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Tonsillectomián átesett páciensek testösszetétel vizsgálata

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Body composition analysis of patients following tonsillectomy

PhD Thesis

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2. List of publications forming the basis of the thesis (indicating classification IF or D, Q)

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Effects of a Dietary Supplement Containing Collagen - L-Arginine - Hyaluronic Acid on General Health in Elderly Patients with Musculoskeletal Complaints, JOURNAL OF ORTHOPAEDICS AND SPORTS MEDICINE 6: 1 pp. 48-61., 14 p. (2024)

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Effects of branched-chain amino acids on changes in body composition during the recovery period following tonsillectomy

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Gut microbiome composition: link between sports performance and protein absorption?

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4. Maszlag, Annamária; Mayer, Lívია; **Fritz, Réka**; Fritz, Péter

A BCAA táplálkozás-élettani hatásai, szerepe a sporttáplálkozásban és a klinikumban.
[Nutritional effects of BCAA, their role in sports nutrition and clinical practice]

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Hungarian male water polo players' body composition can predict specific playing positions and highlight different nutritional needs for optimal sports performance

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3. Introduction

Tonsillectomy is one of the most common otolaryngological surgeries, and at the same time, it is also one of the most painful routine surgeries (Guntinas-Lichius et al, 2016).

In connection with the intervention affecting the beginning of the alimentary tract, a gentle diet is recommended until the wound is completely re-epithelized. In addition, due to the pain of swallowing, patients are also forced to change their eating habits (Erdélyi et al, 2020).

Physical activity and sports are also prohibited during this period.

There are several studies that examined the long-term changes in body weight after tonsillectomy (Rozycki et al, 2015), but there is no research in the international literature that followed the changes in the body composition of the patients in the early postoperative period until the complete removal of the scar.

Predictably, a changed diet and physical inactivity leads to measurable changes in body composition. As muscle loss can occur within 10 days in critical states, swallowing difficulties and inactivity following tonsillectomy may lead to muscle wasting (Puthuchearry et al, 2013).

Branched-chain amino acids (BCAAs) have a special role in sports nutrition, since, unlike other amino acids, the muscles can use them directly and the liver does not need to be involved (Maszlag et al, 2023). They can be used in the muscles as an energy source or for the formation of new muscle proteins.

BCAAs can be quickly digested by themselves, so they can also serve as a source of energy during physical activity. This allows them to spare muscle mass from burning energy, which contributes to the anti-catabolic effect of BCAAs.

There are countless studies in the literature that examine the use of BCAA in various types of surgery and diseases, which I will summarize in the theoretical background section.

However, there is currently no publication in the literature examining the effect of BCAA in relation to interventions affecting the pharynx.

I would like to fill these gaps with the results of my research.

In my PhD thesis, I present in detail, with a literary background, the concepts that the reader will encounter while reading the work.

Theoretical background

Tonsillectomy

Tonsillectomy is one of the most common otolaryngological surgical interventions, and at the same time it is also one of the most painful routine surgeries (Guntinas-Lichius et al, 2016).

Tonsillectomy as a type of surgery was first described by Celsus (25 BC - 50 AD), but even today, the technique of surgery is constantly changing and being refined in connection with the development of new cutting and coagulation devices (Erdélyi et al, 2020).

In the case of extracapsular, cold knife tonsillectomy, swallowing and pharyngeal pain will certainly persist for 14 days, and complete wound healing may take up to 21 days (Erdélyi E. et al, 2020).

Since 1988, reports have been published about weight gain after tonsillectomy. There is a limited number of publications available on whether tonsillectomy can lead to weight gain, and research has not established any cause-and-effect relationship (Wei JL, 2011).

In a research published in 2020, in which the body weight and BMI of children who underwent tonsillectomy were compared before the operation, at 1 and 6 months postoperatively, the result was that the body weight and BMI (Body Mass Index) result after half a year significantly increased compared to the first postoperative month (Abdullah et al, 2020).

According to a Korean study published in 2021, in which the changes in BMI and blood pressure values of tonsillectomy patients were followed for two years compared to a control group that did not undergo the procedure, it was confirmed that there was no difference in either the one-year or the two-year results between the study and control groups in terms of BMI.

It was concluded that tonsillectomy does not lead to long-term weight gain in the Korean population (Wee et al, 2021).

Based on a study conducted in the USA, an average body weight loss of 2.27 kg can be registered in adult patients after tonsillectomy in the postoperative period, after which the patients already reach their pre-operative body weight in about the 5th postoperative month (Stefan Rozycki, Eric M Gessler, 2015).

In summary, a limited number of studies have so far been published in connection with tonsillectomy as a surgical intervention, which monitored changes in body weight. The researches that did have this topic focused on long-term changes in body weight and BMI.

There is no research result in the literature that examines changes in body composition in the postoperative period following tonsillectomy.

BMI

To this day, the most common method for determining nutritional status is the BMI (Body Mass Index) (Caballero, 2019). The BMI was developed between 1830 and 1850 by Adolphe Quetelet. Although it does not indicate the actual body fat percentage, it can be useful to determine the ideal body weight in relation to height. Because it is easy to calculate, BMI is often used to assess obesity in the general population, but it has several shortcomings. In particular, it is unable to determine the distribution of body fat, which would play an important role in characterising the health risk associated with obesity. Furthermore, it does not provide information on the amount of body fat mass and is therefore of limited use for the diagnosis of obesity. Finally, it does not provide insight into the genetic, metabolic, physiological or psychological causes of obesity, nor does it provide insight into the diversity of the disease (Bray, 2023). According to researchers, the body mass index can be misleading in many cases and is of limited use as a professional indicator of health status and the extent of obesity (Bosello - Vanso, 2021).

Body mass index (BMI), which is based on the weight-to-height ratio, is common in medical literature but misleading as it does not differentiate between fats and muscles (Bray, 2023).

In athletes - with above-average lean muscle mass - the figure can be distorted and in unjustified cases indicate overweight. Quetelet already pointed out this correlation when he developed the formula. Since the 2010s, scientists have increasingly criticised the use of BMI (Nordqvist, 2022), but it is still the most commonly used measure of nutritional status in dietetic and clinical practise. Thus, an athlete with high muscle mass may have the same BMI as an individual with obesity of similar height and weight (Fritz R et al, 2023).

