physiological response to the mechanical stress of repeated cyclical loading (Shepherd and Meehan 2003). The point at which this physiological adaptive response becomes pathological is poorly understood and ultimately represents an imbalance in the production and resorption of subchondral bone leading to trabecular thickening (Frost 1994; Boyde 2003). IRU of the plantaro-lateral condyle of MTIII has been documented in Standardbred populations (Martinelli *et al*. 1994; Ross 1998) associated with lameness and the condition recognised in Thoroughbred horses (Shepherd and Pilsworth 1997; Arthur *et al*. 2003; Pilsworth 2003). A similar study to the present report has been presented but involved a smaller number of cases and did not investigate the use of scintigraphy as an indicator of prognosis (Shepherd and Pilsworth 1997). More recently, the term palmar/plantar osteochondral disease (POD) has been used to describe *post mortem* lesions in a Hong Kong Thoroughbred population (Barr *et al*. 2009).

The lateral condyle of the distal third metacarpus/tarsus is the most common site of fatal fracture in UK Thoroughbreds (Parkin *et al*. 2004); however, the link between subchondral bone sclerosis and catastrophic fracture has not been fully elucidated. Subchondral bone is primarily responsible for impact absorption (Radin and Paul 1970) and therefore decreased compliance of the bone theoretically reduces the even distribution of forces through the limb. The macro- and microscopic changes in the subchondral bone have been investigated in horses undergoing training (Pool and Meagher 1990; Riggs and Boyde 1999; Riggs *et al*. 1999a; Dykgraaf *et al*. 2008), in cases with catastrophic condylar fracture (Riggs *et al*. 1999b; Radtke *et al*. 2003; Stepnik *et al*. 2004) and demonstrated in a model of experimentally produced overload arthrosis (Norrdin *et al*. 1998).

Subchondral bone sclerosis has an unclear role in the progression of degenerative joint disease (Kawcak *et al.* 2001; Cruz and Hurtig 2008) but trauma to the subchondral bone has been

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shown to precede cartilage degeneration in a canine experimental model (Lahm *et al*. 2004). There is an increasing awareness of the importance of subchondral bone pathology as a precursor to catastrophic or stress fractures (Davidson and Ross 2003; Muir *et al*. 2006), but these conditions may be challenging to diagnose clinically. Although the term 'subchondral bone' is used extensively in the literature the adjacent trabecular bone is also frequently affected, particularly in clinical cases where abnormal densification of trabecular bone is often present as an extension of subchondral bone plate pathology (Riggs *et al*. 1999b). Nuclear scintigraphy has a high sensitivity for exercise induced bone remodelling and is therefore extremely useful in the diagnosis of subchondral bone disease (Wilcox *et al*. 1977; Roub *et al*. 1979). Early and accurate diagnosis of subchondral bone injury may aid in the treatment and management of the condition. It was hypothesised that quantitative analysis of nuclear scintigraphy would not only aid in the detection of subchondral bone injury but would be an accurate prognostic indicator for return to racing.

Materials and methods

Animals included in the study

Thoroughbred racehorses in training that underwent nuclear scintigraphy at Donnington Grove Veterinary Surgery (DGVS) between 1st January 1999 and 1st July 2008 were available for analysis. All horses were in full training to race on the flat or over jumps, but not all had raced. For inclusion in the series, the horses were required to have hindlimb lameness or gait deficit caused by subchondral bone injury of the plantaro-lateral condyle of MT III, diagnosed using nuclear scintigraphy. Diagnostic analgesia was performed where possible to localise the source of lameness to the metatarsophalangeal region. Horses with IRU at locations that could not be investigated using diagnostic analgesia, multiple sites of lameness confirmed using diagnostic analgesia or radiographic evidence of fracture were excluded from the study.

Data collected included age, sex, trainer, degree of lameness, clinical work-up, radiographic and scintigraphic findings, and treatment regimes. Performance related data included the number of races pre- and post diagnosis, time from diagnosis to next start, average racing post rating (RPR) for 3 starts pre- and post diagnosis and earnings for 3 starts pre- and post diagnosis. Racing data were obtained from the racing post website (http://www.racingpost.com). Follow-up times ranged from 6 months to 9 years.

Diagnostic imaging

Radiographic projections included 4 standard views (dorsoplantar, dorsolateral 45° plantaromedial oblique, dorsomedial 45° plantarolateral oblique and lateromedial), a flexed 120° dorsoplantar view and Dorsal 30° proximal 45° lateral plantarodistal medial oblique, as described previously (Ross *et al*. 1991; Shepherd and Pilsworth 1997; Ross 1998) allowing evaluation of the distal lateral aspect of MTIII.

