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DIFFERENTIAL SCANNING CALORIMETRIC EXAMINATION OF TRANSVERSE CARPAL LIGAMENT IN CARPAL TUNNEL DISEASE

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The carpal tunnel syndrome – compression of the median nerve by the transverse ligament of the wrist – is a serious disease of the human hand. The electrophysiological changes in the median nerve can be easily followed by electroneurography (ENG). The degenerative changes in the collagen structures of the carpal ligament cause shrinking of the ligament and compression of the nerve.

According to the present study we could demonstrate that DSC is a useful and well applicable method for the investigation of collagen tissue of the human carpal transverse ligament. DSC scans clearly demonstrated significant differences between the different types and conditions of samples (control: T_m=61.3°C and ΔH_{cal}=4.04 J g^{-1}, mild: T_m=62°C and ΔH_{cal}=4.3 J g^{-1}, middle: T_m=61.5°C and ΔH_{cal}=5.17 J g^{-1} as well as severe: T_m=61.85°C and ΔH_{cal}=8.44 J g^{-1}). After these investigations we can choose the optimal time of surgical therapy of different clinical level carpal tunnel syndrome too.

Keywords: *carpal tunnel syndrome, DSC, ENG*

Introduction

The carpal tunnel is a common and serious disease of the human hand, a medical condition known as nerve entrapment. Carpal tunnel syndrome (CTS) occurs when the median nerve, which runs from the forearm into the hand, becomes pressed or squeezed at the wrist. The median nerve controls sensations to the palm side of the thumb index and middle fingers, as well as impulses to some small muscles in the hand that allow the fingers and thumb to move. The carpal tunnel – a narrow, rigid passageway of ligament and bones at the base of the hand – houses the median nerve and tendons. Any condition that decreases the size of the carpal tunnel or enlarges the tissues inside the tunnel can produce the symptoms of CTS. Carpal tunnel syndrome is often the result of a combination of factors that increase pressure on the median nerve and tendons in the carpal tunnel, rather than a problem with the nerve itself. The result may be pain, weakness, or numbness in the hand and wrist, radiating up the arm. The aetiology of carpal tunnel syndrome is largely structural, genetic and biological, with environmental and occupational factors such as repetitive hand use. The incidence of this disease is increased year by year in the European countries, because of the monotonous motion of hand such as typing on a computer keyboard or doing assembly work [1, 2].

The diagnosis of carpal tunnel syndrome is usually based on physical examination of the hand, pain, paraesthesia, numbness and weakness are the most important conditions. Instead of physical examination X-ray, MRI and ultrasonography can help to get closer to the correct diagnosis. But only the electro diagnostic tests, the electromyography (EMG) and electroneurography (ENG) can demonstrate the correct and exact electrophysiological changes in the affected median nerve [3–5]. The standard and most informative neurophysiological tests are: sensory nerve conduction velocity (SNCV) and distal motor latency (DML) [6, 7]. The therapy of carpal tunnel syndrome is depended on the seriousness of compliant of the patient and the degree of neurophysiologic changes in the median nerve detected by ENG investigations [8]. The definitive therapy is the surgical decompression of the median nerve with open or endoscope technique [9] (Figs 1 and 2).

The degenerative changes in the collagen structures of the carpal ligament cause shrinking of the ligament and compression of the nerve could be one of the reasons of serious carpal tunnel syndrome. The aetiology of these degenerative changes is still not clear. Earlier examinations have demonstrated that differential scanning calorimetry (DSC) is a useful and well applicable method for demonstration of thermal consequences of local and global conformational changes in the organs of the musculoskeletal system. Besides describing the characteristic DSC scans of the normal hyaline cartilage, the intervertebral discus

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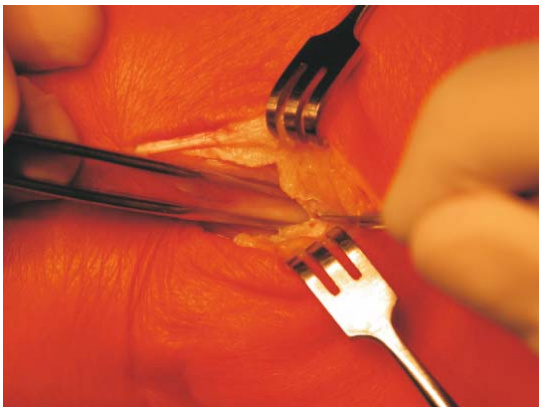

