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# editorial

Dear Readers,

The journal „Zdravotníctvo a sociálna práca“ (Health and Social Work) was renamed in 2021 to International Journal of Health, New Technologies and Social Work.

Our long-term effort is to gradually acquire for the journal European significance and be included in international databases. Starting with issue No. 4 in 2016, the journal accepted the Harvard style of referencing, and changed guidelines for the authors. The aim of the changes was to move closer to the standard in international journals published in English in the area of health and helping professions. The editors are aspiring for registration in other relevant international databases. Since last 2020 the journal has published all articles in English only.

The journal „Zdravotníctvo a sociálna práca“ (Health and Social Work) was established in 2006 at Faculty of Health and Social Work blessed to P. P. Gojdič in Prešov and St. Elizabeth University College of Health and Social Work in Bratislava. In 2021, the journal celebrated its 16<sup>th</sup> year of publication.

Previously professional journal, within 5 years developed into an international, peer-reviewed scholarly journal, published quarterly (4 issues per year). The journal were published by the St. Elizabeth University of Health and Social Work in Bratislava. The journal became international in 2009. The journal was published and distributed in the Slovak Republic and also in the Czech Republic.

Since 2011, the journal is published both in print and as electronic issues, available from: [www.zdravotnictvoasocialnapraca.sk](http://www.zdravotnictvoasocialnapraca.sk). Starting by issue No. 3 in 2014, the scope of the journal has broaden and the journal is covering health sciences, such as Public Health, Nursing, Laboratory Medicine, but also helping professions such as Social Work or Pedagogy. Collaboration with Faculty of Health and Social Work of Trnava University in Trnava was initiated.

The journal is indexed in the following databases: Central and Eastern European Online Library — CEEOL (since 2018), Bibliographia Medica Slovaca (BMS), and Slovak reference database CiBaMed.

The part of journal is Supplementum, to publish abstracts from international conferences organized by the St. Elizabeth University of Health and Social Work in Bratislava. In 2022, the conference will take place in October in Piešťany, in the Slovak Republic.

Prof. Miron Šrámka, MD, DSc.  
*redactor-in-chief*



# Nanoarthroscopy using virtual reality

## Nanoartroskopia s využitím virtuálnej reality

Ján Mašán<sup>1), 2), 5)</sup> Miroslav Kotula<sup>5)</sup> Eugen Ružický<sup>3)</sup> Vladimír Popelka<sup>6)</sup> Miron Šrámka<sup>1), 4)</sup> Ján Lacko<sup>3)</sup>

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### ABSTRACT

**Introduction:** Post-traumatic joint conditions cause trauma and many specific conditions need to be addressed through an intervention. The most often are menisci, ligaments and cartilage that are being damaged and that cannot have a joint total open surgery. At present, there are various surgical methods — techniques (arthroscopic approaches) in which the patient is under full anesthesia or spinal anesthesia during the surgery.

**Objective:** The objective of the study is to highlight the possibilities of using nanoarthroscopy for the knee joint, shoulder joint and ankle using virtual reality.

**Methodology:** They used modified pain perception questionnaires and a Virtual Reality questionnaire for stress assessment.

**Results:** The work describes the theoretical background and current state of application of the latest methods of nanoarthroscopy for the knee joint, shoulder joint and ankle. We supplemented it with positives using the technique of virtual reality, in which the patient is conscious. The possibilities of using virtual reality to relieve pain and stress during surgery are described. The work also addresses the issue of specific technologies that evaluate the patient's condition during the procedure.

**Conclusion:** The case studies of knee arthroscopy focus on the evaluation of nanoarthroscopy using various methods and also using virtual reality. The results of the use of this technology have confirmed the potential of innovative techniques.

**Keywords:** nanoarthroscopy, joint trauma, sports injuries, hypoanalgesia, stress and well-being, digital technologies, virtual reality.

### ABSTRAKT

**Úvod:** Poúrazové stavy kĺbov vyvolávajú trauma a mnohé konkrétne stavy je potrebné riešiť intervenčne. Najčastejšie sa jedná o menisky, väzy a chrupavky, ktoré bývajú poškodené, pri ktorých sa nerobí celková otvorená operácia kĺbu. V súčasnosti existujú rôzne operačné metódy — postupy (artroskopické prístupy), pri ktorých pacient počas operácie je v plnej narkóze, prípadne spinálnej anestézii.

**Cieľ:** Cieľom predkladaného článku je poukázať na možnosti využitia nanoartroskopic pre kolenný kĺb, ramenný kĺb a členok s využitím virtuálnej reality.

**Metodika:** Pro hodnotenie stresu využili upravené dotazníky pre vnímania bolesti a dotazník pre virtuálnu realitu.

**Výsledky:** Práca popisuje teoretické východiská a súčasne stav použitia najnovších metód nanoartroskopic. Doplnili sme ju pozitívnymi s využitím techniky virtuálnej reality, pri ktorej je pacient pri vedomí. Opisujú sa možnosti využitia virtuálnej reality na zmiernenie bolesti a stresu počas operácie. Práca sa dotýka aj problematiky špecifických technológií, ktoré hodnotia stav pacienta počas zákroku.

**Záver:** Prípadové štúdie artroskopic kolena sa zameriavajú na hodnotenie nanoartroskopic pomocou rôznych spôsobov a aj s využitím virtuálnej reality. Výsledky použitia tejto technológie potvrdili potenciál inovatívnych techník.

**Kľúčové slová:** nanoartroskopia, trauma kĺbov, športové úrazy, hypoanalgéria, stres a duševná pohoda, digitálne technológie, virtuálna realita

## INTRODUCTION

The expanding nature of orthopaedics and sports medicine brings new methods and approaches to practice. The pressure on less invasive technologies is constantly increasing. The less invasive technology of arthroscopic treatment of tendons and hip joint labral problems shows excellent results and faster convalescence. A new diagnostic and therapeutic approach of „nano“ arthroscopy allows the use of needle-sized instruments with a local aesthetic.

Professor Kennedy is a world-renowned foot and ankle surgeon and a leading expert in cartilage injuries. Co-founder of ICCRA, which has set the gold standard in treatment algorithms for ankle cartilage surgery. His interests include regenerative medicine and minimally invasive nanoarthroscopy. Professor Kennedy was the first surgeon to perform nano-arthroscopy in an outpatient clinic (ambulance).

NanoScope and the nanoarthroscopy is the latest technology in arthroscopy, which is 1.9 mm in size with the additional benefits of real hole incisions or incisions and can reach all parts of the joint without damaging the structures. The nanoarthroscopy system offers the patient an incision-free experience and unlimited atraumatic access to the joint spaces during diagnostic and treatment procedures. Arthroscopic procedures are minimally invasive surgeries that show faster recovery and lower complications compared to open surgery and can also be performed on an outpatient basis.

The NanoScope system provides an alternative to magnetic resonance imaging and arthroscopy of the second view and offers accurate, direct image-controlled visualization of individual parts and structures of the joint. It works the same as when drugs are instilled into the joint. We can even insert a probe into the joint to identify damaged structures and holes (Colasanti *et al.* 2022). The basic set of NanoScope, to which various additional devices for nanoarthroscopy of the knee, shoulder, elbow and other parts of human joints are added (Figure 1).

As a very advantageous supplement, Entonox is administered to our patients, reducing the patient's stress from the ongoing operation. Thanks to its short-term effect, patients leave the operating room without crutches with a full load on the joint. The whole procedure lasts about 10—20 minutes, after the surgery the patient leaves to home treatment where we recommend a partial ease regime for 3—4 days. The patient leaves independently and is able to drive a car immediately. Thus, 24-hour observation after general/spinal anesthesia and also the risks associated with general anesthesia are eliminated. As for sports activities, if the joint is without a swelling, it is possible to step on the exercise bike the next day and start swimming 10 days after the operation (Dankert *et al.* 2021; Konopka *et al.* 2022).

## MINIMALLY INVASIVE ARTHROSCOPY

One of the obstacles to the treatment of patients with joint diseases is the limited availability of operating rooms. To achieve optimal results, arthroscopic operations require a team of experts, material and space equipment. Thanks to the minimally invasive arthroscopy controlled by Arthrex Nanoscope technology, the whole process can be completed in most facilities — an ambulance with limited staffing requirements.

## NANOARTHROSCOPIC SURGERY

The result is the availability of same-day diagnostics and minimally invasive arthroscopic surgery. Arthrex Nanoscope technology is designed to enable experienced orthopedic surgeons to use advanced techniques, reduce the risk of secondary joint and soft tissue damage, and provide treatment in a comfortable office environment. After the operation, the wound is covered only with a sterile patch, it is not sewn with a classic stitch — there is no need to wait in the outpatient clinic to check and remove the stitches. Immediately after the operation, visco-supplementation in the form of hyaluronic acid or ozone and oxygen O<sub>3</sub> + O<sub>2</sub> can be applied to the joint in the surgery space.

As a patient, you have the opportunity to view images of damaged soft parts of the joint or cartilage in high resolution in real time. Previously, surgeons had to rely on X-rays or MRI scans along with anatomical descriptions to illustrate damage or wear caused by injuries or conditions such as e.g. arthritis. Advanced display of the Arthrex Nanoscope uses a combination of 1 mm sensors, LED illumination, image management and intuitive controls to render the entire image.

These visual elements help/enable patients to play an active role in treatment decisions. When you see progression of meniscus or cartilage damage, it is easier to make decisions that will lead to a better quality of life.

## USE OF VIRTUAL REALITY

Virtual Reality (VR) is a potentially powerful technology for improving mental sensation. At any time or in any place, individuals can be transported to immersive and interactive virtual worlds that are fully under the control of the researcher or therapist. This capability is at the heart of the recent interest in how the VR could be used to improve and, where appropriate, treat and assess mental health or mental health. Reflections on the implementation of the VR in the research and clinical environment are discussed, including current issues with price and approach, developing the evidence base, technical challenges and ethical implications.

It is important to understand the opportunities and challenges of the VR, as researchers and doctors seek to use this technology to improve mental health outcomes.

**Figure 1:** Basic NanoScope set with camera, sharp and blunt obturator (own Photo)



**Figure 2:** Left part: Images shown for the left and right eye. Right part: A patient with the Oculus Quest 2 device looking at the displayed nature in VR (own Photo)



Developments in virtual reality (VR) have the potential to radically change the mental health assessment environment. The immersive VR involves wearing a closed head-mounted device (HMD) that displays three-dimensional images on the screen so that the person is completely immersed in the virtual environment (e.g. Figure 2). Images are constantly rendered with respect to the position of the head and can capture body movements, allowing users to explore and interact with objects and avatars (digital agents) in virtual space. These virtual environments are either programmed using specialized software to create computer-generated, photorealistic images, or shot using specialized cameras to create 360-degree videos of real scenes that can be replayed within VR. Together, these capabilities allow researchers and physicians to observe and record individuals in a highly controlled and near-natural environment in real time.

With technological progress, especially over the last decade, the VR is becoming increasingly immersive. By immersing individuals in real-world situations through the VR, it is possible to make evaluations that better mimic what is happening in everyday life. This capability overcomes the problem of ecological validity, that is, the extent to which the findings of research studies are generalized to the real world. Research constantly shows that individuals respond to virtual environments as if they were experiencing them in real life. It

is known that virtual environments create physiological changes in line with emotional responses to real-world scenarios. There is no risk of injury as in adrenaline sports, but the same emotions.

There is growing evidence that 3D virtual reality is more appropriate than watching a 2D monitor to relieve stress and treat mental disorders such as various anxiety disorders and depression. In the study, Blinkin and colleagues designed a cross-experiment protocol consisting of two emotional, relaxation and excitement environments, which were presented to participants either on a 2D monitor or on a 3D VR display mounted on the head (Blinkin *et al.* 2019). The results clearly supported the use of VR as an effective tool for evoking and regulating emotions compared to a 2D screen. The success of virtual reality (VR) applications used in medical evaluation in rehabilitation depends to a large extent on the patient's sense of presence (Šrámka *et al.* 2020). The VR environment represents a real situation, which can also be used in the rehabilitation of fine motor skills in Parkinson's disease (Ružický *et al.* 2022). In rehabilitation therapy, various categories of parameters were identified, which were evaluated using artificial intelligence methods. It was found that the key elements of virtual reality as a complementary method to therapy are motivation and emotions, which significantly affect the patient's positive attitude to rehabilitation.



In virtual reality, it is important that the patient is supervised and sufficiently immersed in the virtual world and so the cortical neurons are stimulated by simultaneously evoking pleasant feelings with multiple sensations (eyesight, hearing). In this way, we began to use 3D models not only in diagnostics but also in the process of rehabilitation with virtual reality.

A virtual 3D model created from MR images of a patient's shoulder allows us to better assess joint damage, individual muscles, tendon and tendon attachments, the extent of their damage, which are applied when moving the shoulder joint. The virtual arm model created using the software contributed to a better understanding of the localization and progression of the musculoskeletal system disease in comparison with only MR images, which enabled us to target better therapy. In addition, the virtual 3D model allows us to see individual anatomical structures from different sides and, according to our own needs, to differentiate individual structures such as bones, tendons and muscles. We also used this model in the diagnosis and treatment of rotator cuff rupture with a better orientation of the entire shoulder joint (Šrámka 2017).

**Knee joint** — specific clinical scenarios/cases, examples of using diagnostic nanoarthroscopy instead of MRI (and usually immediately followed by therapeutic arthroscopy in the same environment) include: 1. patient after knee block injury and joint infill (haemarthrosis), 2. patient with older positive MRI finding, resp. patient after recurrent injuries such as recurrent dislocation of the shoulder or patella, 3. patient who is contraindicated for MRI, such as a pacemaker or spinal implant, who has clear and obvious clinical findings suggestive of intra-articular pathology, and 4. patient, which will provide us with current views from different angles during the operation and allow us a 360° view. In future, we can imagine a surgery room with several small nanoscopes and multiple imaging monitors that will provide a new three-dimensional world of arthroscopy (Figure 3).