All horses underwent a similar scintigraphy protocol using a Technicare Gemini gamma camera and Sun Ultra[5] hardware on a Link MAPS 10000 acquisition and processing station[1]. Horses were injected with 7.5 GBq of ^{99m}Tc-MDP and images acquired 2–4 h later. All horses underwent full body scintigraphy as standard.

Latero-medial and plantaro-dorsal scintigraphic images of the metatarsus and metatarsophalangeal joint (MTPJ) were acquired for all horses. Region of interest (ROI) counts were obtained from the lateromedial view. ROI values were calculated from an equally sized area over the plantar condyle and the mid-diaphyseal region. The condyle : mid-diaphysis ratio was calculated and values compared against a control group of 48 Thoroughbred horses in full training that had undergone scintigraphic examination with no clinical signs or history of hindlimb lameness. In the affected group, a mean value was calculated for horses with bilateral lameness or poor movement; for unilaterally lame horses the value of the predominantly lame limb was used. For control horses the highest value for both hindlimbs was included in the data.

Following gamma scintigraphy 4 horses underwent magnetic resonance imaging (MRI) examination of the affected fetlocks, using a standing 0.27 Tesla permanent magnet and dedicated radiofrequency coil[2]. Images of the affected MTPJ were obtained in sagittal, transverse and frontal planes with gradient echo (GRE) T1-weighted, GRE T2*-weighted and fast spin echo(FSE) short tau inversion recovery (STIR) sequences, all with motion insensitive correction software.

Statistics

Descriptive analysis was undertaken to examine the distribution of the data. Normal distribution of the data was confirmed using a Kolmogorov-Smirnov test. A 2-sample *t* test was used to assess any differences in ROI ratio between the 2 groups. A Kruskal-Wallis test was performed to investigate any association between the level of radio-nucleotide uptake and likelihood of radiographic findings and prognosis for future racing. Pearson's correlation coefficients were calculated to investigate correlations between lameness and radionucleotide uptake. An ROC curve was calculated to examine the sensitivity and specificity of the scintigraphy. All tests were performed using Minitab (version 15) and STATA 10[5] and a P value of <0.05 was considered significant.

Results

Animals included in the study

In the specified time period, 956 Thoroughbred racehorses in training underwent gamma scintigraphy at DGVS. The inclusion criteria were met by 48 (4.9%) horses. They consisted of 31 males (9 geldings and 22 entire) and 17 females. The mean age at presentation was 3.6 years (range 2–8 years). Forty-four (92%) of the horses were in training to race on the flat at the time of diagnosis, the remaining 4 (8%) were trained for National Hunt racing over jumps. Two horses trained on the flat at diagnosis subsequently changed discipline to National Hunt racing. Cases presented throughout the year in a normal distribution pattern with July as the median month of presentation.

Lameness evaluation

Dynamic lameness evaluation data were available for 47/48 horses. When trotted in a straight line on a hard surface, 25% (12/47) displayed hindlimb gait abnormality (characteristically a bilateral, short-strided, stilted gait) but no lameness attributable to one limb. A predominant left hind lameness was seen in 27% (13/47), a right hind lameness in 32% (16/47). Six horses (12%) had hindlimb gait deficits but were also lame on a forelimb; all 6 of these cases had IRU in all 4 fetlocks. Median lameness score

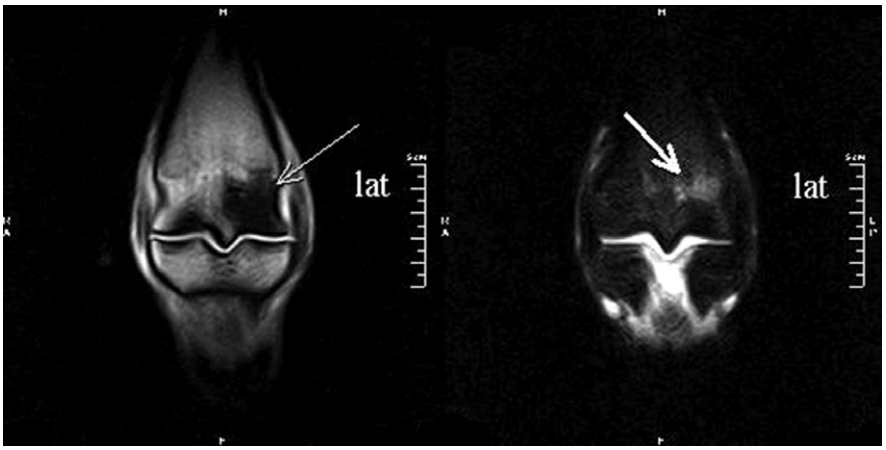

Fig 1: T1-weighted GRE frontal (left) and FSE STIR frontal (right) MRI images of a Thoroughbred MTPJ with subchondral bone sclerosis of the lateral condyle (thin arrow) and bone oedema (thick arrow).

was 2/10 (range 1/10–4/10). There was a positive correlation between the level of the lameness and ROI ratio ($P = 0.024$, $R = 0.438$).