Fig. 1 Intraoperative picture of the incision of the transverse carpal ligament

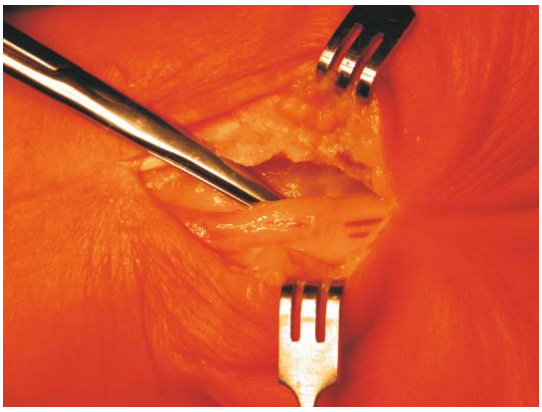

Fig. 2 Intraoperative picture of the decompressed median nerve in the carpal tunnel

and the muscles of lower extremity, different authors have demonstrated thermal effects of degenerative processes in various human tissue samples [10–25]. DSC has never been applied for the investigation of transverse ligament of the wrist.

Our hypothesis was that in carpal tunnel disease there is a clear pathological abnormality in the tissue elements building up the transverse ligament of the wrist, which is responsible for the disease. With DSC we planned to carry out investigations of collagen destruction caused by the disease. The curves may prove and follow the changes in the structure of ligaments collagen in different stages of carpal tunnel disease.

The aim of current study was to set up thermal characteristic of healthy human wrist transverse ligament, to investigate transverse ligaments in case of carpal tunnel syndrome with DSC and to prove with the examinations that there is a definitive difference in the structure of the healthy and pathological ligaments, which can be reproduced. The calorimetric examination of this kind, we hoped could give answer to the following questions:

- is it possible to detect differences between thermal features of the intact and degenerated transverse ligament
- is there any correlation between the thermal effect of the ligament and the nerve electrophysiological condition detected by EMG investigation

Experimental

Material and method

Sample preparation

The healthy transverse ligament of the wrist samples were of cadaver origin. We removed both side transverse ligaments from two cadaver wrists. The donors taken into our study were all under age of 45 at their death, we considered these persons to be free any degenerative changes in their joints. We took samples only from wrists where degeneration of the transverse ligament or post-traumatic changes in the wrist bones could not be verified macroscopically. All the medical intervention were made according to the ethic regulations of the University of Pécs.

The pathologic ligaments were derived during operations of carpal tunnel decompression. During the operations from longitudinal approach of the wrist, we prepared the transverse ligament and cut it in full thickness and length over the median nerve. With this method we could liberate and decompressed the median nerve in full length of the carpal tunnel. All of the operation we made the mentioned open technique instead of close minimally invasive method. We measured 10 pathologic wrist ligament from seven female and 3 male being in average 57 years (36–65) of age.

Histological examination

We removed the central 1×2 cm part of the transverse carpal ligament as one piece and longitudinally cut them into two parts. One part has been sent to histological examinations the other underwent DSC investigation. The later samples were put into physiological saline solution and were stored at 4°C, no longer than 24 h. The samples subject for histological examination were fixed in 4% formaldehyde, longitudinal and cross section slides have been made and stained with haematoxylin and eosin. Light microscopic control has been performed.

EMG-ENG examination

All of operated patients underwent an EMG investigation in a special laboratory of the Neurogical Department of University of Pécs 1 to 2 weeks before the

operation. Neurophysiological 'standard' tests were always performed: median nerve sensory conduction velocity (SNCV) first- and third digit-wrist and distal motor latency (DML). By setting criteria of electrophysiological tests, all patients were classified into mild, moderate and severe degrees of CTS. In 'standard negative' hands disto-proximal ratio technique was performed. Neurophysiological classification: Extreme CTS (absence of median motor, sensory responses), Severe (absence of sensory response, abnormal DML), Moderate (abnormal SNCV, abnormal DML), Mild (abnormal SNCV, normal DML).

DSC investigation

The pieces of different samples have been prepared and measured within 6 h of removal. The calorimetric experiments were done as described earlier . The thermal denaturation was monitored by Setaram Micro DSC-II calorimeter. All the experiments were performed between 0 and 100°C. The heating rate was 0.3 K min^{-1}. Conventional Hastelloy batch vessels were used during the denaturation experiments with 850 μL sample volume (80–240 mg wet mass of ligament samples), on average. The sample and reference vessels were equilibrated with precision of ±0.1 mg and there was no need to do any correction from the point of view of heat capacity between the sample and reference vessels. The data treatment after ASCII conversion was done by Origin 6.0.