There are now more sophisticated methods of assessing the degree of obesity that are more accurate and complex than actual fitness status. These include bioelectrical impedance analysis (BIA), densitometry: hydrodensitometry, whole-body plethysmography, infrared transmission measurements and other medical diagnostic methods such as ultrasound, MR, CT or DEXA (Duren et al.) Some of these more modern methods are based on the principle of ionising radiation, such as DEXA and CT. These two methods also have a technical justification, as DEXA is the most modern method for measuring bone density. CT scans, like MR, are indispensable for the diagnosis of other pathologies and are subject to a waiting list, which makes their use for determining body composition superfluous. The most common instrument for measuring body composition in practice is the BIA. Compared to anthropometric methods, it provides a more accurate picture of body composition and has a lower measurement error. Unlike other medical diagnostic methods, BIA is available in a compact package and can be performed quickly and easily in terms of testing time, making it widely

applicable and offering the advantage of no radiation exposure. In the following, we will take a closer look at the BIA-based devices for measuring body composition InBody.

InBody

The InBody is a non-invasive, fast and accurate body composition analyzer that provides detailed information on body weight, muscle and fat mass and water content. The device sends alternating low and high frequency electrical currents through the body during the measurement, using the body's water content as a conductive medium. This is passed through electrodes in contact with the skin of the palms of the hands and soles of the feet to measure the impedance of the various tissues.

Advantaged over other BIA devices:

Most BIA devices only use a frequency of 50 kHz to measure impedance, which cannot fully penetrate the cells of the body. This makes it impossible to accurately measure the water inside and outside the cell as well as the total body water. This knowledge would be crucial for identifying fluid imbalances that may be associated with acute inflammation or edema. By using different frequencies of the InBody, the device can take much more accurate measurements. In addition, it divides the body into 5 units (right and left arm, torso, right and left leg), whereas other BIA-based devices usually treat it as a single unit. Thus, it provides a much more detailed segmentation of lean body mass and body fat mass by limb (Fritz R. et al, 2024).

Factors for a correct measurement:

The accuracy of the measurement can be affected by a number of factors (temperature, food and fluid intake, exercise, body position, pregnancy, etc.), but the potential for error can be minimised by following certain rules. The manufacturer recommends performing the tests under identical conditions (e.g. the day before the test, make sure you drink enough fluids (avoid alcohol and coffee), and on the day of the test you should consume a maximum of 4.5-5 dl of water 45 minutes before the test, and it is recommended to eat 2-3 hours before the test. Heavy clothing, jewellery and large objects stored in pockets should be removed before the test. It is important that the bare soles of the feet and palms of the hands are in contact with the metal electrodes as much as possible. Conductivity can be improved by using wet wipes, but can also be affected by using various hand creams. It is recommended to wash immediately before application and to adopt a standing position for at least 5 minutes to ensure an even distribution of the liquid fields. However, bathing, sauna bathing and exercise within 3 hours of each other reduce the accuracy of the results. Contraindications for performing the test are wearing implanted heart rate regulators and the absence of limbs.

The InBody result:

These include body weight, muscle and fat mass (and their breakdown at the endothelial level), body fat percentage, visceral fat, water spaces, mineral content, resting basal metabolic rate, estimated calorie requirements and phase angle. The most important parameters of the previous measurements are displayed in a line graph so that changes in body composition can be easily tracked. In addition, the tool's database provides you with a wide range of other data, results and their various interpretations. For an even more detailed analysis, software (LookInBody) is available that provides more detailed data on the entire measurement and transmits the summarised results electronically to the attending physician, the client or other persons involved in the treatment or lifestyle programme after the measurement.

Use of body composition measurement in clinical practice:

Measuring body composition is an important element of dietetic work. On the one hand, it provides a starting point for the beginning of a nutritional intervention and, on the other, it enables more precise tracking during the process. It can also be used in many other areas of healthcare to complement and support various therapies, e.g. oncology, nephrology, diabetology, cardiology, perioperative care, bariatric surgery, occupational medicine, rehabilitation, physiotherapy, lifestyle medicine, etc. Japanese researchers have published several studies on changes in body composition. These have due to its multiple frequencies and is an excellent method for estimating total body composition (Antonio et al. 2019). In a study published in the British Journal of Nutrition 2022, the accuracy of the DSM-BIA (InBody 770) was compared to other methods of measuring body composition (DEXA, ADP, BIS) in 110 participants of different races and ethnic backgrounds. The study found that, in addition to DEXA and ADP, the InBody device measured “excellent to ideal” percent body fat and “ideal” fat-free mass relative to criterion. The devices have the potential to provide valid body composition results for different population groups (Blue et al. 2022).

BCAA

Due to the growing popularity of BCAA (Branch Chain Amino Acid), it is an increasingly widely researched dietary supplement. Its physiological effects are being researched in various diseases and medical conditions at various doses, so it is challenging to provide a comprehensive picture of its mechanism of action. In the field of sports, its effect supporting the growth of performance and muscle mass was observed, while in the clinic it positively influenced the course and outcome of

certain diseases. Depending on the state of health and individual goals, even a daily supplement of 1-60 g can be effective.

So far, there is no publication in the literature examining the effect of BCAA in relation to interventions affecting the pharynx.

BCAA (Branch Chain Amino Acid) is the abbreviation and name of a group of three branched chain amino acids. Amino acids are organic compounds that contain both an amino group (-NH₂) and a carboxyl group (-COOH) and are connected by peptide bonds (Mayer et al, 2023). They can be found in the body in both free and bound form (Kamei et al. 2020). As the building blocks of proteins, amino acids influence their characteristic properties and functions. We count a total of 20 types of protein-building amino acids, of which 9 are considered essential. This means that the body cannot produce them, so it is of utmost importance to replace them with food or, if necessary, with dietary supplements. The remaining 11 are non-essential, i.e. the human body is capable of synthesizing them (Santos – Nascimento, 2019).

BCAA is the common name for leucine, isoleucine and valine ASs, all of which are essential. Their structure is characterized by the fact that they contain a branched side chain consisting of one carbon and three hydrogen atoms (Plotkin et al, 2021). BCAAs make up 50% of the essential amino acids that make up muscle tissue (Santos – Nascimento, 2019).

Skeletal muscle, which is the largest organ of the human body and accounts for ~40% of total body weight, plays an important role in exercise, energy and glucose/amino acid utilization – processes regulated by different amino acids and their metabolites (Kamei et 2020). The most suitable for their dietary intake is the consumption of products of animal origin, such as meat, meat products, fish, milk, dairy products and eggs (Fritz et al. 2017).