Postoperative questionnaire with evaluation, using the Likert scale 1 — 5

**Questionnaire**

1. You felt worried about surgery 1 — 5
2. During the surgery, you were afraid of pain 1 — 5
3. You felt pain during surgery 1 — 5

4. The overall feeling of the surgery 1 — 5
5. Satisfaction with nanoarthroscopy surgery 1 — 5

In the study, they examined people's stability and balance (Slobounov et al. 2015). They confirmed that fully immersive 3D VR induces a higher subjective sense of presence compared to 2D. Our study was conducted with the possibility of an innovative way to harness the positive impact of immersion in virtual reality. For this scenario, we used VR devices that do not require a connection to a computer using VR device Oculus quest 2 (Lacko et al. 2022). Table 1 below shows the values for four patients watching 2D screen and 3D VR.

1. Patient solved by nanoarthroscopy in the area of the knee joint — examination with a classic procedure. Likert scale 1 — 5, total 16 points.
2. Patient solved by nanoarthroscopy while monitoring arthroscopic performance on the screen. Likert scale 1 — 5, total 22 points.
3. Patient solved by nanoarthroscopy combined in the form of virtual reality. Likert scale 1 — 5, total 19 points.
4. Patient solved nanoarthroscopically throughout the whole surgery — VR performance. Likert scale 1 — 5, total 18 points.

The study was done with the possibility of an innovative way using the positive impact of immersion in Virtual Reality.

**NANOARTHROSCOPY OF THE ANKLE JOINT**

Posterior foot disorders include a range of bone, cartilage and soft tissue pathologies. Traditional open surgical techniques are increasingly being replaced by less invasive arthroscopic and endoscopic approaches. Recent innovations, such as the advent of the needle arthroscope, continue to push the boundaries of minimally invasive interventions. This technical note highlights our back foot needle endoscopy technique in common back foot pathologies in an office environment in vigilant state, including indications, and technological advantages.

In the treatment of posterior ankle impingement, it will provide the patient with a unique experience of his pathology and make it easier for him to recover quickly through self-awareness. The use of IONA will accelerate recovery for sports-spe-

**Table 1:** Nanoarthroscopy surgery, patient age, sum of questionnaire points and patient perception during the procedure

Patient	Nanoarthroscopy	Age	Sum of points	Patient perception
1	knee arthroscopy	35	16	operation watching
2	knee arthroscopy	60	22	screen watching
3	knee arthroscopy	82	19	operation watching and VR tracking
4	knee arthroscopy	45	18	only VR tracking

**Figure 3:** Nanoarthroscopy of the knee in the REHAMED PIEŠTANY Ltd. (own Photo)

Patient No. 1 solved by nanoarthroscopy — examination of the knee joint



Patient No. 2 solved by nanoarthroscopy — examination of the knee joint



Patient No. 3 solved by nanoarthroscopy — examination of the knee joint



Patient No. 4 solved by nanoarthroscopy — examination of the knee joint



cific activities compared to standard arthroscopic procedures. A retrospective cohort study of patients who underwent IONA for posterior ankle impingement between 2019 and 2020. Clinical outcomes were assessed using the following preoperative and follow-up methods: The Foot and Ankle Outcome Scores (FAOS) and Patient-Reported Outcomes.

Domains of pain interference and pain intensity in the measurement information system (PROMIS). At the final follow-up, a five-point Likert scale on patient satisfaction was assessed. The Wilcoxon test was performed to compare pre-surgery and postsurgery outcomes. Ten patients, including 4 men and 6 women, were enrolled in this study. The average PROMIS Pain Interference T-score decreased from  $69.0 \pm 5.8$  before surgery to  $63.1 \pm 5.8$  at final follow-up ( $p < 0001$ ). Before the IONA-arthroscopy procedure, 7 patients took part in the sports activity. Of these, 7 patients (100 %) returned to sports activities. The median of time of return to sports was 4.1 weeks (range 1 to 14 weeks). Finally, 10 patients (100 %) expressed a willingness to undergo the same procedure again. The current study demonstrates that treatment of IONA posterior ankle impingement leads to significant pain reduction, low complication rates, and excellent outcomes reported to patients with a high rate of return to work/sports (Konopka *et al.* 2022).

## CONCLUSION

NanoScope is a diagnostic procedure with the possibility of immediate treatment of problems in the first phase, whether at pain or condition after the joint injury, without the need to wait for further paraclinical examinations and without general/spinal anaesthesia, shortening the treatment time with the problem (no need for presurgery examination, magnetic resonance imaging, etc.).

Nanoarthroscopy (or needle arthroscopy) is suitable for the diagnosis as well as for the injury treatment, it brings high patient satisfaction associated with a timely rate of return to work and sports. Due to the relatively significant influence and importance of the VR, we want to continue the introduction of this method in nanoarthroscopes and, to confirm this, carry out a study in this direction.

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# Knee joint diagnostics using in-depth sensory tests

## Diagnostika kolenného kĺbu s využitím hlbkových senzorických testov

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### ABSTRACT

**Introduction:** The return to functional performance of the lower limbs in patients with degenerative diseases after orthopedic surgery and neurological and sports injuries is associated with the stimulation of proprioceptive perception with neuromuscular control. The resumption of gait depends on a deep feeling, an alternative known as a proprioceptive feeling, and on the mechanisms that control the muscles. Sensory processed information in the nervous system forces an appropriate response of the muscular system through a system of feedback, controlled balance. An effectively functioning sensor integration system enables gait reeducation.

**Aim:** The aim of the present article is to point out the necessity of performing deep sensory tests in the knee joint during diagnosis and physiotherapeutic activities in patients with lower limb dysfunction and after operations.

**Methods:** A normal, passive lifestyle and limited motor activity reduce the possibility of receptor stimulation, leading to a gradual impairment of proprioceptive perception. Deterioration of deep sensation is observed in virtually all patients after prolonged immobilization, surgery and, for example, after neurological events.

**Results:** Deep sensory impairment in the knee joints manifests itself in several ways. The most commonly observed gait is a departure from physiological gait, insufficient joint stabilization, muscle weakness or muscle stiffness. Patients often have difficulty locating the limb. The paper presents selected tests of deep sensation, taking into account the ability to reproduce the position of the knee joint as well as a test of the strength and speed of the performed movement. In the diagnosis of proprioception and the evaluation of progress in the physiotherapeutic improvement of the lower limbs, it has been proposed to use a treadmill and a stabilometric platform. Assessment of proprioceptive sensation is essential in the rehabilitation of patients with lower limb dysfunction and, in combination with other diagnostic tests, will allow physiotherapy to focus on what is most and most important in terms of the patient's needs. When deep sensation worsens, you should immediately begin the recommended exercise and daily activities, taking into account the patient's contraindications and current motor skills.

**Conclusion:** Numerous lower limb dysfunctions, injuries and the need for surgical procedures in society require the use of reliable and reliable tests during comprehensive rehabilitation. The proprioception tests presented in the article are not only an element of diagnostics, but also an objective assessment of ongoing improvement.

**Key words:** Knee joint diagnostics, deep sensory tests, physiotherapy



**Úvod:** Návrat k funkčnej výkonnosti dolných končatín u pacientov s degeneratívnymi ochoreniami po ortopedických operáciách a neurologických a športových úrazoch je spojený so stimuláciou propioceptívneho vnímania s nervovosvalovou kontrolou. Obnova chôdze závisí od hlbokého pocitu, alternatívneho známeho ako propioceptívny pocit, a od mechanizmov, ktoré ovládajú svaly. Sensoricky spracované informácie v nervovom systéme vynucujú primeranú reakciu svalového systému prostredníctvom systému spätnej väzby, riadenej rovnováhy. Efektívne fungujúci sensorický integračný systém umožňuje reedukáciu chôdze.

**Cieľ:** Cieľom predkladaného článku je poukázať na nevyhnutnosť vykonania hlbokých sensorických testov v kolennom kĺbe pri diagnostike a fyzioterapeutickej činnosti u pacientov s dysfunkciou dolných končatín a po operáciách.

**Metódy:** Bežný, pasívny životný štýl a obmedzená motorická aktivita znižujú možnosť stimulácie receptorov, čo vedie k postupnej poruche propioceptívneho vnímania. Zhoršenie hlbokého cítenia pozorujeme prakticky u všetkých pacientov po dlhšej imobilizácii, operáciách a napríklad po neurologických príhodách.

**Výsledky:** Hĺbková sensorická porucha v kolenných kĺboch sa prejavuje viacerými spôsobmi. Najčastejšie pozorovanou je odchýlka od fyziologickej chôdze, nedostatočná stabilizácia kĺbov, svalová slabosť alebo svalová stuhnutosť. Pacienti majú často ťažkosti s určením polohy končatiny. V príspevku sú prezentované vybrané testy hlbokého cítenia s prihliadnutím na schopnosť reprodukovat polohu kolenného kĺbu ako aj test sily a rýchlosti vykonávaného pohybu. V diagnostike propiocepce a hodnotení pokroku vo fyzioterapeutickom zlepšení dolných končatín bolo navrhnuté použiť bežiaci pás a stabilometrickú platformu. Hodnotenie propioceptívneho cítenia je nevyhnutné pri rehabilitácii pacientov s dysfunkciou dolných končatín a v kombinácii s ďalšími diagnostickými vyšetreniami umožní zamerať fyzioterapeutickú činnosť na to najdôležitejšie a najdôležitejšie z hľadiska potrieb pacienta. Keď sa hĺbkové cítenie zhorší, mali by ste okamžite začať vykonávať odporúčané fyzické cvičenia a denné aktivity, berúc do úvahy kontraindikácie a aktuálne motorické schopnosti pacienta.

**Záver:** Početné poruchy funkcií dolných končatín, úrazy a nevyhnutnosť chirurgických výkonov v spoločnosti si vyžadujú používanie spoľahlivých testov počas komplexnej rehabilitácie. Propriocepčné testy prezentované v článku sú nielen prvkom diagnostiky, ale aj objektívnym hodnotením prebiehajúceho zlepšovania.

**Kľúčové slová:** Diagnostika kolenného kĺbu, hlbkové sensorické testy, fyzioterapia

## INTRODUCTION

The ability to achieve independent and free movement is the primary goal of all therapies and proves the effectiveness of physiotherapy. Rehabilitation is often a very long process, it depends mainly on the cause of the dysfunction, at the same time it requires the patient's own activity. Rehabilitation teams, in turn, involved tedious individualization at work. Difficulty returning to lower limb function occurs in the elderly and in neurological patients who have lost this possibility due to a vascular event or long-term illness.

Reindeer with eating disorders can also have problems with mobility and strain on muscular and skeletal structures (Budayová 2021).

Any restoration of lower limb function is closely related to stimulation of proprioceptive perception and neuromuscular control. The effectiveness of this process affects patients with degenerative diseases, after orthopedic surgery and neurological diseases and injuries, as well as athletes after injuries. The resumption of physiological gait depends on a deep sensation in the lower limbs, an alternative known

as a proprioceptive sensation, and on the mechanisms that control the muscles. In the 1970 s, it was believed that improved gait was associated with improved musculoskeletal structures. Based on research, it is currently assumed that joint stability is more of a neurological nature (Stolarczyk, Śmigielski, Adamczyk 2000). The very mechanism of proper functioning of the neurological system is feedback, the beginning of which is found in the joint structures, tendons and muscles of the lower limbs. The performance of any motor act is associated with a constant flow of information from the circuit. The sources of this information are localized and recorded in muscle proprioceptors (sensitive to muscle strain), capsular (angular position statistics) and receptors located in the semicircular canals and atrium. Efficient receptors with continuity of nerve pathways transmit information that allows walking without visual control while maintaining a suitable vertical position and determining the position of the individual parts of the limbs relative to each other. Additional information about data from telereceptors and exteroceptive stimuli (eg from the substrate) is transmitted to the CNS (Nowotny, Nowotny-Czupryna, Czupryna 2015), where they are merged. The sensory information processed in the CNS forces an appropriate response of the muscular

system through a system of feedback and controlled balance. A fully functional sensory integration system enables gait reeducation, thus significantly improving patients' quality of life.

Posture and gait are related to sensory information, are regulated dynamically, and are constantly changing with changing environmental conditions during these motor tasks. Under conditions of upright posture and flat ground, afferent somatosensory information accounts for approximately 70 % of the information needed for complete control, vestibular information is approximately 20 %, and visual information is only 10 % (Peterka 2002). Visual and atrial data are becoming a more important source for sensory integration, for example when walking on uneven and unstable terrain (the role of stimuli coming from the body decreases), when walking in the dark the role of somatosensory stimuli and information from the body, the atrium is elevated. All sensory information from the proprioceptive system is characterized by a rapid response time at the spine level, often without or to a small extent that the patient is aware of (Ciechowicz Lewkowicz 2005).

## RESEARCH OBJECTIVES

The aim of the study is to point out the necessity of performing in-depth sensory tests in the area of the knee joint during physiotherapeutic activities in patients with lower limb dysfunction and after operations. The tests performed are objective results, both during the initial diagnosis and provide information about the effects of the rehabilitation.

## DEEP FEELING IN THE KNEE JOINT

Deep sensitivity consists of feeling the positioning, movement and vibration of body parts, evaluating their position relative to each other and in space, at rest and in motion. Information about deep sensation comes from the proprioceptors of joints and tendons (Styczyński, Gasik, Pyskło 2007; Klu-kowski, Nowotny, Czamara 2014), while those found in the deeper layers of the skin and fascia are traditionally perceived as complementary sources (Lin *et al.* 2015).