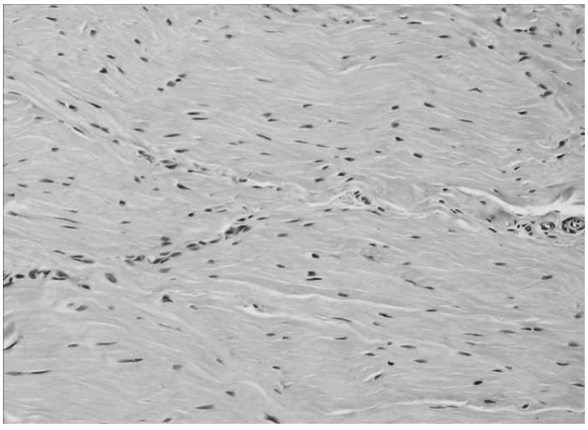

Fig. 3 Longitudinal section of collagen fibers of healthy transverse ligament of the hand (HE, 100×)

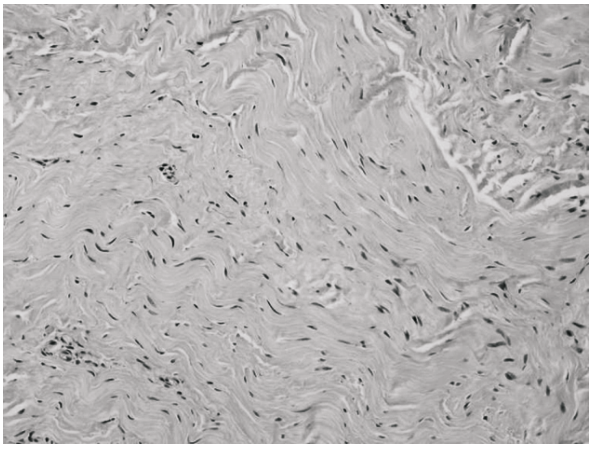

Fig. 4 Longitudinal section of collagen fibers of transverse ligament of the hand in carpal tunnel syndrome: moderately degenerated fibers (HE, 200×)

Results and discussion

With our histological examination we could demonstrate that transverse carpal ligaments tissues showed no sign of degeneration, regular collagenous structure could be seen (Fig. 3.) The pathologic samples showed only mild signs of degeneration microscopically (Fig. 4.).

The thermal denaturation results can be seen in Fig. 5. It was surprising at one hand, that in all cases we could detect only mild decrease in heat capacity after denaturation, without significant differences. On the other hand in case of calorimetric enthalpy of unfolding the DSC scans clearly demonstrated the significant differences between the different stages of samples (Table 1: control: T_m=61.3°C and ΔH_{cal}= 4.04 J g^{-1}, mild: T_m=62°C and ΔH_{cal}=4.3 J g^{-1}, middle: T_m=61.5°C and ΔH_{cal}=5.17 J g^{-1}, as well as in severe stage: T_m=61.85°C and ΔH_{cal}=8.44 J g^{-1}). The DSC scans are good mirror of clinical manifestation of syndrome.

With our investigations we can clearly demonstrate that there are strong significances between the different stages of nerve degeneration which can be demonstrated by the EMG results (Table 1 the decrease of the conduction velocity and the increase of distal motor latency) and the structural changes in the transverse ligament tissues. With the classical histo-

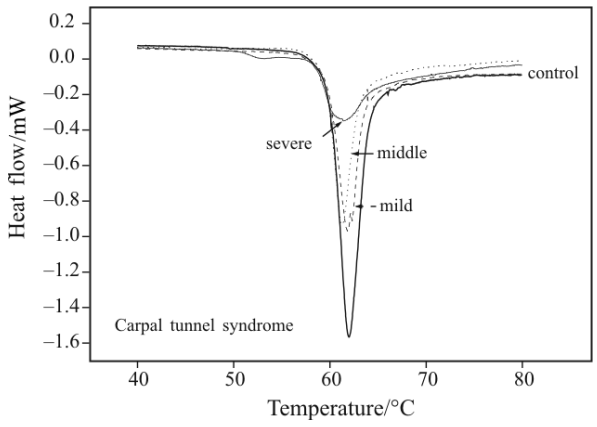

Fig. 5 Thermal denaturation scans of normal and pathologic transverse carpal ligaments in different level of median nerve compression in carpal tunnel disease

Table 1 The neurological and thermal parameters of carpal-tunnel disease

Seriousness of CTS	Number of samples	Distal motor latency/msec	Conduction velocity/m s^{-1}	T_m/°C	ΔH_{cal}/J g^{-1}
Control	4	<1	>50	61.3	4.04
Mild	3	1–2	50–45	62	4.3
Middle	5	2–6	45–35	61.5	5.17
Severe	2	>6	<35	61.85	8.44

logical investigations we could not demonstrate relevant difference between the intact and pathologic transverse ligament, but the increase of thermal parameter the calorimetric enthalpy proved the degeneration and structural changes in the ligaments tissues.

We believe that the variability in the clinical presentation of CTS is largely due to the presence of associated diseases and our results provide information which could help to better define the clinical criteria used in the diagnosis of this syndrome.

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