Metabolism of the BCAAs

Unlike most amino acids, the initial step of BCAA catabolism does not take place in the liver, but in the skeletal muscle, because the concentration of BCAA aminotransferase, the enzyme responsible for the initial step of BCAA breakdown, is high in skeletal muscle, while it is low in the liver. For this reason, after protein intake, BCAA levels increase rapidly in the systemic circulation and are readily available to extrahepatic tissues. This phenomenon gives BCAA-based dietary supplement formulas a unique advantage over other products, especially those targeting the brain and muscles. As the last step of metabolism in skeletal muscle, they can be used as an energy source or for the formation of new muscle proteins. BCAAs have a stimulating effect on protein synthesis (Holeček, 2018). To increase muscle mass, the rate of muscle protein synthesis must exceed the rate of

breakdown. Myofibrillar muscle protein synthesis can be enhanced both by the intake of essential amino acids and by resistance training through the activation of the rapamycin complex-1 (mTORC1) signaling pathway (Jackman et al. 2017). Furthermore, they have an inhibitory effect on proteolysis, i.e. the hydrolysis of the peptide bonds holding proteins together. Since the latter process could result in the breakdown of proteins into their key components, peptides and amino acids, the role of BCAAs in maintaining muscle is known (Holeček, 2018). However, research investigating the effectiveness of isolated BCAA intake on human muscle hypertrophy does not always show the same results (Santos – Nascimento, 2019).

Areas of use of the BCAAs:

1. Sport

Source of Energy: BCAAs can be digested quickly, so they can serve as an energy source during physical activity. They are able to prevent the burning of muscle mass for energy. This results in the anti-catabolic effect of BCAAs (Holeček, 2018).

Performance Matsumoto et al investigated the effect of BCAA supplementation on lactate threshold. Although the number of cases was very low (n=8), the results suggest that BCAA supplementation can effectively increase endurance training capacity (Matsumoto et al. 2009). In accordance with this, in the research of Manaf et al., acute BCAA supplementation significantly improved performance in cycling time trials among recreational athletes compared to the placebo group (Manaf et al. 2021). Serotonin also plays a major role in fatigue during exercise. BCAA supplementation is believed to reduce serotonin production, thereby contributing to athletic performance (Holeček, 2018). Thus, it can be particularly useful for endurance athletes. During a 40-week research on elderly people, BCAA supplementation was also used in addition to a multi-component exercise program. Based on the results, BCAA supplementation alone had no effect on functional fitness, but within a short period of time (16 weeks) it contributed to the reduction of weakness and may reduce the negative impact of the non-training period on functional capacity (Caldo-Silva et al. 2021).

2. Muscle damage and regeneration

According to current evidence-based information, it can be one of the most important dietary supplements in sports circles. The use of BCAA is more effective than passive recovery or rest after strenuous exercise, as it alleviates post-exercise muscle soreness and improves muscle function (Rahimi et al. 2017). A 2011 double-blind, randomized cross-sectional study investigated the effects of BCAAs in athletes. As a result of the supplement, the individuals receiving the supplement tired later compared to the members of the control group, and BCAA promoted the oxidation of fatty acids

when the amount of muscle glycogen had already decreased (Gualano et al. 2011). Kim et al investigated the effect of BCAA administration on parameters indicating fatigue (serotonin, ammonia and lactate), causing muscle damage (CK and LDH) and energy metabolism (free fatty acid and glucose) after endurance exercise in 26 fatal adult men. Their results show that BCAA supplementation reduced serum concentrations of intramuscular enzymes such as CK and LDH. This observation suggests that BCAAs may reduce muscle damage caused by endurance exercise (Kim et al. 2013). The timing of BCAA supplementation has also been investigated in relation to muscle soreness and muscle damage. The supplementation took place at 3 times (before training, after training, placebo), of which supplementation before training resulted in the greatest improvement in delayed-onset muscle soreness (DOMS), upper arm circumference, and elbow range of motion. Furthermore, the level of parameters indicating muscle damage (CK, LDH, aldolase) significantly decreased compared to the control group (Ra et al. 2018).

Based on research by Sharp and Pearson, serum testosterone levels were significantly higher, while cortisol and creatine kinase levels were significantly lower in the BCAA group during and after resistance training. These results suggest that short-term amino acid supplementation with high BCAA content may result in a net anabolic hormone profile while mitigating increases in exercise-induced muscle tissue damage (Sharp-Pearson, 2010). Based on a review by Pourgharib Shahi et al., BCAA supplementation can reduce the body's cortisol concentration and improve muscle function 2 hours after exercise, thereby contributing to better regeneration (Pourgharib Shahi et al. 2022). In a 2021 systematic review by Weber et al., they investigated the effect of BCAA supplementation on exercise-induced muscle damage (EIMD) and delayed-onset muscle soreness (DOMS). BCAA has proven to be useful in promoting muscle regeneration even after a workout, reducing the degree of DOMS, therefore its supplementation is recommended not only after the EIMD protocol (Weber et al. 2021). On the other hand, in some researches examining long-term endurance athletes, it was not possible to prove the positive effects of BCAA supplementation. Areces et al. tested BCAA supplementation against an isocaloric placebo in 49 marathon runners. BCAA supplementation of 5g/day for one week did not improve marathon running performance, nor was it more effective in protecting muscles or preventing muscle damage and muscle soreness, compared to the control group (Areces et al. 2014). Knechtle et al concluded that 20g BCAA supplementation before and during a 100 km ultramarathon had no effect on performance, skeletal muscle damage and renal function compared to a control group (Knechtle et al. 2012). And Bigard et al found that BCAA supplementation was ineffective compared to carbohydrate supplementation during six consecutive (6-8 hour, 2500-4000m ascent) tours of 24 highly trained ski mountaineers. BCAA did not significantly affect changes in body composition or muscle performance during isometric contraction

(Bigard et al. 1996). Body weight control BCAAs can support the preservation of muscle mass in caloric deficit through the glucose-alanine cycle (aka Cahill cycle) (Holeček, 2018). In the research conducted by Dudgeon et al. in 2016, they examined the effect of BCAA (2x14g, or carbohydrate placebo) supplementation in addition to a calorie-reduced diet and resistance training, administered before and after training. A greater loss of body weight and dry muscle mass was measured in the carbohydrate group, while in the group receiving BCAA supplementation there was no change in the amount of muscle mass, and a greater decrease in body fat was measured. At the same time, the increase in muscle strength measured in both the upper and lower body was greater (Dudgeon - Kelley - Scheett, 2016).

Another randomized controlled trial conducted in 2018 was conducted with the participation of 42 overweight and obese women. Based on the results, dietary supplementation with 6 g of BCAA and 40 mg of vitamin B6 per day helped preserve the dry muscle mass of the lower limbs with a calorie-reduced diet, and reduced the waist-to-hip ratio (Novin - Ghavamzadeh - Mehdizadeh, 2018).