Diagnostic analgesia

Diagnostic local analgesia was performed in 83% (40/48) of cases and in all of these was positive for the MTPJ region; in the remaining 8 cases nerve blocks were not performed at the request of the trainer or due to the refractory nature of the animal but none had IRU at other anatomical locations. Intra-articular analgesia of the MTPJ produced an improvement in 95% (19/20) of the cases in which it was performed but in some cases required up to 30 min for the response to be seen. Perineural analgesia of the lateral plantar metatarsal nerve at the distal button of the fourth metatarsal bone (Bassage and Ross 2003) produced a positive response in 84% (22/26) horses. A perineural ring block or 'low 6-point' (at the distal metatarsal region) produced a positive response in 10/10 (100%) horses.

Diagnostic imaging

Radiographs were obtained from 45 horses. No radiographic abnormalities were reported in 66% (30/45) of cases. In the remaining 15 horses a subtle loss of trabecular pattern and sclerosis of the subchondral bone in the plantar distal aspect of the lateral condyle of MTIII were evident. Two horses had small osseous fragments in the plantar pouch of the joint associated with the proximal plantar aspect of the first phalanx; both had a round chronic appearance and were not considered clinically significant. One horse had a small chronic apical fracture of the medial sesamoid bone; this too was considered not to be significant. There was a trend towards radiographic findings and level of IRU using the Kruskal-Wallis test but this was not statistically significant ($P = 0.051$).

Magnetic resonance imaging findings in the 4 horses studied included marked bone densification of the lateral condyle visible primarily on T1-weighted images and hyperintense signal proximal to the sclerotic region visible on the STIR-sequence, thought to be consistent with bone oedema (Fig 1). MRI also allowed identification of microcracks within the subchondral bone and defects of the articular cartilage not visible using digital radiography.

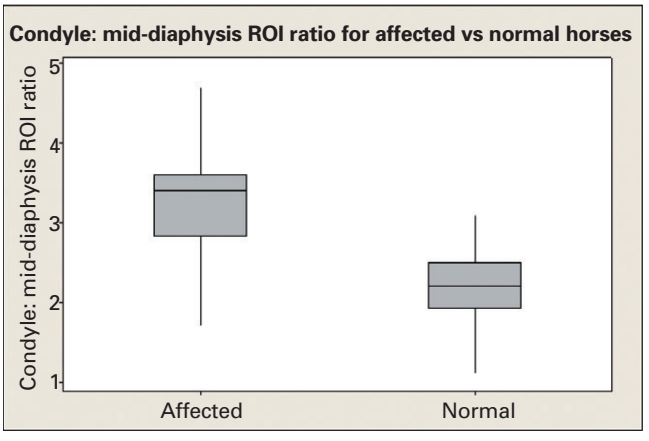

Fig 2: Box and whisker plot of condyle : mid-diaphysis ROI ratio for affected vs. normal horses.

In the 29 horses with unilateral hindlimb lameness the ROI count ratio was highest for the affected limb in 76% (22/29). The mean ± s.d. condyle: mid-diaphysis ROI ratio for the affected group (3.3 ± 0.8972) was significantly higher than the mean for the normal group (2.2 $P<0.001$) (Fig 2). The ratio for clinically affected horses ranged from 1.5–6 compared to 0.9–3.1 for control horses. The ROC value was 0.89, with a 95% confidence interval of 0.83–0.96 (Fig 3).

Therapeutics

Treatment options were varied and included rest (range 2–25 weeks), radial extra-corporeal shockwave therapy, systemic nonsteroidal anti-inflammatory medication (phenylbutazone), tiludronate, aspirin and intra-articular medication. Intra-articular therapeutic agents included triamcinalone acetonide, methyl-prednisolone acetate, polysulphated glycosaminoglycans, sodium hyaluronate and autologous conditioned serum (IRAP[3]). The variation in treatment regimes was too great to allow meaningful statistical evaluation.