When the lower limb is positioned and standing or walking, the receptors inform about changes in human tissues, turn into nerve signals, and are sent to the CNS via sensory pathways (Grigg 1994). The importance of various mechanoreceptors is constantly monitored and studied. In the last two decades, it has been thought that proprioception is mainly the result of signaling from muscle spindles, and that tension information comes from the tendon organ of the Goldie apparatus (Proske 2006). Joint receptors play an active role only in the extreme positions of the range of motion, and not in the middle ranges of movement in the joint. Skin receptors behave in the same way (Goble *et al.* 2009). The muscle spindle actively informs you in the entire range of

motion. These observations are confirmed by researchers who have evaluated the role of receptors in the mid-range of motion (1 050, 1 200, 1 350). They reported that joint and skin receptors were not very active and contributed little to proprioception. In addition, they found that the sense of strength depended more on sensory inputs from the Golgi tendons, and the sense of movement depended more on information from muscle spindles. The position feeling, in turn, is based on double input from the muscle spindles and the Golgi organ (Lin *et al.* 2015).

Receptors (Ruffini's, Pacini's nerve endings, Goldi's organ) are damaged as a result of an ACL injury, resulting in a failure to transmit the correct information to the CNS (Dhillon, Bali, and Prabhakar, 2012) and a reduction in the excitability of the thigh muscle spindles (Lephart, Abt and Ferris 2002).

A normal, passive lifestyle and limited motor activity reduce the possibility of receptor stimulation, which causes a gradual impairment of proprioceptive perception. Deterioration of deep sensation is observed in virtually all patients after prolonged immobilization, surgery and, for example, after neurological events. Disruption of the deep feeling in the knee joints manifests itself in many ways. The most commonly observed gait is a departure from physiological gait, insufficient joint stabilization, muscle weakness or muscle stiffness. Patients often have difficulty locating the limb.

## RESULTS

There are many ways to assess knee proprioception. However, it is always necessary to use tests focused on a specific problem, such as feeling the position of the knee, its instability, or insufficient sense of movement (Li *et al.* 2016), or its direction. When planning the performance of the tests, it is necessary to determine the possibility of performing them, including the position of the body to be taken by the examined person (sitting or lying position). Additional conditions for performing the tests are related to the problem of loading the knee joint or whether to perform the movement without loading it. Other possibilities are the elimination of visual information during the examination.

There are deep sensation tests that take into account the feeling of constant force over a short period of time (Baert *et al.* 2018), with the ability to distinguish between loads (Chu Vwt 2017) or with the ability to actively reproduce. passive motion rate (Nagai *et al.* 2016). Another is the ability to map different knee joints after passive movement (Waddington, Adams 1999). Treadmills are recommended as a good diagnostic tool for qualitative evaluation of gait and for monitoring the progress of patient rehabilitation (Krekor, Czernicki 2009). Stabilometric platforms are also a valuable complement to physiotherapy courses and diagnostics (Bugajski, Czernicki 2013; Jankowska *et al.* 2021).

**Figure 1:** Assessment of the difference in degrees between the target angle and the angle obtained by the subject (A), the inclinometer (B)



A



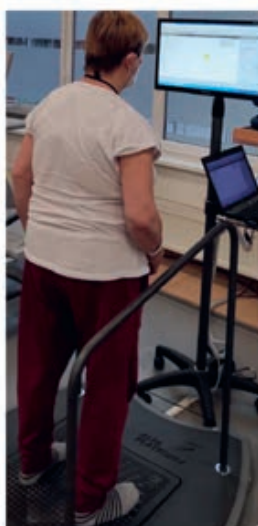
B

**Figure 2:** Evaluation of passive transport

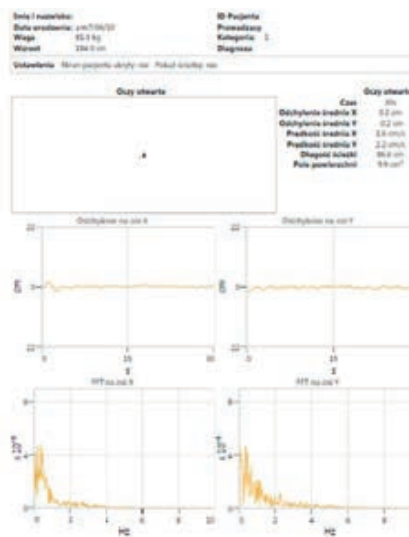


Stabilometric platform diagnostics, together with reports to distinguish deep lower limb sensations, are shown in Figures 3

**Figure 3.** Stabilometric platform test (A), reports on: stability test — open eyes (B), dynamic (C), load distribution (D)



A



B



C



D



Figure 4: Treadmill test (A), treadmill exercise report (B)

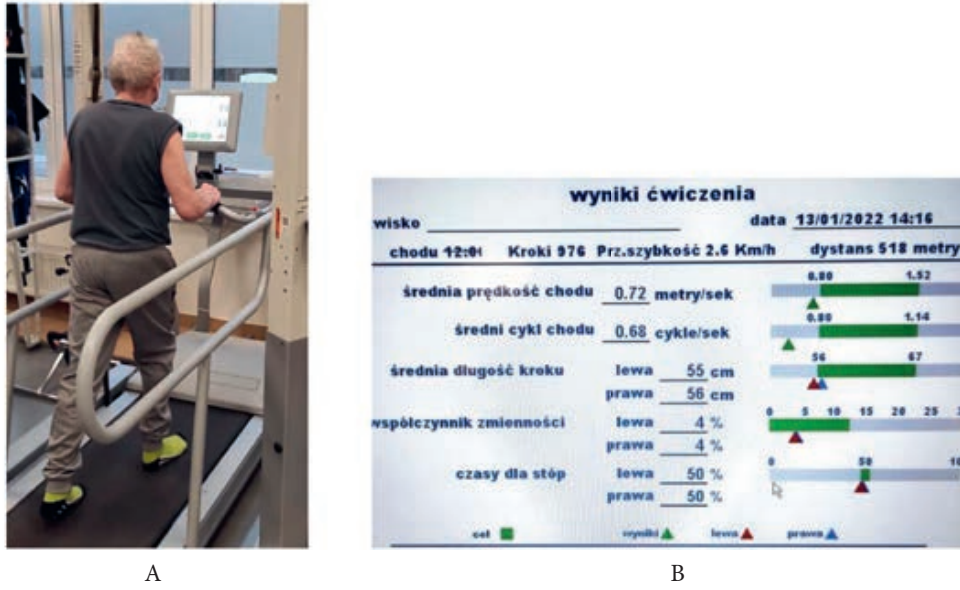
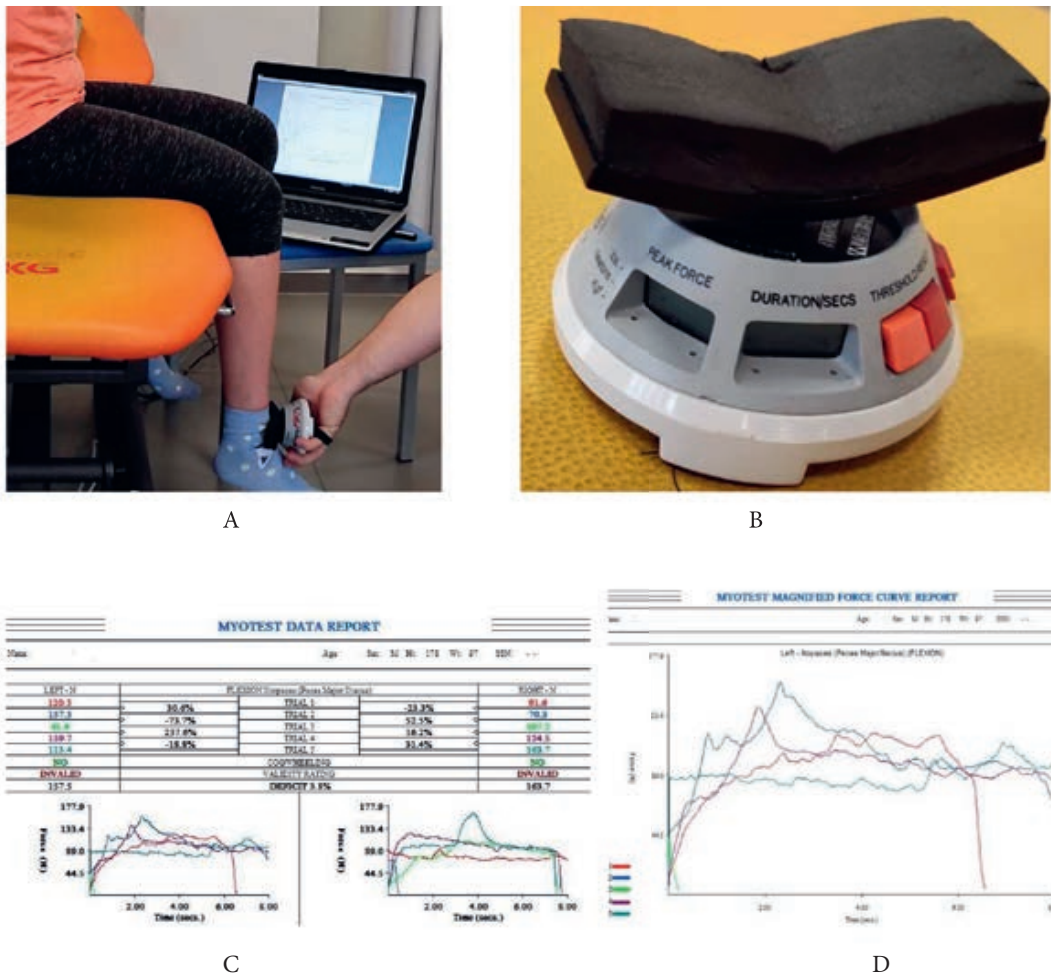


Figure 5: Short-term constant force sensing and speed reproduction test (A), micrFET 2 dynamometer (B) and lower limb comparison (C) and test protocols (D)





One of the most popular methods is to assess the position of the knee joint using an inclinometer (Figure 1). It consists in performing an active or passive movement up to the bending angle of the knee joint. The test result is a difference in degrees between the target angle and the angle obtained by the subject (Baert *et al.* 2018). Another test is the detection of passive movement (Figure 2), which consists in performing a passive movement by the therapist to a certain angle with the direction of movement. The bar only supports the assessment of how the subject has reached the desired angle. During this time, the subject is blindfolded. The test result is the time between the start of the movement and the indication of the angular position by the test person. The condition for a positive test is the correct direction of movement (Nagai *et al.* 2016).

Figure 4 presents a tread assessment report in patients with lower limb dysfunction.

Evaluations of muscle strength, knee movement speed, and lower limb differences are shown in Figure 5

## DISCUSSION

The effectiveness of walking depends on a properly functioning sensory integration, a correctly (no pathology) interpreted deep feeling is the basis of movement planning in the first place. This is followed by the regulation of muscle tone, motor coordination and, in the extreme case, the right movement is performed. Evaluation of proprioceptive feeling is essential in the rehabilitation of patients after peripheral and central nervous system injuries, limb injuries and orthopedic procedures. Together with other diagnostic tests, it will make it possible to focus rehabilitation activities on the most important and important ones from the point of view of the patient's needs.

Balancing platform exercises with current biological feedback can be used for motor improvement, which should be a permanent element of physiotherapy in patients with lower limb dysfunction in any rehabilitation period (Kurkowska 2009).

Pathology in the area of deep perception requires the immediate initiation of recommended physical exercises, taking into account the contraindications and current motor abilities of the patient. In the first place, it requires regular exercise and constant verification of progress in improvement while modifying physiotherapy exercises. Returning to full condition can prove to be long-term and not always successful. Improving proprioception intersects with the whole process of physical therapy, which includes exercises for muscle function, mobility, coordination, balance and locomotion. Classes like yoga or tai chi can be a valuable addition. Comprehensive rehabilitation also uses other physical treatments. Current patient education, including information on the cause of dysfunction,

therapy and health recommendations, including ergonomic ones for the future, should be an essential element of comprehensive rehabilitation.

Rehabilitation activities should not be conducted in the same way and all patients need individualization and a separate approach to each patient's health problems. Physiotherapists responsible for the effectiveness of therapy should pay attention to the age of the patients. Involutionary changes in the elderly also adversely affect the deep sensory system, deterioration of nervous system performance, degenerative joint diseases, and deterioration of receptor function (Rottermund *et al.* 2015). Therefore, especially in this age group, proprioception training should be supported during daily physical and physical activity. Restriction of neuromuscular control in turn causes joint instability, impairs balance and motor skills, and subsequently disrupts the statics of the patient's body, which contributes to postural instability (Riva *et al.* 2013). The combination of improvement exercise with mild aerobic activity should be indicated to contribute to improved motor function (Tognolo *et al.* 2022).

## CONCLUSION

Disorders of the lower limbs are increasing in society. The injuries result in the need to undergo surgery. The period of convalescence and economic effects determine the use of modern techniques and physiotherapeutic methods. Therefore, timely and comprehensive rehabilitation requires the use of reliable and reliable tests. The proprioception tests presented in the article are not only an element of diagnostics, but also an objective assessment of ongoing improvement.

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# The prebiotic of dried powder tomato pomace and its impact on experimental atherogenesis and cancerogenesis

## Vplyv prebiotika z paradajkových výliskov na experimentálnu aterogénu a kancerogénu

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### ABSTRACT

**Objective:** The effect of dietary cellulose (5 or 15 %) and dried powder tomato pomace (15 %) on the development of atherogenesis and colon carcinoma was studied in male Wistar rats.

**Methods:** The animals were fed with diet containing 0,3 % cholesterol and received 12 doses of dimethylhydrazine (20 mg.kg<sup>-1</sup>) subcutaneously in one-week intervals. Fiber content in tomato peels was 47,2 g/100 g of dry matter, 10,3 % of which was in water-soluble form. Immediately after killing the animals, the colon was removed, opened longitudinally, flushed with saline, and the presence of tumors and lymphoid aggregates was assessed macro and microscopically.