3. Insulin sensitivity:

In athletes, regular exercise increases the efficiency of BCAA oxidation in the mitochondria, thus improving insulin sensitivity. On the other hand, 2 studies report on the effect of BCAA increasing insulin resistance. The background of this phenomenon may be the activating effect of the BCAA mTORC1 protein complex, as well as the accumulation of intermediate products resulting from the insufficient breakdown of BCAA. All this was mostly observed in the absence of exercise or among obese people (Yoon, 2016).

4. Use of BCAA in clinical practice:

Immune system:

It can be useful in supporting the immune system, as in a study by Bassit et al., BCAA supplementation (2x6 g before training, 3 g before competition, 3 g in the morning for 1 week after testing) reversed the decrease in serum glutamine concentration observed after long-term, intense training among triathletes. As a result, their bodies were more resistant to infections and the symptoms of diseases appeared with a lower incidence (33.84%) (Bassit et al. 2000).

There are countless studies in the literature that examine the use of BCAA in different types of surgery and diseases. Since it reduces or prevents the degradation of muscle tissue, it can be seen as one of the nutritional foundations of surgical preparation for cancer (Choudry HA et al., 2006).

Cardiovascular system:

Hotta et al. concluded that whey peptides and BCAA supplementation could be a useful treatment for patients with chronic heart failure, as it increased physical performance (Hotta et al. 2021). However, in any case, its introduction into the diet requires careful consideration, as the body's BCAA metabolism may differ from individual to individual. In some cases, it can even negatively affect the outcome of the disease (Narita – Amiya, 2021).

Liver diseases:

BCAAs enter the brain via the same carrier as AAAs (aromatic amino acids: phenylalanine, tyrosine, tryptophan). The competition between BCAAs and AAAs can affect the synthesis of some neurotransmitters (dopamine, norepinephrine, serotonin). This phenomenon justifies the use of BCAAs in patients with liver cirrhosis, where a decrease in the ratio of BCAAs to AAAs plays a role in the pathogenesis of hepatic encephalopathy (Holeček, 2018).

Based on several studies, we can conclude that the prophylactic use of BCAA seems to be safe (side effects cannot be confirmed) and can improve the survival chances of liver cirrhosis patients, as well as be useful in minimizing or reversing catabolic processes. However, these phenomena still require further research (van Dijk et al. 2023) (Maddrey, 1985). In addition, it also produced positive results for hepatocellular carcinoma patients, as a large percentage (80-90%) of them had a cirrhotic state (Lo et al. 2022). BCAA-enriched oral supplementation improved the morbidity and quality of life of patients undergoing severe liver resection and chemoembolization, and had a positive effect on muscle wasting.

BCAA supplementation significantly improves disease prognostic factors in patients with cirrhosis and has a potentially positive effect on mortality (Konstantis, G et al. 2022).

Gastric resection:

Multidisciplinary approaches play a key role in the surgical management of elderly patients. Postoperative exercise and nutritional therapy with BCAA-rich nutritional supplements may benefit elderly patients after gastrectomy by reducing muscle loss and quality of life impairment (Nishida Y et al. 2023).

BCAA-enriched parenteral nutrition significantly improved the loss of muscle mass in gastric resection patients starting from the early postoperative period (Sakuraya M et al. 2023).

Sepsis:

Based on the review by De Bandt and Cynober, BCAA supplementation improved the nutritional status of the subjects and the outcome of their disease in septic patients in two prospective, controlled

studies (De Band et al, 2006). Chronic renal failure In dialysis patients, oral BCAA supplementation improved appetite and nutritional status. BCAA and BCKA (branched chain keto acids) supplements have been used to reduce additional dietary protein intake while maintaining adequate nutritional status. In this situation, BCAAs and BCKAs were not used alone, but in combination with other essential AS or keto analogues, so the corresponding effect of BCAAs and/or BCKAs was not investigated separately. Protein restriction together with ketoacids and/or essential AS improved insulin sensitivity and hyperparathyroidism and supported maintenance of nutritional status (Cano–Fouque–Leverve, 2006).

It is also suitable for reducing the development of isomatrophy and preventing the development of a septic condition (Hou YC et al 2023).

Milan Holeček reached a similar result based on research conducted on mice. According to his claim, BCAA supplementation may be necessary in addition to a low-protein diet, for example in patients with chronic kidney failure or urea cycle disorders (Holeček, 2018).

Tumor prevention:

Mikalayeva and her colleagues investigated the effect of BCAA supplementation on tumor cells. During the research, they found a cell type in whose proliferation the breakdown of BCAA can be an important source of energy and carbon. However, cancer cell types can be very different from a metabolic point of view, therefore the therapeutic targeting of BCAA raises an interesting opportunity to reduce tumor growth and may be an important area of research in the future (Mikalayeva et al. 2021). Mental functions Based on the study by Elliott et al., dietary supplementation with 30 g of BCAA twice a day seemed to be effective in the treatment of insomnia and objective sleep disorders in veterans with traumatic brain injury. In the future, it may be a promising intervention alternative in the treatment of the aforementioned conditions (Elliott et al. 2022).

4. Purposes

We examine the body composition of patients who underwent tonsillectomy as a planned operation, determined by bioimpedance-based measurements immediately before surgery and on the 7th and 21st days of the postoperative period.

Also, on the 7th and 21st days of the postoperative period, blood count, liver and kidney function parameters, blood fat level (cholesterol: HDL-LDL, Triglyceride), total protein, albumin, Na, Ca, K, and Mg are determined.

In order to eliminate or similarly reduce the loss of muscle mass assumed due to the physical care to be maintained in the first 3 weeks postoperatively and eating habits due to post-operative

pharyngeal pain and pain, BCAA (Branch Chained Amino Acids) administration was administered in a control group with a composition study group.

Based on our results, future targeted dietary recommendations can be prepared for patients preparing for a similar intervention, in order to avoid or reduce negative test composition changes.

Primary purpose:

- Examining what differences can be registered in the body composition after the surgical intervention compared to the pre-operative state.
- Is there a statistically verifiable difference in the parameters tested at the time of blood sampling compared to the pre-operative state on the 7th and 21st postoperative day.

Secondary purpose:

- Any correlation or difference in body composition attributable to the BCAA used by the study group can be detected.

Hypothesis:

- **H₀**: A loss of muscle mass can be verified during measurements in the postoperative period.
- **H₁**: Significant fat loss cannot be verified during measurements in the postoperative period.
- **H₂**: In the case of the study group, the loss of muscle mass will be less significant.