Racing performance

Racing performance data were available for 47/48 horses. 85% (40/47) had raced prior to diagnosis, mean number of starts was 6.8

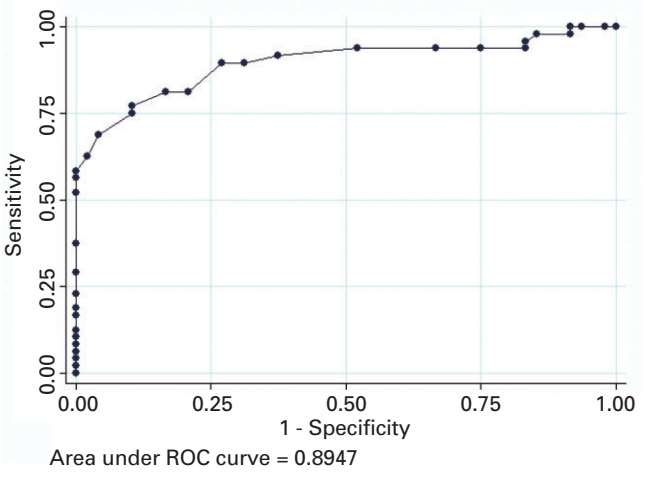

Fig 3: ROC curve for condyle : mid-diaphysis ROI ratio for affected vs. normal horses.

(range 0–21). There was a tendency for those horses that had not raced before diagnosis to have lower ROI counts but this was not significant (P = 0.055). Post diagnosis 17% (8/47) horses retired without racing again, 44% (20/47) did not start >3 times and 51% (24/47) did not start >5 times. There was no correlation between ROI count and retirement (P = 0.278), failing to start >3 times (P = 0.640) or failing to start >5 times (P = 0.728). For those horses that raced again, the mean time to next start was 196 days (range 36–464 days). There was no correlation between the ROI count and the time to the next start (P = 0.247).

Discussion

Increased uptake of radionucleotide of the metatarsal condyles is a common scintigraphic finding; however, the true prevalence and significance of subchondral bone injury of the metatarsal condyles is difficult to ascertain. Barr *et al*. (2009) found a 67% prevalence of POD at routine *post mortem* examination but did not examine the clinical significance of these lesions. Many horses will have multiple sites of IRU identified using nuclear scintigraphy consistent with stress fractures which may preclude further clinical investigation and concurrent IRU in the fetlocks of these animals cannot be fully investigated. Earlier studies into this condition have looked at a greater number of cases in Standardbred horses but without such specific inclusion criteria (Martinelli *et al*. 1994; Ross 1998). Similarly, a diagnosis of subchondral bone injury may be reached without the use of nuclear scintigraphy, particularly in animals with advanced radiographic changes, and these cases have also not been included. However, the purpose of this study was to describe a population of horses that were only affected with subchondral bone injury diagnosed using nuclear scintigraphy and investigate the use of quantitative analysis as an indicator of prognosis. Nuclear scintigraphy was useful in the detection of the condition but was a poor indicator of prognosis. In reality, many horses in race training may have an element of subclinical or unrecognised subchondral bone injury but investigation of this population is hard to achieve due to subtle clinical signs and multiple confounding factors.

Monthly distribution of cases is similar to those previously reported in the UK (Shepherd and Pilsworth 1997) with the majority of cases presenting between June and September. This clearly represents a time when flat racehorses are in full training on hard ground and is not unexpected. Given the nature of subchondral bone injury a surprisingly high percentage of cases (95% of the 20 horses in which this block was performed) showed a positive response to intra-articular anaesthesia of the MTPJ, which is contrary to a previous report (Davidson and Ross 2003). In the current study, a positive response was considered an improvement rather than resolution of the lameness. Furthermore, a number of horses required a long (>30 min) period of time to take effect, which would suggest significant periarticular diffusion of local anaesthetic could have taken place. If, as is currently postulated (Lahm *et al*. 2004; Mrosek *et al*. 2006), subchondral bone injury is an initiating factor for cartilage damage and osteoarthritis, a rapid response to anaesthesia could be due to the alleviation of secondary synovitis. If defects are present in the articular cartilage or a long response time is seen then the local anaesthetic may well be directly desensitising the subchondral bone. In refractory animals where a single perineural nerve block is desired, analgesia of the lateral plantar nerve at the level of the distal aspect of MTIV is a useful alternative with 84% of the 26 cases in which this block was performed responding. As expected, a low plantar 6 point nerve block was 100% successful but it should be noted that this block was only performed in 10 horses.