**Results and Conclusions:** Tomato pomace in the diet caused a reduction of liver content conjugated dienes by 40 % and activities of superoxide dismutase and glutathione peroxidase in liver increased two-fold. Similarly caused a significant reduction of average occurrence of pre-neoplastic lesions and incidence of dominant type of tumors as well as the total volume of tumors.

**Keywords:** prebiotics, tomato pomace, atherogenesis, cancerogenesis.

### ABSTRAKT

**Cieľ:** U samcov potkanov (Wistar) sa sledoval vplyv diéty celulózy alebo sušených mletých paradajkových výliskov, na rozvoj hypercholesterolemie a karcinómu hrubého čreva.

**Metóda:** Samci potkanov (Wistar) boli kŕmení diétou s 0,3 % cholesterolu, a 12-krát v týždňových intervaloch subkutánne sa im aplikoval dimetylhydrazín (20 mg.kg<sup>-1</sup>). Ďalej im bola podávaná diéta s 15 % celulózu alebo s 15 % sušenými mletými paradajkovými výliskami. Paradajkové výlisky obsahovali 47,2 g vlákniny na 100 g sušiny, z čoho 10,3 % bolo vo vodorozpustnej forme. Okamžite po usmrtení bola vykonaná pitva a materiál bol vyšetrený makroskopicky a mikroskopicky.

**Výsledky a záver:** Paradajkové výlisky znížili obsah konjugovaných diénov v pečeni o 40 % a na dvojnásobok zvýšili aktivitu superoxidodismutázy a glutathionperoxidázy. Podobne signifikantne znížili priemerný výskyt preneoplastických lézií v porovnaní s diétou s 5 % celulózy. Oproti tejto diéte sa pod vplyvom paradajkových výliskov znížila incidencia infiltrujúcich nádorov a v rovnakej miere aj objem všetkých nádorov.

**Kľúčové slová:** prebiotiká, paradajkové výlisky, aterogéna, kancerogéna

## INTRODUCTION

Tomatoes and their processing products, in particular as crucial nutritional sources of antioxidantly acting active carotenoid — lycopene, are of interest. Of the 72 epidemiological studies in 54 of them, an inverse relationship between tomato and tomato product consumption and the risk of carcinoma were confirmed (Giovannucci E 1999). In this work, we focused on dried powder tomato pomace, waste products in the industrial processing of tomatoes, which are a hitherto unused source of food fibre. The results of epidemiological, clinical and experimental studies indicate a protective effect of fibre in both cancer etiopathogenesis and cardiovascular diseases (Abushita AA, Daood HG, Biacs A 2000), which are the main causes of morbidity and mortality in many countries (Eastwood M, Kritchevsky D 2004). It can be inferred from the above that the issues of fibre consumption are issues of a common strategy for the nutritional prevention of both atherosclerosis and cancer. From the point of view of etiopathogenesis, one aspect that connects both diseases is the abnormal course of oxidation marches generating increasingly reactive oxygen products (Dreher D, Junod AF 1996). Based on the above context, we investigated the impact of a diet high in dried powder tomato pomace on nutritionally induced hypercholesterolaemia, chemically induced colon cancerogenesis and the antioxidant status of the organism in rats.

## MATERIAL AND METHODS

In the experiment, we used male rats (Wistar strain, Top-Velaz, Czech Republic,  $n = 34$ ) with an initial weight of about 60 g, reared under standard conditions without affecting the light regime. The animals had continuous access to drinking water and food of the following composition (in %): starch 61, casein 18, lard 10, cellulose 5, mineral mixture 4, vitamin mixture 1, fel tauri (commercial dried bile) 0.55, cholesterol 0.3 and choline chloride 0.15 (control diet with 5 % cellulose). In another control group, we increased the cellulose content to 15 % in the same diet at the expense of starch. In the experimental group, we replaced cellulose with 15 % of tomato compacts obtained during the industrial processing of tomatoes into juice and dried in laboratory conditions at 60 — 70 °C. We determined the content of insoluble and soluble fiber in the compacts by enzyme-gravimetric methods (McCleary BV, DeVries JW, Rader JJ, et al. 2010). After dieting, animals of all groups were subcutaneously administered 20 mg.kg<sup>-1</sup> weighted 1,2-dimethylhydrazine hydrochloride (DMH) (Aldrich) in saline 12 times at weekly intervals. At an additional 14 weeks after the end of DMH administration, the animals were sacrificed by decapitation under light ether anesthesia after 18 hours of weaning.

We determined the cholesterol content in serum, lipoproteins and chloroform-methanol (2 : 1) extract, in the heart and aorta, and the content of triacylglycerols in serum, heart and li-

ver (Oxochrom Chol 2 150 E, TG 450 T and Bio-La-Test sets, respectively), Czech Republic). We determined the content of conjugated dienes in plasma, erythrocytes and liver. We determined the activities of superoxide dismutase (SOD) (Randox Lab. Ltd., UK), catalase (KAT), glutathione peroxidase (GSH-PX) activities in erythrocytes, liver and colon wall. In addition, we determined glutathione reductase (GR) and glutathione-S-transferase (GST) activities in erythrocytes and liver. We determined the protein content in the liver and in the wall of the colon. We determined the content of reduced glutathione (GSH) in erythrocytes, liver and intestine. Immediately after killing the animals, the colon was removed, opened longitudinally, flushed with saline, and the presence of tumors and lymphoid aggregates was assessed macroscopically. The intestine was then divided into 5 sections (7 cm proximal section, 5 cm main flexure, 2 × 3 cm distal section and the rest of the colorectal segment). Individual parts of the colon were stretched on a paraffin pad and fixed in neutral 10 % buffered formula for 24 hours. After fixation, samples were left in Giemsa solution (6 ml/50 ml phosphate buffer) for 15 min. The Giemsa solution was then replaced with buffer and the samples were examined under a stereomicroscope (at 40 × magnification) to assess the occurrence of aberrant crypt foci (ACF) Figure 1. We recorded the total number of ACFs as well as their characteristics with respect to the size, shape and thickness of the lining epithelium. We distinguished ACF small (1 — 3 crypts), medium (4 — 6 crypts) and large (7 or more crypts). Further histological examination was performed by the technique of paraffin sections stained with hematoxylin-eosin. We evaluated the total number of tumors, including the proportion of carcinoma in situ (CIS: tumor foci of highly differentiated adenocarcinoma growing exophytically without signs of lamina basalis penetration) Figure 2. and infiltrating carcinoma (ICA: tumor cell penetration through lamina basalis with spread to all layers of the intestinal wall) Figure 3. Processing of material for morphometric measurement: the whole histological object (tumor) was cut with serial sections of known section thickness (10 μ). Using a histomorphometric device (IMPOR, Image Digitization and Video Analysis System, Quant, SR), we measured the area of each section, multiplied it by the section thickness and calculated the volume for the entire histological object. Results were statistically evaluated by one-way analysis of variance (Instat) and Fisher's exact two-tailed test (Epi Info).

## RESULTS

Tomato pomace contained 47.2 g of total fiber per 100 g of dry matter, of which 10.3 % was in water-soluble form. The composition of the diets did not significantly affect the final weight of the animals. Compared to the physiological level, the multiple elevated serum cholesterol levels were not affected by the cellulose content in the diet, but under the influence of tomato pomace they decreased significantly by 30 %. The decrease in cholesterol was broken down into all lipopro-



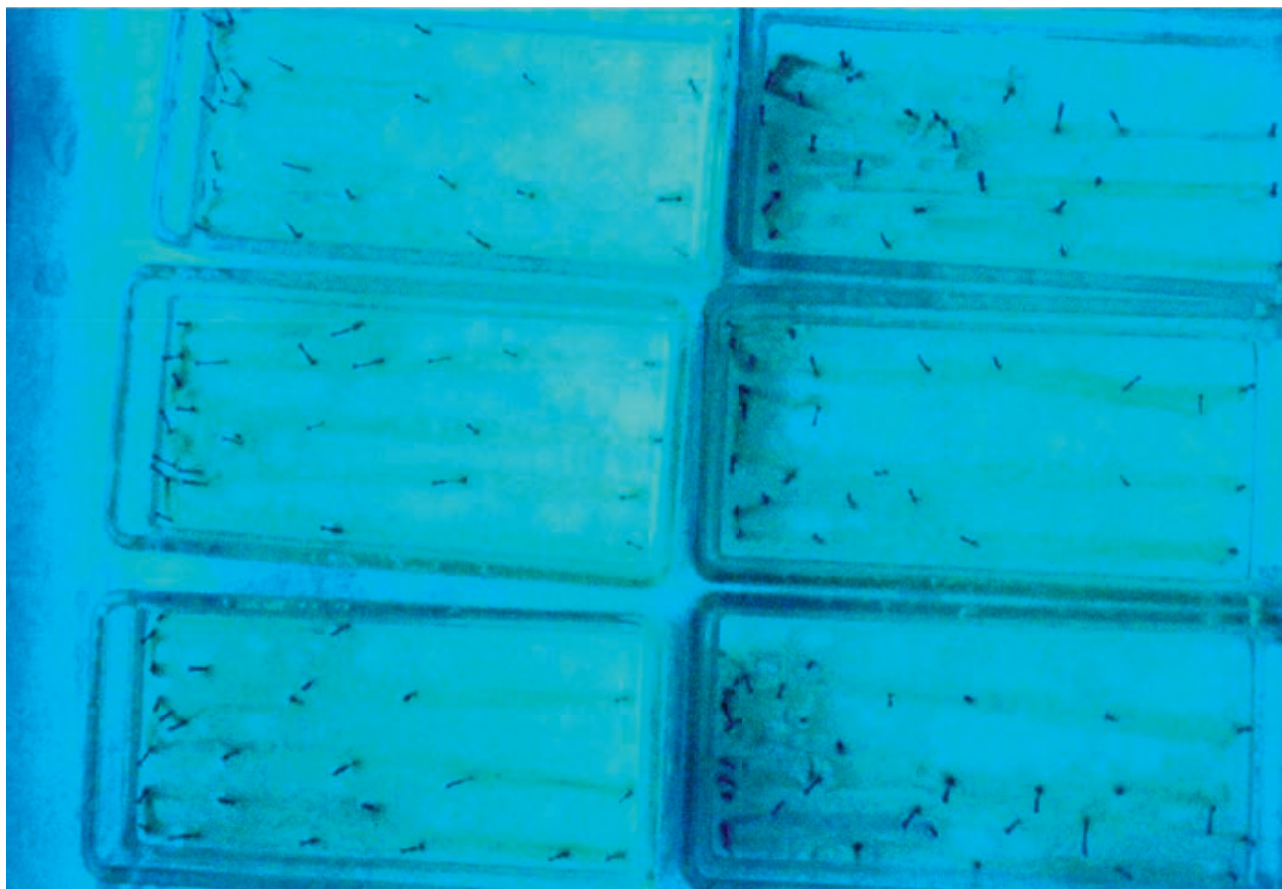
tein fractions, so there were no changes in the cholesterol distribution in the lipoproteins. Neither the cellulose content nor the tomato pomace in the diet affected the cholesterol content in the liver or heart, but reduced it by 30 % in the aorta. Tomato pomace doubled the content of triacylglycerols in the heart, while there were no significant changes in serum and liver. An increase in the cellulose content of the diet led to a significant decrease in conjugated dienes in the liver. At the same time, the activity of KAT in the liver doubled and, conversely, the activity of GSH-PX in this organ decreased to the same extent and the content of GSH decreased. Tomato pomace, compared to a diet with the same cellulose content, led to a decrease in the content of conjugated dienes in the liver, while in this organ the activities of SOD and GSH-PX increased significantly and the activity of KAT decreased. Tomato pomace significantly increased the activity of KAT and GR in erythrocytes, but did not affect the GSH content in erythrocytes and monitored organs. All animals exposed to DMH developed precancerous aberrant crypts foci in the colon. Tomato pomace and an increase of the cellulose content of the diet significantly reduced the incidence of these pathological changes compared to animals on a diet with 5 % cellulose. Tomato pomace halved the incidence of numerically dominant infiltrating tumors (ICA), with the total number and volume

of all tumors combined being lower. A lower number of tumors was found even when the cellulose content increased to 15 %. The latter data were not statistically significant for large variance (Tables 1 and 2).