5. Materials and methods

This prospective interventional controlled study, which was conducted from September to December 2023, at the Ear-Nose-Throat and head and Neck Surgery Department of University of Szeged, included 48 participants and adhered to ethical guidelines. This study was approved by the Regional and Institutional Committee of Science and Research Ethics and the Hungarian Medical Research Council (OGYÉI/56432-2/2023) and registered on Clinical Trials (NCT06247436). Participants included those aged 20–40 years who were scheduled for tonsillectomy. Those with metabolic or bleeding disorders were excluded.

Involvement in the research took place exclusively through voluntary participation, the selected person received detailed information about the research both in writing and orally, after which she/he could decide on her participation, which she/he certified with a declaration of consent.

All participants underwent **extracapsular tonsillectomy using the “cold knife” technique**, which involves dissecting the tonsil and its capsule from the surrounding tissues using Cooper scissors, rasp, bipolar forceps, and bindings, if necessary. The inferior pole of the tonsil is removed using a snare (Erdélyi et al, 2020).

Body composition measurements and blood tests were performed three times: preoperatively, on day 7, and on day 21 postoperatively. The wound is completely re-epithelialized at the latest 3 weeks postoperatively; therefore, the second check-up is frequently scheduled between the 14th and 21st postoperative day. We opted for the last data collection on day 21.

The following were the elements of the blood test: total cholesterol, high-density lipoprotein, low-density lipoprotein, gamma-glutamyl transferase, glutamic oxaloacetic transaminase, glutamate pyruvate transaminase, triglyceride, carbamide, creatinine, estimated glomerular filtration rate, albumin, sodium, potassium, magnesium, and calcium.

Body composition was analyzed using the InBody 270 (InBody Co., Ltd., South Korea) device, which operates on the principle of bioimpedance and is a noninvasive, fast, and accurate body composition analyzer that provides detailed information on body weight, muscle, fat mass, and water content. During the measurement, the device sends alternating low- and high-frequency electrical currents throughout the body, using the body’s water content as a conductive medium. These electrical currents are passed through electrodes in contact with the skin of the palms of the hands and soles of the feet to measure the impedance of various tissues (Fritz R et al, 2023).

The following were the parameters measured: weight (kg), total body water (L), body fat mass (kg), skeletal muscle mass (kg), percent body fat (%), visceral fat level, mineral mass (kg), bone mineral content (kg), protein mass (kg), basal metabolic rate (kcal), and total fitness (InBody Score). The device stores patient measurements for tracking changes over time.

Postoperatively, the study group took 2×4 g of BCAA powder daily. The BCAA product contained leucine, isoleucine, and valine in a ratio of 2:1:1.

Physical activity habits were recorded, and patients were divided into subgroups on the basis of whether they exercised at least three times a week.

In accordance with our preliminary plans, 48 people participated in the study.

There were 24 people in the control group (average age: 28.5 years \pm 6.46, initial weight: 74.0 kg \pm 17.43), and 24 people in the study group (average age: 27.8 years \pm 6.65, initial weight: 73.6 kg \pm 13.56) was randomly selected.

There were 16 women in the control group (average age: 29.6 \pm 6.28, initial weight 64.2 \pm 10.53). Among them, 12 were non-athletes (average age: 30.7 \pm 6.11, initial weight: 65.1 \pm 11.44), 4 athletes (average age: 26.5 \pm 6.56, average age: 61 .8 \pm 7.99) was.

There were 8 men in the control group (average age: 26.3 \pm 6.63, initial weight 93.6 \pm 10.16). Among them, 2 non-athletes (average age: 32.5 \pm 6.36, initial weight: 93.2 \pm 9.12), 6 athletes (average age: 24.2 \pm 5.71, initial weight: 93.8 \pm 11.30).

There were 13 women in the study group (average age: 30.8 \pm 5.94, initial weight 65.0 \pm 8.06). Among them, 11 were non-athletes (average age: 31.8 \pm 5.93, initial weight: 67.0 \pm 6.93), 2 athletes (average age: 25.5 \pm 2.12, initial weight: 54.1 \pm 4.17).

There were 11 men in the study group (average age: 24.2 \pm 5.72, initial weight 83.7 \pm 11.69). Among them, 4 were non-athletes (average age: 23.5 \pm 1.00, initial weight: 81.7 \pm 16.31), 7 athletes (average age: 24.6 \pm 7.32, initial weight: 84.8 \pm 9.51).

Table 1 Characteristics of participants in the study

		Control			Experimental			Total		
		Inactive	Active	Total	Inactive	Active	Total	Inactive	Active	Total
N	Female	12	4	16	11	2	13	23	6	29
	Male	2	6	8	4	7	11	6	13	19
	Total	14	10	24	15	9	24	29	19	48
average age	Female	30,7	26,5	29,6	31,8	25,5	30,8	31,2	26,2	30,2
	Male	32,5	24,2	26,3	23,5	24,6	24,2	26,5	24,4	25,1
	Total	30,9	25,1	28,5	29,6	24,8	27,8	30,2	24,9	28,1
SD	Female	6,11	6,56	6,28	5,93	2,12	5,94	5,92	5,19	6,05
	Male	6,36	5,71	6,63	1	7,32	5,72	5,5	6,36	6,03
	Total	5,93	5,82	6,46	6,31	6,4	6,65	6,06	5,93	6,49
average weight	Female	65,1	61,8	64,2	67	54,1	65	66	59,2	64,6
	Male	93,2	93,8	93,6	81,7	84,8	83,7	85,5	89	87,9
	Total	69,1	81	74	70,9	78	73,6	70	79,6	73,8
SD	Female	11,44	7,99	10,53	6,93	4,17	8,06	9,39	7,6	9,35
	Male	9,12	11,3	10,16	16,31	9,51	11,69	14,54	10,95	11,89
	Total	14,87	19,1	17,43	11,69	15,94	13,56	13,11	17,25	15,45

where C is control group and E is experimental group; I is inactive and A is active. F is for female and M for men.

Statistical methods

Two- and three-variate analysis of variance (ANOVA) was used to examine the correlations between the results of the three time points and the grouping variables (test/control and active/inactive), univariate and repeated ANOVA to determine the simple main effect, and the Chi-square test to examine the deviation of the individual laboratory results from the reference range.

The prerequisites for the tests were examined using the following tests: the Shapiro–Wilk test for normality, the boxplot test for examining extreme values, Levene’s test for testing the equality of standard deviations, Mauchly’s test for testing the equality of variances (sphericity), Greenhouse–Geisser correction when the sphericity was damaged, partial η^2 (eta) for measuring the effects of relationships that were significant following ANOVA, and Cramer’s V coefficient for measuring the effects of significant relationships following the Chi-square test.

All statistical analyses were performed using Statistical Package for the Social Sciences (version 25, IBM, Armonk, NY, USA).