This positive response to intra-articular analgesia suggests that intra-articular therapy could be beneficial; however, clinical cases often show a poor response to intra-articular medication (Ross 2003; Davidson and Ross 2003). Intra-articular medication can be expected at best to address secondary aspects of the condition and is not likely to address the underlying subchondral bone pathology. The treatment options and regimes recorded in this study were too varied for statistical analysis and further work is needed in this area. An experimental form of overload arthrosis has been developed (Norrdin *et al*. 1998) and this model could be used to investigate various prophylactic training regimes and treatment options in a prospective randomised trial.

Nuclear scintigraphy was instrumental in the diagnosis of all 48 of the cases while radiography of the fetlocks had poor sensitivity for the condition, even with the use of specific down-angled oblique views. Some authors suggest that Thoroughbreds may be less likely to develop subchondral lucency than Standardbreds (Ross 2003) which may account for the low detection rate of radiographic change. Cases with advanced concurrent osteoarthritic change in the MTPJ are also more likely to be diagnosed using survey radiography and may therefore not have been presented for nuclear scintigraphy.

Quantitative scintigraphy has been used to evaluate various anatomic regions in lame horses including the tibia (Valdez-Martinez *et al*. 2008), distal tarsus (Murray *et al*. 2005) and sacroiliac region (Tucker *et al*. 1998). Weekes *et al*. (2004) examined the metacarpophalangeal and metatarsophalangeal joints in clinically sound horses and found a mean ± s.d. condyle: mid-diaphysis ROI ratio of 2 ± 0.46. The slightly higher mean (2.2) and upper range (3.1) values in the present study may reflect a population of racehorses in training compared with a sports horse population. Shepherd and Pilsworth (1997) presented a similar study in 26 UK Thoroughbreds in training and obtained comparable ROI ratios for both clinically affected (mean = 3.39, range 1.8–8.4) and control (mean = 2.13, range 0.9–3.0) populations. The use of fixed positive profile analysis of scintigraphy images of the metacarpo/metatarsophalangeal joints demonstrated a different pattern of radiopharmaceutical uptake in lame horses but was not helpful diagnostically (Biggi *et al*. 2009).

In contrast, the ROC value indicates that quantitative analysis of ROI ratios may be useful in the identification of clinically significant IRU. A cut off ratio of 3.2 will give 100% specificity but only 58% sensitivity; reducing this value to 2.9 gives 90% specificity and 75% sensitivity. This may be particularly useful for assessing the significance of, and also prognosis for, IRU in the plantar lateral condyles of distal MTIII where other sites of pathology are present which preclude further investigation such as pelvic or tibial stress fractures. In the 25% of clinical cases which fall below this value then further diagnostic investigation is necessary.

Subchondral bone injury of the plantarolateral condyles of MTIII is a challenging condition to manage with nearly half of all horses diagnosed failing to start more than 3 times post diagnosis. For those horses that do race again successfully it represents a significant number of lost training days. Quantitative analysis of nuclear scintigraphy was not a useful indicator of prognosis in clinical cases. The use of other imaging modalities to investigate subchondral bone pathology is becoming more widespread; MRI has proved useful in the 4 cases in this study and in other studies (Zubrod *et al*. 2004; Sherlock *et al*. 2009). Morgan *et al*. (2006) used computed tomography to assess metacarpo/metatarsophalangeal joint pathology. Further work is necessary to assess the use of these modalities for the management of clinical cases and assessment of prognosis but recent reports suggest they may prove useful (Murray 2009).

The limitations of this study design include the absence of *post mortem* information on the clinical cases, which would be required to provide a gold standard diagnosis, and the variation in diagnostic protocols for each case, particularly regarding diagnostic analgesia where the blocks performed are clinician and case dependent. Such is to be expected in a retrospective study using clinical data and prospective studies using the overload model described by Norrdin *et al*. (1998) may prove valuable.

Subchondral bone injury of the plantar lateral condyles of MTIII is a significant cause of lameness in the UK Thoroughbred population. Radiography is a poor imaging modality for detection of the condition, whereas nuclear scintigraphy has a high sensitivity and specificity for the condition and is useful for identifying clinical cases. A significant number of training days may be lost and successful management of the condition may be challenging. Quantitative analysis of nuclear scintigraphy was a poor indicator of prognosis or convalescence time. Further work is needed to establish the link between lameness, IRU and *post mortem* findings and prospective follow-up studies investigating training regimes and treatment regimes would be beneficial.

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Manufacturers' addresses

[1]Link Medical Ltd, Bramshill, Hampshire, UK.
[2]Hallmarq Veterinary Imaging Ltd, Guildford, Surrey, UK.
[3]Genitrix Ltd, Billingshurst, Surrey, UK.
[4]Minitab Inc, State College, Pennsylvania, USA.
[5]STATA, College Station, Texas, USA.

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