## DISCUSSION

Tomato pomace could be expected to have a significantly less nutritional effect than the fiber source. The significant hypocholesterolemic effect of tomato pomace (in the absence of a diet with the same cellulose content) is in line with the finding that soluble fiber components are most effective (Anderson TPM, 1991), although the positive effect is also attributed to insoluble fiber (He K, Merchant A, Rimm EB *et al.* 2003). The effect is obviously dose-dependent, as it was absent at a 5 % dose of both products in the diet. Both products modified the lipoprotein profile to a decrease in proatherogenic fractions (VLDL and LDL) and to a more than twofold increase in the proportion of HDL in cholesterol transport. Tomato pomace reduced the level of conjugated dienes (primary products of lipoperoxidation) and increased by 40–80 % the activity of SOD, which catalyzes the conversion of superoxide radicals to hydroperoxide and thus has an inhibitory effect in the initial phase of lipoperoxida-

**Figure 1:** Cut rat colon samples prepared for counting aberrant focal crypts. Giemsa staining

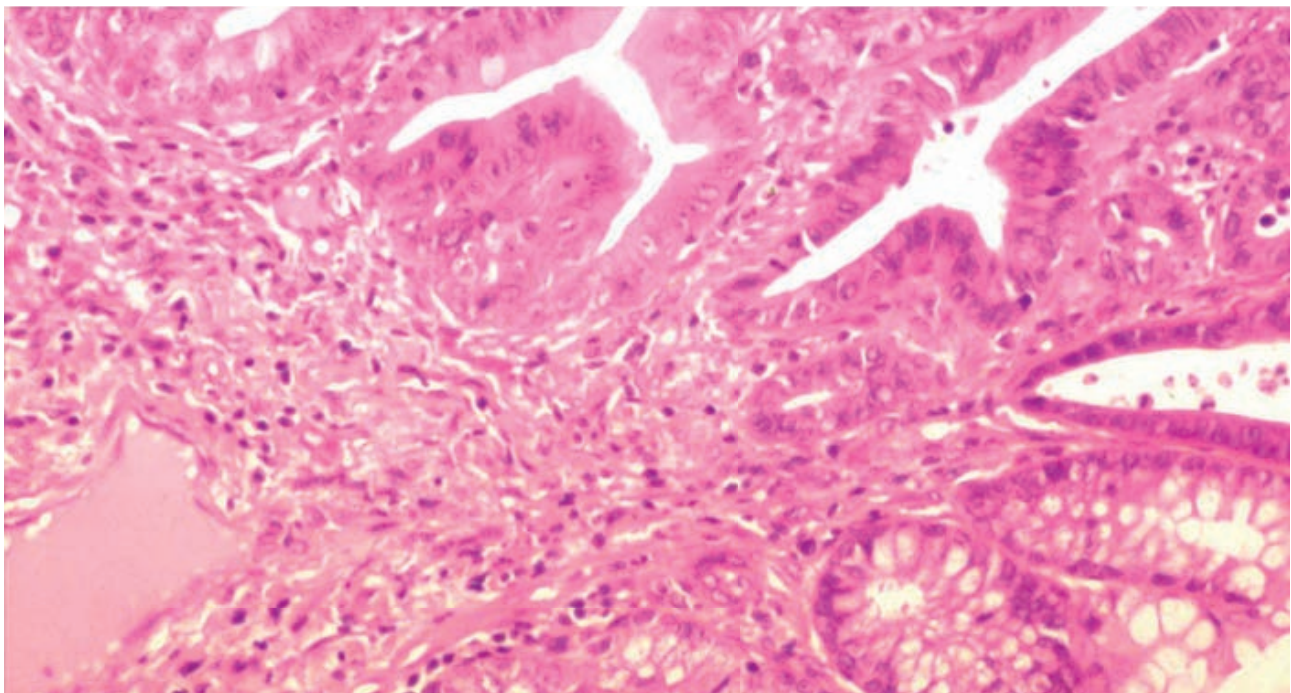


**Table 1:** Incidence and characteristic of aberrant crypt foci in rat

Parameter <sup>1</sup>	Diet <sup>2</sup>		
	Cellulose, 5 % <sup>3</sup>	Cellulose, 15 % <sup>4</sup>	Tomato pomace 15 % <sup>5</sup>
n	11	12	11
Aberrant crypt foci: <sup>6</sup>			
Small <sup>7</sup>	123 ± 3	91 ± 7A	109 ± 8
Medium <sup>8</sup>	34,2 ± 2,7	22,4 ± 3,9A	20,7 ± 3,9A
Large <sup>9</sup>	4,1 ± 0,9	3,2 ± 1,0	3,3 ± 1,1
Total <sup>10</sup>	161 ± 3	117 ± 11B	133 ± 11A

Values are means ± SEM for n animals in group

<sup>A,B</sup> Statistical significance as evidence against group with 5 % cellulose, <sup>A</sup>p < 0,05, <sup>B</sup>p < 0,02

**Figure 2:** Adenocarcinoma in situ without infiltration of lamina submucosa. Hematoxylin-eosin Mg. 200x**Table 2:** Incidence, characteristic and volume of tumours in rat

Parameter <sup>1</sup>	Diet <sup>2</sup>		
	Cellulose, 5 % <sup>3</sup>	Cellulose, 15 % <sup>4</sup>	Tomato pomace 15 % <sup>5</sup>
n	11	12	11
Tumours <sup>6</sup>			
CIS*	2/18	2/17	3/27
ICA*	8/73	6/50	4/36
Total: <sup>7</sup>	8/73	7/58	6/55
-Count <sup>8</sup>	1,91 ± 0,74	0,75 ± 0,22	0,91 ± 0,37
-Volume (mm <sup>3</sup> ) <sup>9</sup>	59.6 ± 21.2	54.2 ± 25.9	22.2 ± 8.4

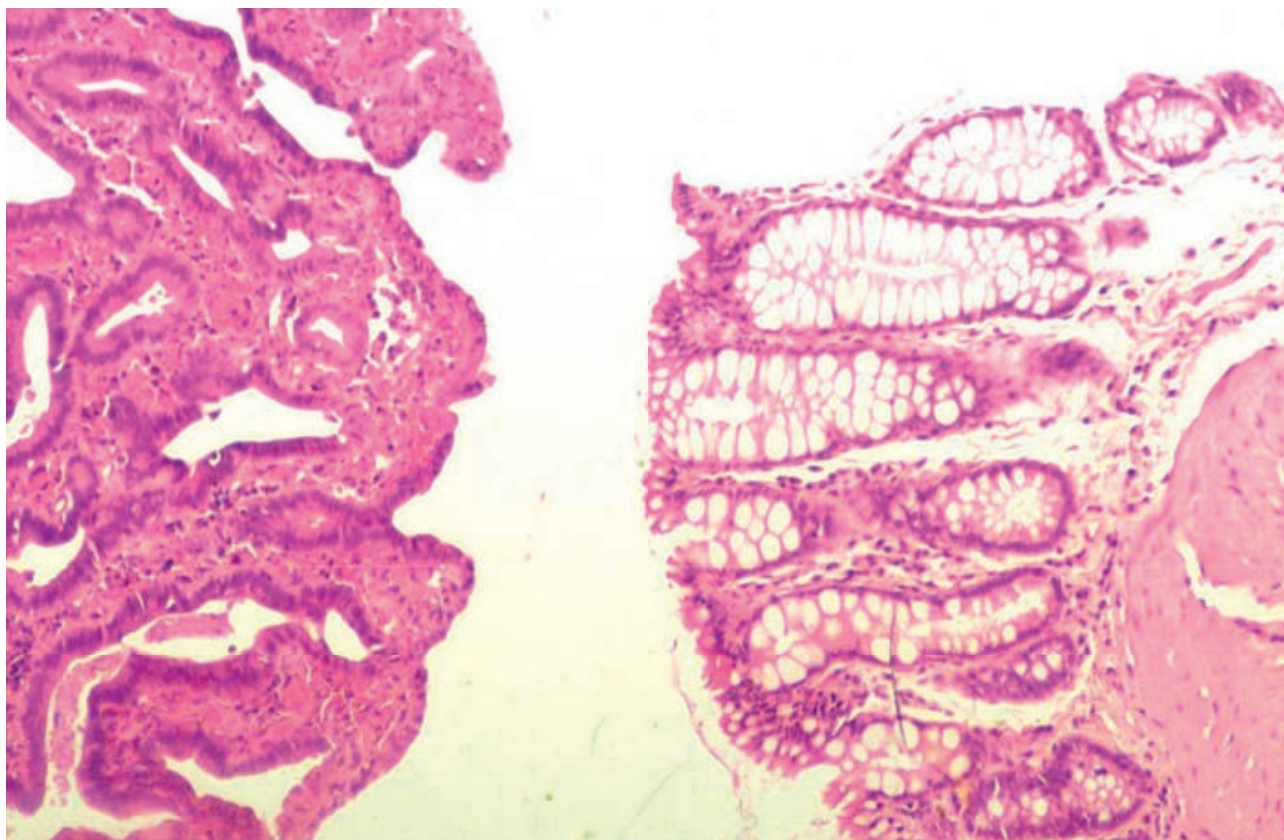
Values are means ± SEM for n animals in group

\*Presented data are number of animals with pathological findings/ % from the whole animals in the group (%)

CIS: Carcinoma in Situ

ICA: Carcinoma Infiltrans



**Figure 3:** Left side infiltrating adenocarcinoma. Right side normal mucosa of colon. HE 200x

tion. Fiber, resp. its raw materials, it can act both antioxidant and non-enzymatic as a medium for the transport of bioactive phytochemicals such as lycopene, vitamins, polyphenols, flavonides, carotenoids, which may have been present in the quantities we did not find in the compacts. In any case, this effect is positive in terms of the etiopathogenesis of both diseases. The antioxidant properties of the compacts may be important due to the mechanism of action of the carcinogen used. As DMH is an electrophilic carcinogen, in this respect the increase in SOD activities should have a protective effect in carcinogenesis. The results of most epidemiological, clinical and experimental studies indicate a protective effect of fiber in carcinogenesis (He M, Hong J, Yang YX, Shen X 2005). However, several conflicting data do not yet allow to define the type of protective fiber, nor to clearly determine the mechanism of this effect. The scheme of the protective effect of fiber leads to a reduction in the exposure of the intestinal mucosa to bile acids and other carcinogens or promoters of exogenous or endogenous origin, their binding to fiber and the acceleration of excretion (Ferguson LR, Chavan RR, Harris PJ 2001). Some authors have not confirmed a relationship between fiber intake, bile acid excretion, and carcinogenesis (Radakovich K, Heilbrun LK, Venkatramamoorthy 2006).

In our study, increases in the content of cellulose and tomato pomace in the diet significantly reduced the incidence of

aberrant crypts foci, which most authors consider real preneoplastic lesions and their evaluation as a reliable end method of experiments of this type (Bird RP, Good CK 2000). Animals on a tomato-pressed diet had a half-incidence of numerically dominant tumors, a lower total number of tumors and the lowest tumor volume. The lower incidence and number of tumors resulted in an increase in cellulose content to 15%. However, the latter results were in most cases only on the verge of statistical evidence. It is questionable what results would be obtained with another methodological arrangement when, after 10–12 applications of DMH, the experiment lasts about 30 weeks before induction (Begleiter A, Sivanathan K, Lefas GM 2009). It is stated that in relation to the source of fiber, its anticarcinogenic effect is limited by the fiber content in the diet, which can be up to 25% (Schwartz B, Birk Y, Raz A, Madar Z 2004).

## CONCLUSION

Issues of improving our chronic deficient fiber intake motivate the search for and study of non-traditional, economically undemanding sources of this nutritional component. A look at the food market in developed countries shows a trend of using fiber from various sources to prepare foods with dietary properties. The results of numerous epidemiological, clinical and experimental studies show that fiber's ability to enter

the metabolism of cholesterol, bile acids and other substances in the intestinal tract can have a hypocholesterolemic effect and have a protective effect in carcinogenesis. Therefore, several authors consider fiber to be one of several possible components of joint nutritional prevention of atherosclerosis and cancer. In connection with the risk of carcinogenesis, the defense effect of an enzymatic system bound to the most important non-enzymatic intracellular antioxidant — GSH — is most often mentioned. GSH is a substrate of GSH-PX, which eliminates toxic peroxides and GST mediates conjugation with glutathione, which is a crucial step in the detoxification of electrophilic decomposition products from the reactions of reactive oxygen species with lipids and DNA.

In our country, the fulfillment of the recommended doses of dietary fiber is lagging behind, probably also due to the seasonal economic demands of resources, vegetables and fruits. On the other hand, the production of unused waste in the industrial processing of fruit and vegetables, which are a rich source of dietary fiber, is increasing. Our results indicated that the range of dietary fiber sources, so far represented mainly by cereals and to a lesser extent seasonally economically demanding fruits and vegetables, can be expanded and another, economically undemanding source with an interesting biological effect.

#### Autorship

All authors have read and approved the final version of the manuscript and all authors listed as co-workers met the criteria for author ship.

#### Conflict of Interest

The authors declared no conflict of interest in relation to the article.

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# Risks of cardiotoxicity in targeted biological therapy

## Riziká kardiotoxicity cielenej biologickej liečby

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### ABSTRACT

**Introduction:** Targeted biological therapy is a new treatment for various cancers, it leads to the improvement of survival of oncological patients and may be associated with the occurrence of cardiovascular side effects. Cardiotoxicity can be manifested as cardiac failure, ischemic heart disease, arrhythmias, QTc prolongation, arterial hypertension, thromboembolic and peripheral vascular diseases.

**Core of the work:** Targeted drugs (small molecules, monoclonal antibodies, proteasome inhibitors) act on various receptors, signal molecules and transcription factors that play a role in tumor pathogenesis and also favorably affect the normal growth and survival of cardiomyocytes, endothelial cells and other cells in the heart and vessels. Giving targeted biological therapy is associated with several cardiovascular complications and consequences. This article points out the toxicity of targeted antiHER2 therapy in HER2-positive breast cancer, where the risk of cardiotoxicity increases even in combination with cardiotoxic chemotherapy of anthracyclines and taxanes.

**Conclusion:** When indicating targeted biological therapy, it is necessary to think not only about the effect of this treatment but also the risks of cardiotoxicity. The patient should be monitored regularly in collaboration with a cardiologist to prevent serious cardiac damage.

**Keywords:** Cardiotoxicity, targeted biological therapy, small molecules, monoclonal antibodies, proteasome inhibitors

### ABSTRAKT

**Úvod:** Cielená biologická liečba je novým liečebným postupom pri rôznych nádorových ochoreniach a vedie k zlepšeniu prežívania onkologických pacientov a môže byť spojená s výskytom kardiovaskulárnych nežiadúcich účinkov. Kardiotoxicita sa môže prejavovať ako kardiálne zlyhanie, ischemická choroba srdca, arytmie, predĺženie QTc intervalu, arteriálna hypertenzia, tromboembolické a periférne vaskulárne ochorenia.