- partial η^2 (eta) for measuring the effects of relationships:

<u>effect</u>	<u>parctial η^2</u>
light	<0,01
medium	0,01-0,06
strong	>0,06

Table.2

- and Cramer’s V coefficient for measuring the effects of significant relationships following the Chi-square test

<u>effect</u>	<u>Cramer’s V</u>
light	<0,2
medium	0,2 - 0,6
strong	>0,6

Table 3.

Data protection: according to SZTE GDPR regulations. The rules for managing and accessing the participant's data. In the research, the data of the participants was treated confidentially throughout,

in accordance with the relevant legislation (Data Protection Act CXII of 2011 on the right to informational self-determination and freedom of information; Act XLVII of 1997 on the management and protection of health and related personal data).

After signing the consent form, each volunteer participant filled out a data sheet in the evening. Each participant was provided with a unique code, the data processed during the examination were always shown in code on the data sheet, the patient's identity cannot be established from them.

6. Results

Table 4. Results of two-way repeated-measures analysis of variance for three time points (the day of surgery, a week after surgery, and two weeks after surgery), and groups (control and experimental) and activity (physically active and physically inactive).

		F	df	df (Error (time))	p	η^2
Body Weight	Time \times Groups	1.049	2	88	0.355	0.023
	Time \times Groups \times Activity	0.646	2	88	<0,0005	0.429
BMI	Time \times Groups	0.576	1.985	87.33	0.563	0.013
	Time \times Groups \times Activity	0.199	1.985	88	<0,0005	0.276
SMM/Body Weight ratio	Time \times Groups	41.795	2	88	<0,0005	0.487
	Time \times Groups \times Activity	9.672	2	88	0.001	0.156
BFM/Body weight ratio	Time \times Groups	16.782	2	88	<0,0005	0.276
	Time \times Groups \times Activity	0.997	2	88	<0,0005	0.186
Visceral Fat level	Time \times Groups	8.434	1.966	86.523	<0,0005	0.161
	Time \times Groups \times Activity	8.135	1.966	85.017	<0,0005	0.416
Total Body water/Body weight ratio	Time \times Groups	8.133	2	88	0.001	0.156
	Time \times Groups \times Activity	1.547	2	0	0.526	0.014
InBody Score	Time \times Groups	31.32	1.932	85.017	<0,0005	0.416
	Time \times Groups \times Activity	1.952	1.932	88	<0,0005	0.487

Table 4. Results of two-way repeated-measures ANOVA for the three time points (the day of surgery, 1 week postoperatively, and 2 weeks postoperatively), and groups (control and experimental) and activity (physically active and inactive). The table reports results of the two-way ANOVA, including F-values, degrees of freedom (df), error degrees of freedom (df Error), p-values, and partial eta squared (η^2), to evaluate the main and interaction effects of the independent variables on the dependent variable, along with their statistical significance and effect sizes.

A two-variable ANOVA was performed to understand the effects of BCAA on the different elements of body composition postoperatively. Furthermore, a three-variable ANOVA was performed to determine the potential influence of exercise habits.

We examined the conditions for the tests. Body composition data, except for SMM and TBW, were normally distributed ($p > 0.05$) according to the Shapiro–Wilk test. Moreover, examining the boxplots showed no extreme values in the data. Homogeneity of standard deviations (by group) existed for all body composition items and time points, with the exception of one case (InBody Score at time point 2), as determined by Levene’s test for the equality of standard deviations. The equality of variances (sphericity) was performed using Mauchly’s sphericity test. The Greenhouse–Geisser correction was used in the interaction analysis when the equality of variances was violated.

We presented the results of the seven body composition elements on the basis of the prerequisite test. For the body composition results, we presented the interaction of the results of the test and control groups measured at three time points, and when a significant three-way relationship with exercise habits was demonstrated, their results were also presented.

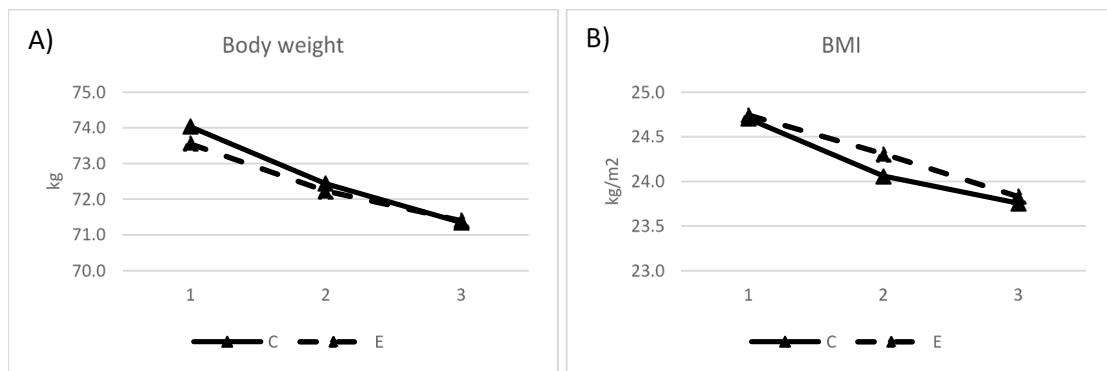


Figure 1 Comparison of changes in Body weight (A) and BMI (B) of control (C) and experimental (E) groups

The mean body weight continuously decreased in both groups and less in the study group; however, no significant ($p = 0.341$) interaction was noted between the changes in body weight of patients who took supplements and those who did not.

Regarding BMI, no significant interaction ($p = 0.565$) was observed between the two groups and the values measured at the three time points.

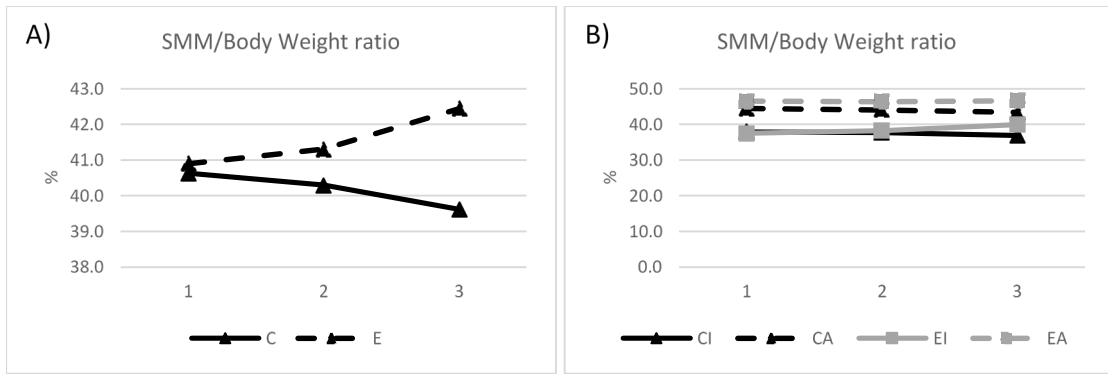


Figure 2. Comparison of changes in SMM/Body weight ratio (A) of control (C) and experimental (E) groups and (B) Control, Inactive (CI), Control, Active (CA), Experimental, Inactive (EI) and Experimental, Active (EA) groups