**Jadro práce:** Cielené lieky (malé molekuly, monoklonálne protilátky, inhibítory proteazómu) pôsobia na rôzne receptory, signálne molekuly a transkripčné faktory, ktoré majú úlohu v patogenéze nádorov a taktiež priaznivo ovplyvňujú normálny rast a prežívanie kardiomyocytov, endotelových buniek a iných buniek v srdci a cievach. Podávanie cielenej biologickej liečby je spojené s viacerými kardiovaskulárnymi komplikáciami a následkami. Článok poukazuje na toxicitu cielenej antiHER2 liečby u HER2 pozitívneho karcinómu prsníka, kde sa zvyšuje riziko kardiotoxicity aj kombináciou s kardiotoxickou chemoterapiou antracyklínmi a taxanmi.

**Záver:** Pri indikácii cielenej biologickej liečby je potrebné myslieť nielen na efekt tejto liečby ale aj riziká kardiotoxicity. Pacienta je potrebné pravidelne monitorovať v spolupráci s kardiológom, aby sme predišli závažnému kardiálnemu poškodeniu.

**Kľúčové slová:** kardiotoxicita, cielená biologická liečba, malé molekuly, monoklonálne protilátky, inhibítory proteazómu

## INTRODUCTION

New treatment methods (radiotherapy, chemotherapy, targeted biological therapy and immunotherapy) improve the survival of cancer patients but, on the other hand, these successes of new treatments are accompanied by more frequent side effects (such as cardiotoxicity). In cardiac injury, various mechanisms are in place that can potentiate each other. Cardiotoxicity in the treatment of breast cancer can significantly affect in a negative way the outcome of our therapeutic efforts and affect the quality of life of patients. Beáta Mladosičová (2014, p. 27) states: „that there is currently no generally accepted definition of cardiotoxicity in clinical practice. Cardiotoxicity should also be evaluated taking into account clinical symptoms and laboratory parameters. The situation is particularly difficult in defining cardiotoxicity in targeted biological therapy. Historically, cardiotoxicity has been defined as anthracycline cardiomyopathy, which was first observed in 1960. „The first and basic condition for optimal management of chemotherapeutic treatment in relation to possible heart damage is knowledge of the mechanisms of toxicity of individual anticancer drugs, in respect to their combinations and other modalities (radiotherapy, immunotherapy and targeted biological therapy)“ (Slanina and Kmec 2015, p. 1). Cardiotoxicity occurs in association with the application of targeted drugs of *small molecules*, *monoclonal antibodies* and *inducers of apoptosis* (see Table 1). The aim of this study is to elucidate the mechanisms of effects and risks of cardiac toxicity and to point out the toxicity of targeted therapy of HER 2-positive breast cancer.

## TARGETED BIOLOGICAL THERAPY

Targeted biological therapy (targeted molecular therapy, see Figure 1) is a new treatment for various cancers. It is used more often and more successfully in more and more patients, which shows that these patients live longer. The study *Targeted Biological Therapy of the Most Common Cancer and Its Side Effects* (Beržinec 2009) states that this treatment is „used to label substances and procedures that selectively act on disease-specific targets with no or minimal effect on normal cells. In cancer, several tumor-specific cellular and molecular targets have been identified for different types of tumors. Conventional chemotherapy targets virtually any proliferating cell, whether tumorous or not. The result is systemic toxicity. Targeted therapy is focused on specific goals so it has fewer side effects, which are mostly (not always) mild and many are specific“ (Beržinec 2009, p. 80).

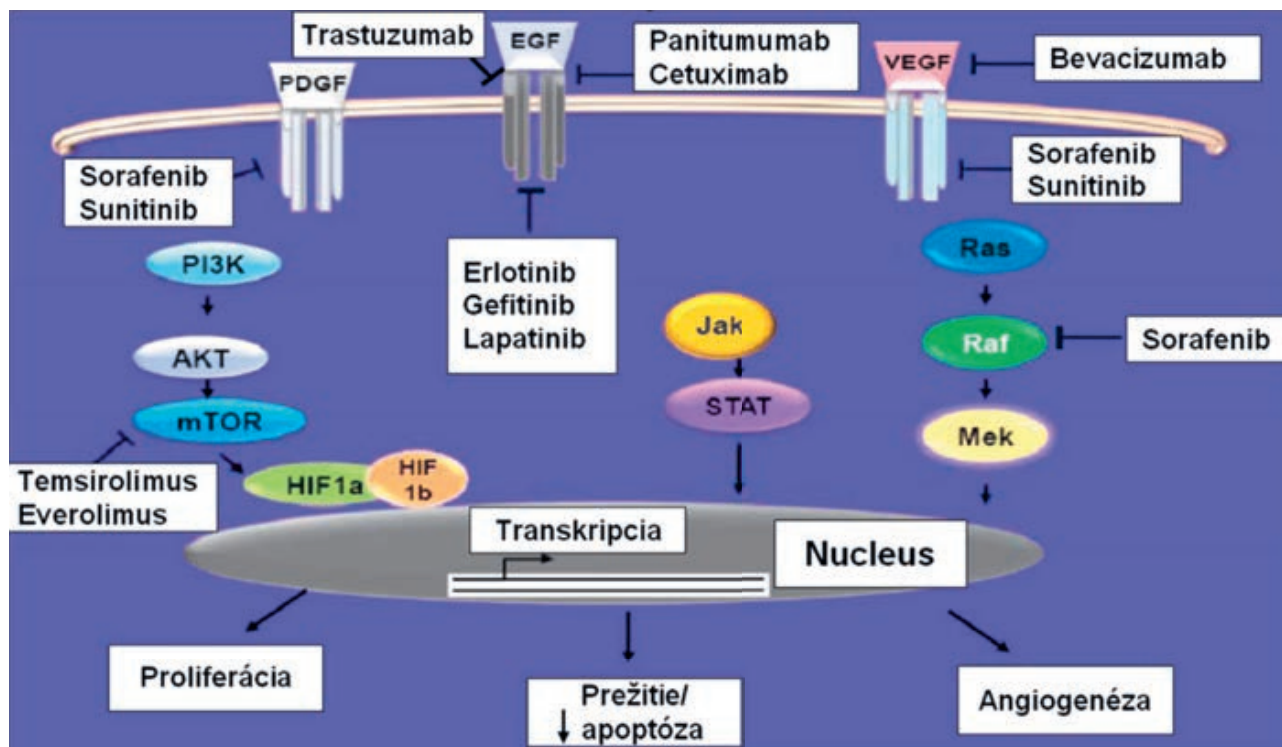
The authors of the study *Cardiotoxicity of Targeted Tumor Treatment* (Mladosičová and Rečková 2013) point out that „knowledge about the cardiotoxicity of monoclonal antibodies against growth factors and receptors and signaling molecules is increasing dramatically. What is unexpected is the detection of pathophysiological contexts that suggest that several ligands, receptors, signal molecules and transcription factors, which play a role in tumor pathogenesis, favorably affect the normal growth and survival of cardiomyocytes, endothelial cells and other cells in the heart and blood vessels. Targeted therapy is associated with several cardiovascular complications and consequences.

**Table 1:** Cardiovascular toxicity of selected targeted drugs (according to Carver JR and Desai CHJ 2010 and Chaudhary P and Garja A 2010)

Targeted anticancer drugs	Cardiovascular toxicity
<b>Monoclonal antibodies</b>	
rituximab	infusion-induced hypotension, atrial or ventricular arrhythmias, angina pectoris, acute myocardial infarction
cetuximab	arrhythmia (probably induced by hypomagnesaemia), cardiomyopathy, acute myocardial infarction, heart failure, hypotension, sudden cardiac death
alemtuzumab	infusion-induced hypotension, heart failure
trastuzumab	asymptomatic or symptomatic decrease in ejection fraction, cardiomyopathy
bevacizumab	hypertension, venous or arterial thromboembolism, heart failure
<b>Tyrosine kinase inhibitors</b>	
imatinib	heart failure in a patient with risk factors, possibly cardiomyopathy
sunitinib	hypertension, myocardial infarction, heart failure, cardiomyopathy
sorafenib	hypertension
lapatinib	asymptomatic decrease in the ejection fraction of the left ventricle, possible cardiomyopathy
<b>Proteasome inhibitors</b>	
bortezomib	heart failure, prolonged QTc interval, angina pectoris, atrioventricular block

Note: The table does not provide an overview of all cardiovascular consequences of anticancer drugs. (Source: Mladosičová, 2014)

Figure 1: Targeted biological therapy — some successful drugs



Legend: VEGF — vascular endothelial growth factor, PDGF — platelet derived growth factor, EGF — epidermal growth factor, proliferácia (proliferation), transkripcia (transcription), prežitie/apoptóza (survival/apoptosis), angiogenéza (angiogenesis)

(Source: Beržinec: Cílená biologická liečba najčastejších nádorových ochorení a jej vedľajšie účinky, 2009)

Experimental and clinical work have confirmed that the RAS-RAFMAPK-ERK1/2 signaling pathway plays a role in maintaining myofibrillar structure, RAF and BRAF kinases play a role in myocyte survival, EGFR helps maintain proper left ventricular function and mTOR kinase plays a role in cardiomyocyte cellular metabolism and in the process of conserving their energy reserves. HER2 signaling is necessary for the physiological growth and survival of cardiomyocytes, it is important in protecting against various situations burdening the the myocardium with oxidative stress, ischemia, pressure overload and other offenses. VEGF and PDGF are important in adequate cardiac perfusion during stressful situations in cardiac remodeling. C-kit kinase is important in the signaling needed to mobilize repair cells in the heart — in the differentiation of progenitor cells in the heart and in the maturation of cardiomyocytes. By blocking these and other molecules by targeted therapy, cardiovascular damage may be indicated“ (Mladosičová and Rečková 2013, p. 10).

## SMALL MOLECULES

*Sunitinib* inhibits numerous receptor tyrosine kinases (RTKs), which are involved in tumor growth, neoangiogenesis and metastatic tumor spread. Sunitinib has been identi-

fied as an inhibitor of platelet-derived growth factor receptors (PDGFR $\alpha$  and PDGFR $\beta$ ), vascular endothelial growth factor receptors (VEGFR1, VEGFR2 and VEGFR3), stem cell factor receptor (KIT), Fms-like tyrosine kinase 3 (FLT3), colony stimulating factor (CSF-1R) and glial cell line-derived neurotrophic factor receptors (RET). It is indicated for the treatment of unresectable and/or metastatic malignant gastrointestinal stromal tumor (GIST) in adults after failure of imatinib treatment. It is also used in the treatment of metastatic renal cell carcinoma (MRCC) and well-differentiated unresectable or metastatic pancreatic neuroendocrine tumors (pNET).

The most common side effects with sunitinib include: fatigue, diarrhea, hand-foot syndrome, hypertension, stomatitis, hypothyroidism and myelotoxicity. Sunitinib treatment increases the risk of heart failure and myocardial infarction. Hypertension was a very common adverse reaction reported in clinical trials, occurring in approximately 33.9 % of patients. 4.7 % of patients with solid tumors experienced severe hypertension (> 200 mmHg systolic or 110 mmHg diastolic blood pressure). Hypertension is a risk factor for heart failure, so close monitoring and treatment of hypertension is essential to reduce the risk of serious cardiovascular complications. Hypertension is also considered a predictor of treatment efficacy and can be expected with other targeted drugs that af-

fect the VEGF pathway. Sunitinib increases the risk of cardiomyopathy. In clinical studies, decreases in LVEF of  $\geq 20\%$ , resp. below the lower limit of the standard occur in approximately 2 % of GIST patients treated with SUTENT, 4 % of patients with cytokine-resistant MRCC, and 2 % of GIST patients in the placebo group. This decrease in LVEF did not show signs of progression and was often corrected with continued treatment. Sunitinib may cause QTc prolongation beyond 500 ms and may lead to an increased risk of ventricular arrhythmias, including torsade de pointes. Sunitinib should be used with caution in patients with an anamnesis of QTc interval prolongation, in patients taking antiarrhythmics or drugs that may prolong the QTc interval, or in patients with pre-existing severe heart conditions, bradycardia or electrolyte imbalance. In a prospective study from 2017, the risk of cardiotoxicity was assessed using ECHOkg and biomarkers (highly sensitive troponin I (hsTnI) and B-type natriuretic peptide (BNP)) in 90 patients. These patients were found to show only a slight decrease in LVEF and negligible changes in hsTnI and BNP. Approximately 9.7 % to 18.9 % of patients experienced more severe abnormalities. These changes occur early and can be largely cured by careful monitoring (Narayan *et al.* 2017, p. 2).

*Sorafenib* is a multikinase inhibitor that has been shown to have antiproliferative and antiangiogenic properties, inhibiting the activity of target objects present in tumor cells (CRAF, BRAF, V600 BRAF, c-KIT and FLT-3) and in the vascular system of the tumor (CRAF, VEGFR-2, VEGFR-3 and PDGFR- $\beta$ ). RAF kinases are serine/threonine kinases, while c-KIT, FLT-3, VEGFR-2, VEGFR-3 and PDGFR- $\beta$  are receptor tyrosine kinases. The clinical safety and efficacy of sorafenib have been studied in patients with hepatocellular carcinoma (HCC), in patients with advanced renal cell carcinoma (RCC) and in patients with differentiated thyroid carcinoma (DTC). The most common adverse reactions were diarrhea, fatigue, alopecia, infection, hand-foot skin reaction and rashes. The most important serious adverse reactions were myocardial infarction/ischemia, gastrointestinal perforation, drug-induced hepatitis, haemorrhage and hypertension/hypertensive crisis. Hypertension was a very common adverse reaction reported in clinical trials, occurring in approximately 43 % of patients. There is an increase in systolic and diastolic blood pressure. The risk of coronary syndrome and acute coronary events during sorafenib treatment is reported to be in the range of 2.7 – 4.9 %.

*Lapatinib*, 4-anilinequinazoline, is an inhibitor of intracellular tyrosine kinase of the domains of both the EGFR (ErbB1) and HER2 (ErbB2) receptors. It is indicated for the treatment of adult patients with breast cancer whose tumors report an excessive expression of HER2 (ErbB2); in combination with capecitabine for patients with advanced or metastatic disease with a progression after previous treatment, which must have had included anthracyclines, taxanes and trastuzumab, it

may also be applied in combination with trastuzumab and an aromatase inhibitor for postmenopausal women with a metastatic disease with hormonal receptor positivity, for whom chemotherapy is not currently planned. The most common adverse reactions (> 25 %) during treatment with lapatinib were gastrointestinal events (such as diarrhea, nausea and vomiting) and rash. Palmar-plantar erythrodysesthesia [PPE] was also common (> 25 %) when lapatinib was given in combination with capecitabine. Decreased LVEF was reported in approximately 1 % of patients receiving lapatinib and was asymptomatic in more than 70 % of cases. Symptomatic reductions in LVEF were observed in approximately 0.3 % of patients receiving lapatinib in monotherapy, 2.5 % of patients receiving lapatinib in combination with capecitabine, 3.1 % of patients receiving lapatinib in combination with letrozole, and 6.7 % of patients receiving lapatinib in combination with trastuzumab. Observed adverse reactions included dyspnoea, heart failure and palpitations. In a total of 58 % of patients these symptoms disappeared.

## MONOCLONAL ANTIBODIES

*Bevacizumab* is a monoclonal antibody that binds itself to the vascular endothelial growth factor (VEGF), a key activator of vasculogenesis and angiogenesis, thereby inhibiting EGF binding to Flt-1 (VEGFR-1) and KDR (VEGFR-2) receptors on the surface of endothelial cells. Neutralization of the VEGF biological activity causes a regression of tumor vascularization, normalizes the remaining vascular supply of the tumor and prevents the formation of new vascular supply of the tumor, thus inhibiting tumor growth. It is used in combination with other drugs against cancer to treat adults with the following types of cancer: metastatic colorectal cancer, metastatic breast cancer, advanced non-small cell lung cancer, metastatic kidney cancer, metastatic ovarian cancer and cervical cancer.

The most serious side effects were: gastrointestinal perforations, bleeding including haemoptysis, which was more common in patients with non-small cell lung cancer, arterial thromboembolism. The most common side effects were arterial hypertension, fatigue or asthenia, diarrhea and abdominal pain, proteinuria. Cardiovascular adverse effects of bevacizumab include arterial hypertension, congestive cardiac failure and deep vein thrombosis. It was also observed an increased incidence of arterial thromboembolic reactions, including cerebrovascular incidents, myocardial infarction, transient ischemic attacks and other arterial thromboembolic reactions in up to 3.8 % in the groups with bevacizumab compared to 2.1 % in the control groups with chemotherapy. Congestive heart failure occurred in approximately 3 % of patients and was probably related to the lack of angiogenesis required to manage stress reactions. The incidence of arterial hypertension ranged from 4 – 35 %, with stage 3 hypertension represented 11 – 18 %.



*Trastuzumab* is a recombinant humanized monoclonal antibody of the type IgG1 against the receptor 2 of the human epidermal growth factor (HER2). It binds itself to the extracellular domain of the HER2 receptor, preventing dimerization of the receptor and subsequent phosphorylation of the intracellular domain of the receptor and the initiation of intracellular signaling, thereby inhibiting the proliferation and survival of cells with an increased expression of HER2. It is used in the treatment of metastatic HER2-positive breast cancer, in the treatment of early HER2-positive breast cancer (neoadjuvant and adjuvant application) and in the treatment of metastatic HER2-positive stomach cancer. The issues of the pathophysiology of cardiotoxicity of Trastuzumab, as well as the pathophysiology of cardiotoxicity of Pertuzumab, is discussed in more detail in the study *Efficacy and risk of cardiotoxicity of targeted antiHER2 treatment in adjuvanting HER2-positive breast cancer* (Lešková 2020, pp. 44 — 50).

The most serious and/or most common adverse reactions reported to date with the use of Herceptin (for intravenous and subcutaneous administration) include cardiac dysfunction, infusion-related reactions, haematotoxicity (especially neutropenia), infections and pulmonary adverse reactions. „The cardiac toxicity of trastuzumab usually manifests itself as an asymptomatic decrease in ejection fraction of the left ventricle, or as a symptomatic congestive cardiac failure“ (Novotný *et al.* 2019, p. 639).

The overall incidence of cardiac toxicity is variable and depends on the definition used in various clinical studies. „The risk is 2—7 % for trastuzumab monotherapy, 2—13 % for the combination of trastuzumab and paclitaxel and up to 27 % in combination with anthracyclines (the risk depends on the cumulative dose of anthracycline). Prior use of anthracyclines, especially at high cumulative doses (more than 250 mg/m<sup>2</sup> of doxorubicin or more than 600 mg/m<sup>2</sup> of epirubicin) may be the most important risk factor for subsequent cardiac dysfunction“ (Florido *et al.* 2017, p. 7). Equally risky is concomitant anthracycline administration or a short period (3 weeks versus 3 months) between anthracycline use and trastuzumab administration, which in some studies increases the risk of cardiac adverse events (Florido *et al.* 2017, p. 7). In study N9831, older age (> 60 years), lower baseline LVEF and use of antihypertensives were associated with an increased risk of cardiotoxicity. In another study, NSABP-31, older age and lower baseline LVEF of 50—54 % were associated with trastuzumab-induced cardiotoxicity. The risk of cardiotoxicity increases with age, as confirmed by some studies. Higher body weight also significantly increases the likelihood of anthracycline-related cardiac dysfunction or gradual anthracycline and trastuzumab treatment. In a meta-analysis of 15 studies, a body mass index > than 25 was associated with 1.32 × and a body mass index greater than 30 with 1.47-fold (95 % CI, 0.95 — 2.28) higher cardiotoxicity than in patients with normal body weight values. Other risk factors include:

age, hypertension, diabetes mellitus, ischemic heart disease, atrial fibrillation or flutter, renal dysfunction and the use of adjuvant chemotherapy.

## PROTEASOME INHIBITORS

*Bortezomide* is a ubiquitin-proteasome complex (UPK) inhibitor and is used in the treatment of multiple myeloma and mantle cell lymphoma. The most commonly reported adverse reactions during treatment are nausea, diarrhea, constipation, vomiting, fatigue, pyrexia, thrombocytopenia, anemia, neutropenia, peripheral neuropathy (including sensory), headache, paraesthesia, decreased appetite, dyspnoea, rash, herpes zoster and myalgia. Cardiac failure is one of the serious side effects, occurring in 5 % of patients. Prolonged QTc interval, angina pectoris and AV block occur sporadically.

## CONCLUSION

At the end of the study it can be stated that the more significant development of oncological treatment in recent time leads to the improvement of survival of oncological patients, but also to increased morbidity and mortality due to the side effects of this treatment. One of the most serious side effects is cardiotoxicity, which can significantly affect in a negative way the outcome of our therapeutic efforts. Cardiac complications associated with treatment against cancer, or cancer itself, become so complex that they cease to be a priority of one field. At present, a new discipline is profiling in several renowned workplaces around the world (it is still absent in Slovak Republic), in which cardiology intersects with oncology — cardiooncology (Mladosičová 2014). The aim of this field is to maintain the good quality of the cardiovascular condition of oncological patients while maintaining the effectiveness of treatment.

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The authors declare no conflict of interest.

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# The association between the quality of life and BMI among adults

## Vztah kvality života a BMI u dospělých osob

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### ABSTRACT

**Introduction:** For the assessment of a body weight, we can use measuring the body composition, various anthropometric measurements, but a very simple tool may comprise the assessment according to the body mass index (BMI).

**Objectives:** The objective of the study was to determine the association between BMI values and the quality of life.

**Methods:** We used the body mass index (BMI) for the assessment according to body weight. We also used a standardised WHOQOL-BREF questionnaire of the quality of life (the brief version) of the World Health Organization. The study sample included 323 adults aged 18 — 65. The study sample was divided into two groups based on the BMI values and gender — BMI lower than 25 kg/m<sup>2</sup> and BMI of 25 kg/m<sup>2</sup> or higher.

**Results and conclusions:** In the group of respondents with BMI <25 kg/m<sup>2</sup>, higher values were achieved in the domains assessing the quality of life. In the experiencing area, lower values were achieved. In the domain of social relationships, the values tend to be close to the population standard, where higher values were achieved with respect to respondents with BMI <25 kg/m<sup>2</sup>. In the environmental domain, higher values than the population standard were achieved in both groups.

**Keywords:** Quality of life, WHOQOL-BREF, BMI, adults

### ABSTRAKT

**Úvod:** Pro hodnocení tělesné hmotnosti můžeme využít měření tělesného složení, různá antropometrická měření, velmi jednoduchým nástrojem ale může být hodnocení dle indexu tělesné hmotnosti (BMI).

**Cíl práce:** Cílem práce bylo zjistit, jaký je vztah mezi hodnotami BMI a kvalitou života.

**Metodika:** Pro hodnocení dle tělesné hmotnosti jsme využili index tělesné hmotnosti (BMI). Dále jsme využili standardizovaný dotazník kvality života (zkrácenou verzi) Světové zdravotnické organizace WHOQOL-BREF. Výzkumný soubor tvořilo 323 dospělých osob ve věku 18 — 65 let. Soubor byl rozdělen dle hodnot BMI a pohlaví do dvou skupin: BMI nižší než 25 kg/m<sup>2</sup> a BMI 25 kg/m<sup>2</sup> nebo vyšší.

**Výsledky a závěr:** U skupiny respondentů s BMI <25 kg/m<sup>2</sup> bylo dosaženo vyšších hodnot v doménách hodnocení kvality života. V oblasti prožívání bylo dosaženo nižších hodnot. V doméně sociálních vztahů se hodnoty blíží populační normě, přičemž u respondentů s BMI <25 kg/m<sup>2</sup> bylo dosaženo vyšších hodnot. V doméně prostředí bylo u obou skupin dosaženo vyšších hodnot, než je populační průměr.

**Klíčová slova:** kvalita života, WHOQOL-BREF, BMI, dospělé osoby

## Introduction

Excess weight and obesity is recognised as a chronic non-communicable disease, the occurrence of which is continuously increasing. In consideration of the occurrence and potential complications, this means a global pandemic, causes of death of many people. More people die as a result of being overweight or obese than people dying because of malnutrition (WHO, Obesity 2021).

According to the World Health Organization (WHO 2021), excess weight is defined as BMI higher or equal to 25 kg/m<sup>2</sup>, and obesity as BMI higher or equal to 30 kg/m<sup>2</sup>. The basic characteristic is increased adipose tissue in the organism. If the BMI value is between 18.5 and 24.9 kg/m<sup>2</sup>, then the weight is assessed as normal, physiological or healthy. A lower BMI value, then, would mean underweight.

BMI (Body Mass Index), or the Quetelet's index of body mass, indicates the relation between a body weight and body height.

$$\text{BMI} = \frac{\text{body weight (kg)}}{\text{height}^2 \text{ (m)}}$$

BMI is a basic index for fast, simple and effective assessment of the nutritional status of individuals. BMI is a more suitable index for the assessment of a large group, or an entire population, than for the assessment of an individual. Nevertheless, BMI will usually provide a correct assessment of an individual in the majority of cases as well.

The World Health Organization (WHO 2022) defines quality of life as individual perception of one's own position in life in the context of the culture and system of values, in which an individual lives and in relation to individual objectives, expectations, standards and interests. The quality of life is determined by personal satisfaction, feeling of well-being and opportunity to fulfil the different functions in the society, the modern society brings different views on the importance of the quality of life (Ludvigh Cintulová, Budayová, Buzařová 2022).

The globalisation, demographic revolution and increasing poverty over the world bring different view to the quality of life, there are subjective and objective factors influencing the life standard that linked to changing the society and personal value orientation (Budayová, Ludvigh Cintulová, Chanas 2018).

WHO experts created a standardised tool, a questionnaire, which is to assess the quality of life. The WHOQOL-100 questionnaire contains 100 questions, which, however, might be too much and too demanding to fill out, and therefore a brief version, WHOQOL-BREF, was created. This questionnaire contains 26 questions, of which 4 domains are subsequently

created and two questions are assessed separately. The domains are as follows: physical health, experiencing (mental health), social relationships and environment (living conditions). The two questions assessed separately concern the quality of life and health satisfaction (Dragomirecká and Bartoňová 2006). The questionnaire finds out information about the respondent's lives in the last 14 days. Respondents always choose answer 1 to 5. Respondents assess their health and quality of life, how they experience certain things, the extent in which they can perform different activities, how happy or satisfied they are in different areas of their lives or how often they experience certain feelings. The higher the values achieved in individual domains, the higher is the satisfaction of respondents in the relevant area.

## MATERIAL AND METHODS

The study sample included adults aged 18—65. Total 323 individuals participated, of which 156 were men and 167 were women. All respondents were divided into groups based on the BMI, the first group included individuals with BMI <25 kg/m<sup>2</sup>, the second group included individuals with BMI ≥25 kg/m<sup>2</sup>.

All respondents completed the WHOQOL-BREF questionnaire, consisting of 26 questions. The WHOQOL-BREF quality of life questionnaire was prepared according to the instructions and six scales were determined — the quality of life, health satisfaction and four domains created by summing up: physical health (D1; including seven items), experiencing (D2; including six items), social relationships (D3; including three items), and environment (D4; including eight items). To enable a better comparison, the domain scores are presented in a transformed status to a 0—100 scale. To enable a comparison with other studies, the values are also transformed to a 4—20 scale.

For the purposes of description, the group of respondents was divided into two groups based on BMI (<25 kg/m<sup>2</sup>, ≥25 kg/m<sup>2</sup>), in which the differences in gender representation were assessed by a chi-squared test, and the differences in average age or scores by a two-sample t test. The impact of gender, age and BMI of respondents on their scores was evaluated by a regression analysis (Enter method). The data was processed in the IBM SPSS 26.0 statistical programme. The selected significance level was  $\alpha = 0,05$ .