A significant and strong two-way interaction was demonstrated between the two groups in terms of the muscle mass-to-body weight ratio ($F [1.458, 64.164] = 41.795, p < 0.0005, \text{partial } \eta^2 = 0.487$). A continuous increase in the ratio of muscle mass to body weight was observed in the patients of the study group, whereas those in the control group exhibited a continuous decrease. A significant and strong interaction was noted between the changes in the muscle mass-to-body weight ratio, dietary supplement consumption, and exercise habits ($F [1.458, 64.164] = 9.672, p = 0.001, \text{partial } \eta^2 = 0.180$). In the study group, a significant increase was observed in the inactives, stagnation in the actives in the study group, and a decrease in both inactives and actives in the control group.

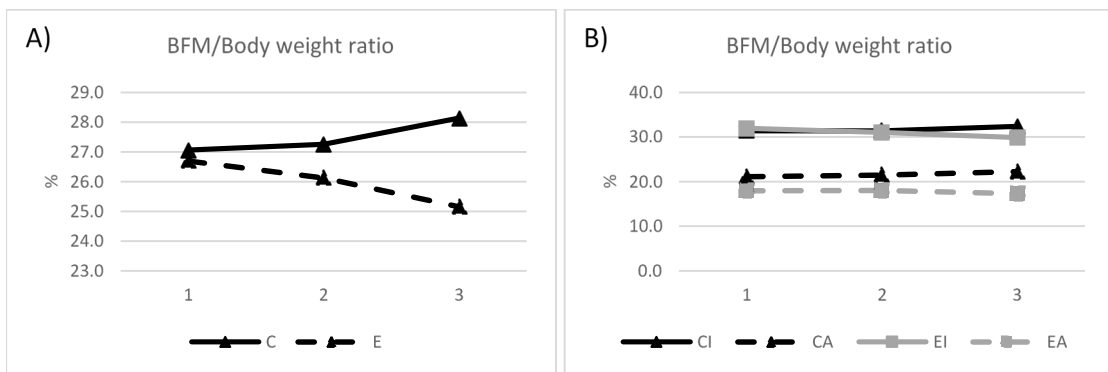


Figure 3 Comparison of changes in BFM/Body weight ratio (A) of control (C) and experimental (E) groups and (B) Control, Inactive (CI), Control, Active (CA), Experimental, Inactive (EI) and Experimental, Active (EA) groups

A significant and strong two-way interaction was demonstrated between the changes in the body fat-to-body weight ratio over time and dietary supplement consumption ($F [1.461, 64.272] = 16.782, p < 0.0005, \text{partial } \eta^2 = 0.276$). The percentage of body fat significantly decreased in the study group, whereas it significantly increased in the control group. The influencing factor for exercise could not be detected using the three-variable ANOVA ($p = 0.352$). In the study group, both actives and inactives lost weight, whereas the body fat percentage increased in both cases in the control group.

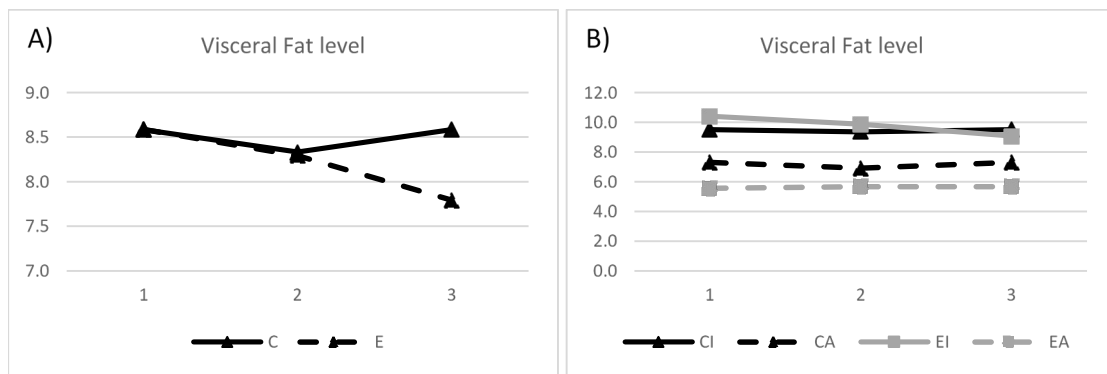


Figure 4 Comparison of changes in Visceral Fat level (A) of control (C) and experimental (E) groups and (B) Control, Inactive (CI), Control, Active (CA), Experimental, Inactive (EI) and Experimental, Active (EA) groups

A two- and three-way significant interaction was noted between the measured value, dietary supplement, and effects of sport in terms of the visceral fat level. The two-sided correlation was significant, and the degree of interaction was high ($F = [2, 88] = 8.434, p < 0.0005, \text{partial } \eta^2 = 0.161$). The visceral fat level decreased in both groups at the second examination time point; however, it decreased further at the third examination time point. Additionally, an increasing rate was noted among the participants in the study group, whereas the direction of change was reversed among those in the control group, and it increased to a level above the initial value.

The three-way significant relationship was also strong. ($F(2, 88) = 8.135, p=0.001, \text{partial } \eta^2 = 0.156$). In this case, the actives in the study group were stagnated, the inactives in the study group continued to decrease, and both actives and inactives in the control group initially experienced a decrease and a subsequent increase to the original value.