For the evaluation of the collected data, population standards were used, as obtained from the manual for the users of the Czech version of the WHOQOL questionnaire (Dragomirecká and Bartoňová 2006, p. 42). Radkova and Ludvigh Cintulova (2018) accept the quantitative research as the great tool to attain greater knowledge and understanding of the aspects and determination of the quality of life, it also allows to do variation to look for the relation between various variables.



## RESULTS

At first the average scores of individual domains were calculated, which were transported to a 4–20 scale, then to a 0–100 scale in order to enable the comparison of the results with other studies. The scale range of individual questionnaire items was always 1–5, where 5 means a better quality in the given area in most questions. Several questions are assessed vice versa, i.e. 5 means the worst quality, namely questions 3, 4 and 26 (assessment of pain, the medical care needed and experiencing negative emotions).

Table 1 contains the results of respondents transported to a 0–100 scale. The group of individuals with BMI <25 kg/m<sup>2</sup> included more women, on the contrary, the group with BMI ≥25 kg/m<sup>2</sup> included more men. The average age in individual groups is 35.9, and 39.0. The representation of respondents in groups based on age in groups with a different BMI is identical. The average scores of all four domains and two separately assessed questions differ between the groups based on BMI. You can see the differences in table 1 and in the graphs.

**Table 1:** Division into two groups based on BMI. Score 0–100

		BMI < 25		BMI ≥ 25		Achieved level of significance
		frequency	percentage	frequency	percentage	
Gender	male	69	42.6 %	87	54.0 %	0.040 <sup>b</sup>
	female	93	57.4 %	74	46.0 %	
		mean	st. deviation	mean	st. deviation	
Age		35.9	13.5	39.0	14.8	0.052 <sup>c</sup>
Quality of life		4.1	0.6	3.9	0.7	0.003 <sup>c</sup>
Health satisfaction		4.0	0.7	3.5	0.8	<0.001 <sup>c</sup>
D1 <sup>a</sup>		63.2	14.0	59.4	13.3	0.013 <sup>c</sup>
D2 <sup>a</sup>		65.4	13.3	61.4	13.5	0.009 <sup>c</sup>
D3 <sup>a</sup>		72.6	15.7	66.8	19.1	0.003 <sup>c</sup>
D4 <sup>a</sup>		71.9	11.1	68.0	13.5	0.004 <sup>c</sup>

*a* the score of scales transformed to a 0–100 scale (for better comparison, because the scales do not contain the same number of questions)

*b* chi-squared test — the representation of gender is different in the two BMI groups (more overweight men)

*c* *t*-test — the average age in the two BMI groups is identical; the average score of all six scales is different in the two BMI groups (the scores of overweight respondents are always lower — see the graphs)

\* Own results

**Table 2:** Division into two groups based on BMI. Score 4–20

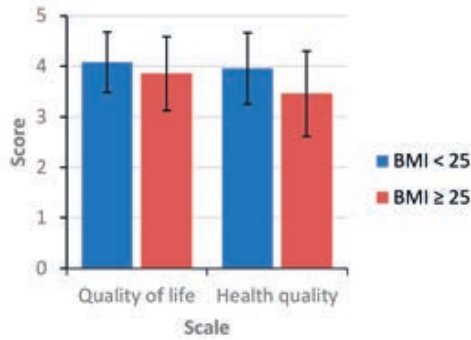
		BMI <25		BMI ≥25		Achieved level of significance	Population standards* ( <i>n</i> = 308, or <i>n</i> = 310 <sup>d</sup> )
		frequency	percentage	frequency	percentage		
Gender	male	69	42.6 %	87	54.0 %	0.040 <sup>b</sup>	
	female	93	57.4 %	74	46.0 %		
		mean	st. deviation	mean	st. deviation		
Age		35.9	13.5	39.0	14.8	0.052 <sup>c</sup>	
Quality of life		4.1	0.6	3.9	0.7	0.003 <sup>c</sup>	3.82 ± 0.72d
Health satisfaction		4.0	0.7	3.5	0.8	<0.001 <sup>c</sup>	3.68 ± 0.85d
D1		14.1	2.2	13.5	2.1	0.013 <sup>c</sup>	15.55 ± 2.55
D2		14.5	2.1	13.8	2.2	0.009 <sup>c</sup>	14.78 ± 2.43
D3		15.6	2.5	14.7	3.1	0.003 <sup>c</sup>	14.98 ± 2.89
D4		15.5	1.8	14.9	2.2	0.004 <sup>c</sup>	13.30 ± 2.08

*b* chi-squared test — the representation of gender is different in the two BMI groups (more overweight men)

*c* *t*-test — the average age in the two BMI groups is identical; the average score of all six scales is different in the two BMI groups (the scores of overweight respondents are always lower — see the graphs 1 and 2)

\* Dragomirecká and Bartoňová, 2006; Own results

**Graph 1:** The average score of quality of life and health quality in the two BMI groups (own results)



In two separately assessed questions, but also in all four domains, we see that the group of respondents with BMI  $\geq 25$  kg/m<sup>2</sup> achieved lower values. All the differences found among the monitored respondents, or groups, are statistically significant.

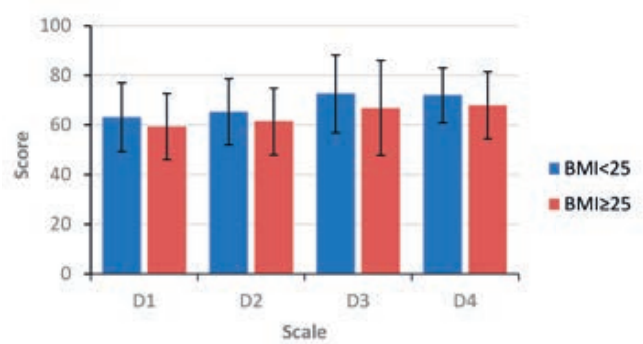
To enable comparison of our results with other studies, the values in table 2 are transformed to a 4 — 20 scale. The range for the assessment of the two separately assessed questions remains 1 — 5.

It is apparent from table 2 that in terms of the quality of life, all our respondents, regardless the BMI value, achieved higher values in comparison with the population standard. In health satisfaction, there is a difference, respondents with BMI <25 kg/m<sup>2</sup> achieved higher values, on the contrary, overweight and obese respondents achieved lower values in comparison with the population standard. In the physical health and experiencing domains, our respondents with any BMI achieved lower values in comparison with the population standard. In the domain of social relationships, our respondents with BMI <25 kg/m<sup>2</sup> achieved higher values, on the contrary, respondents with BMI  $\geq 25$  kg/m<sup>2</sup> achieved lower values in comparison with the population standards. In the last domain, the living conditions or environment, all our respondents achieved higher values.

Comparison of the achieved values with various groups of individuals according to Dragomirecká and Bartoňová (2006). For this part of comparison, a transformed 4 — 20 scale was used. If we compare in individual domains the values achieved by our group of respondents and respondents according to Dragomirecká, Bartoňová (2006) — 60+, U3V, students, bariatry, pancreas, schizophrenia and Parkinson's.

In the physical health domain, our respondents with BMI <25 kg/m<sup>2</sup> achieved worse values in comparison with the population average, and also than U3V and students, on the contrary, they achieved better values than individuals with any medical condition and elderly (60+). With the achieved value (13.5), our respondents with BMI  $\geq 25$  kg/m<sup>2</sup> achieved similar values as individuals from the „pancreas“ group, worse values

**Graph 2:** The average score of all four scales in the two BMI groups (own results)



than individuals 60+, U3V, students, and better values than the bariatry, schizophrenia and Parkinson's groups.

In the exercising domain, the value achieved in the group with BMI <25 kg/m<sup>2</sup> reaches similar values as the U3V group, the group with BMI  $\geq 25$  kg/m<sup>2</sup> then similar values as the 60+ group, a lower score in this domain was achieved only by the „schizophrenia“ and „Parkinson's“ groups.

In the social relationships domain, the average value achieved by the group with BMI <25 kg/m<sup>2</sup> is higher than the values achieved by all the mentioned groups, the group with BMI  $\geq 25$  kg/m<sup>2</sup> is then closest to the general population (18 — 59).

In the last domain, the environment, both our groups achieve higher values than all the mentioned groups, where the closest values were achieved by the U3V group.

## DISCUSSION

Stephenson et al. (2021) assessed quality of life among obese individuals by HRQoL, and came to the conclusion that with the increasing obesity degree, HRQoL was decreasing, but the difference between overweight individuals and individuals with normal body weight was very small. In our respondents, statistically significant differences were observed in all domains, as well as in the two separately assessed questions (i.e. including quality of life), and the dependence is negative, i.e. the higher the BMI value, the lower the score. The strongest dependence was in the quality of life and health quality. In this context, we could say that we came to the same result in part, but our respondents were divided into two main groups (BMI <25 kg/m<sup>2</sup> and BMI  $\geq 25$  kg/m<sup>2</sup>).

Bužgová et al. (2014) states that when assessing the quality of life of obese patients, their quality of life was lower than the population standards before bariatric surgery, namely in the physical health and experiencing (mental health) domains ( $p < 0001$ ). After bariatric surgery (3 months and 6 months), the results in these domains were identical to the population standards ( $n = 308$ ; 18 — 59). In the physical health domain,

our respondents achieved lower values in comparison with the populations standards, namely both groups (any BMI); in the experiencing (mental health) domain, both groups of respondents also achieved lower values. When comparing the values with the standard of patients before and after surgical treatment of obesity ( $n = 17$ ), our respondents with BMI  $\geq 25$  kg/m<sup>2</sup> achieved similar values as respondents before bariatric surgery (Dragomirecká and Bartoňová 2006, p. 40).

Among respondents of Bužgová *et al.* (2014), the quality of life according to the domain of social relationships was identical in patients with morbid obesity and in the population (the population standard) already before bariatric surgery. The environmental domain was significantly better in obese respondents (Bužgová, Buzga, Holeczy 2014). In the domain of social relationships, our respondents with BMI  $< 25$  kg/m<sup>2</sup> achieved higher values, but respondents with BMI  $\geq 25$  kg/m<sup>2</sup> achieved a lower score in comparison with the population standards. In the environmental domain, better values were achieved by all.

Toselli *et al.* (2020). monitored the quality of life of elderly Italians. In comparison with their findings, our respondents achieved higher values in the experiencing domain and the domain of social relationships, but in the physical health domain, all our respondents achieved lower values. In spite of the fact that Toselli *et al.* (2020) monitored a group of individuals aged 65 and older, and our respondents were aged between 18 and 65. In the environmental domain, our respondents with BMI  $< 25$  kg/m<sup>2</sup> achieved similar values as women, and our respondents with BMI  $\geq 25$  kg/m<sup>2</sup> achieved similar values as men of the study sample of Toselli *et al.* (2020).

Gholami *et al.* (2013) monitored the quality of life among health professionals. As far as the average age is concerned, their study sample was similar to our study sample (21 — 65 years, average age  $35.1 \pm 7.7$  years). In the physical health domain, medical professionals achieved higher values than our respondents ( $15.26 \pm 2.74$ ); in the experiencing domain, our respondent achieved higher values (medical professionals:  $13.68 \pm 2.64$ ); in the domain of social relationships, our respondents also achieved higher values (medical professionals:  $14.15 \pm 2.8$ ); and in the environmental domain, the values we obtained were also higher (medical professionals:  $13.09 \pm 2.37$ ) (Gholami *et al.* 2013).

Chang *et al.* (2010) monitored obese individuals, they divided the patients based on the BMI into groups 32 — 40 kg/m<sup>2</sup> and obese individuals with BMI  $> 40$  kg/m<sup>2</sup>. In addition to the subjects, a control group was also included. In the assessment of quality of life and health quality, healthy individuals with BMI  $< 25$  kg/m<sup>2</sup> achieved lower values than our respondents with identical BMI values. In the healthy group with higher BMI, the values were more similar to our values. In terms of the quality of life, our respondents with BMI  $\geq 25$  kg/m<sup>2</sup> achieved

a higher value than the control group with BMI 25 — 32 kg/m<sup>2</sup> monitored here. In terms of the health quality, the values are almost identical (our respondents with BMI  $\geq 25$  kg/m<sup>2</sup>:  $3.5 \pm 0.8$ , and the healthy control group:  $3.58 \pm 0.50$ ). In terms of the physical health, our respondents with any BMI achieved lower values than the healthy control group of the study conducted by Chang *et al.* (2010). In other domains, the group of respondents we monitored (with any BMI) achieved higher values than healthy subjects (control group of Chang *et al.* (2010) with BMI  $< 25$  kg/m<sup>2</sup>, but also with BMI 25 — 32 kg/m<sup>2</sup>). In comparison with respondents before bariatric surgery included in the same study, our respondents achieved again lower values in the physical health domain, and comparable values with respondents with BMI  $\geq 40$  kg/m<sup>2</sup> (in comparison with our respondents with BMI  $\geq 25$  kg/m<sup>2</sup>). In other domains, our respondents with any BMI achieved higher values; in the two separately assessed questions, the score achieved by our respondents was also higher.

## CONCLUSIONS

The resulting values of the quality of life differ between respondents with BMI  $< 25$  kg/m<sup>2</sup> and respondents with BMI  $\geq 25$  kg/m<sup>2</sup>. All the differences are statistically significant. It applies that with the increasing BMI, the achieved values are lower, i.e. the quality of life is decreasing. In all the assessed domains, as well as in the two separately assessed questions, respondents with BMI  $< 25$  kg/m<sup>2</sup> achieved higher values than the second group of respondents. It seems that in order to increase the quality of life, it is important to follow the recommendations regarding lifestyle and recommendations regarding body weight, etc., i.e. to maintain the adequate body weight.

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### Conflicts of interests

The authors declare no conflict of interests.

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