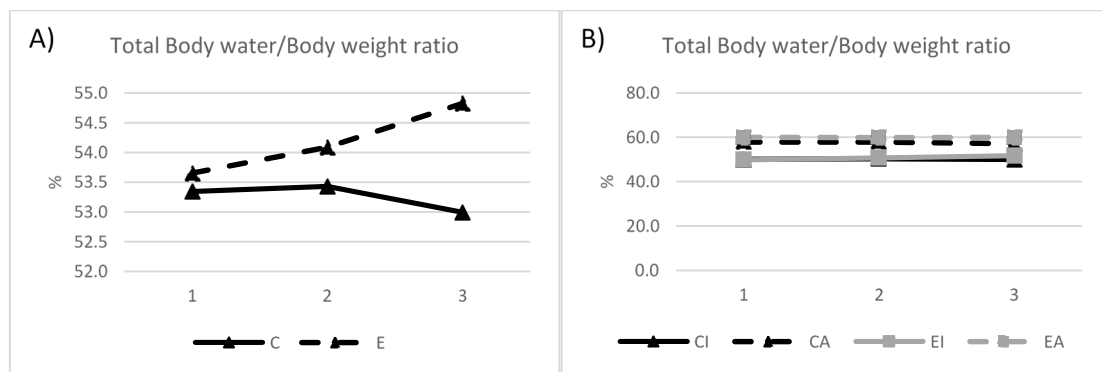


Figure 5 Comparison of changes in Total Body water/Body weight ratio (A) of control (C) and experimental (E) groups and (B) Control, Inactive (CI), Control, Active (CA), Experimental, Inactive (EI) and Experimental, Active (EA) groups

The interaction between the body water-to-body weight ratio and dietary supplement consumption was strong and significant ($F = [1.501, 66.061] = 8.133, p = 0.002, \text{partial } \eta^2 = 0.156$). The percentage of body water increased in those who consumed BCAA, whereas an average increase of 0.1% was observed in the control group at the first time point, followed by a decrease. Exercise had no effect (the three-way interaction was not significant, $p = 0.222$). Regardless of the sporting lifestyle, the body water percentage value increased in the participants in the study group, whereas it decreased in those in the control group.

The InBody Score reflects a general assessment of the body composition. Using this score, a significant two-way interaction was observed in relation to dietary supplement consumption ($F = [2, 88] = 31.320, p < 0.0005, \text{partial } \eta^2 = 0.416$). At the second measurement time point, the value decreased in both groups; however, at the third time point, the measured value of the control group continued to decrease, whereas it increased above the original value in the study group. No significant three-way interaction was observed ($p = 0.148$). However, among the actives in the study group, the value increased following the initial decrease, whereas among the inactives, a continuous increase was noted. In both cases, a continuous decrease was observed in the control group.

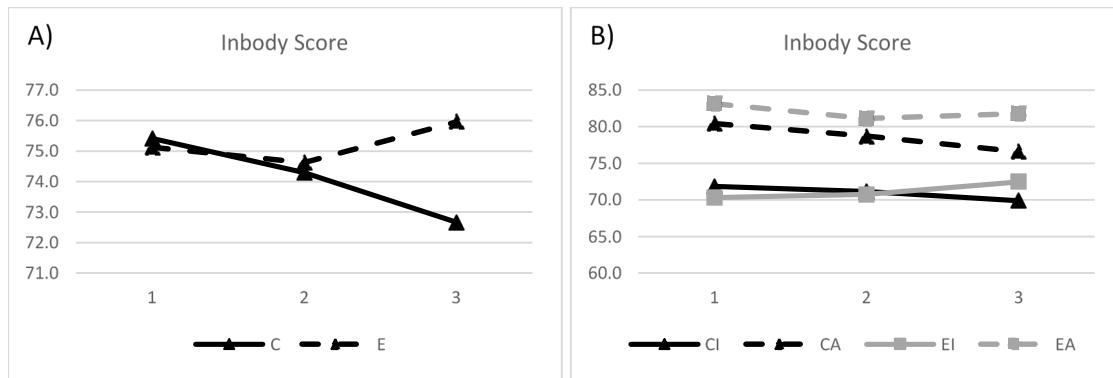


Figure 6 Comparison of changes in InBody score (A) of control (C) and experimental (E) groups and (B) Control, Inactive (CI), Control, Active (CA), Experimental, Inactive (EI) and Experimental, Active (EA) groups

Regarding body composition test results wherein a significant two-way interaction was noted, we also examined the simple main effects to understand the extent and direction of the individual factors (control/test and time) influencing the dependent variable, independent of the other factor.

No significant main effects were observed between the control and study groups in any case (for any of the body composition indicators and for any of the time points); however, a significant change over time was noted in all cases.

Regarding laboratory results, the deviation from the reference range was measured using the Chi-square test, whereas the strength of the relationship was measured using Cramer's V coefficient.

Regarding blood test results, significant changes in the examined elements were not noted. Neither dietary supplement consumption nor the grouping based on lifestyle activity revealed any differences between the groups.

7. Discussion

This study aimed to evaluate the changes in body composition in adult patients in the recovery period following tonsillectomy.

Analyzing body composition instead of relying on BMI and body weight, which have been the most commonly used methods for nutritional status assessment, is a novel concept. Individuals with the same age, height, and weight (therefore, the same BMI [kg/m²]) can have different body shapes, body composition, energy requirements, and metabolic profiles (Lemos et al, 2017).

Regarding tonsillectomy, and pharyngeal surgeries in general, there are no published studies in the literature that focus on body composition.

The muscle is the body's primary glycogen store; during critical periods such as the recovery period following tonsillectomy, energy is primarily sourced from muscles rather than fats (Shiose et al, 2022).

In this prospective interventional controlled study, we introduced the use of BCAA to our study group to prevent muscle mass degradation. This approach ensured that the energy requirement was met by utilizing fat, thereby preserving muscle mass.

BCAAs including leucine, isoleucine, and valine are unique in sports nutrition as muscles can directly use them without liver involvement. They are quickly digested, providing energy and preserving muscle mass, thereby contributing to their anticatabolic effect (Holecek et al, 2018), as confirmed in our study.

No clear dosage recommendation for BCAAs is reported in the literature. Depending on the state of health and individual goals, a 1–60 g daily supplement may even be effective (Mayer et al, 2023).

In the literature, some researchers examined the effects of this dietary supplement on the body using 2×6 g of BCAA daily (Bassit et al, 2000), others used 2×14 g daily (Dudgeon et al, 2016), whereas another group used 6 g of BCAA daily (Novin et al, 2018).

Considering these different data and the fact that the patients in our study are in a strict physical rest period, but also in the wound healing phase, which puts a strain on the body, we decided on 8 mg (2×4 mg) BCAA daily.

Considering patients' physical activity habits is the strength of the present study, as active individuals generally have higher muscle mass. Notably, our active patients had an initial muscle mass of 36.2 kg, which was significantly higher than the 26.4 kg of the inactive group, consistent with literature findings.

This approach allowed us to identify significant differences not only between the control and study groups but also between physically active and inactive patients.

Moreover, the most valuable component of our research results is that we examined not only the changes in specific body composition elements within each group but also the changes in these parameters compared with patients' body weight. Comparing these values to each other and expressing them in proportion for each patient helps to eliminate the possibility of error caused by potentially large anthropometric differences between individual patients.

We examined the elements determined using the InBody 270 that can significantly change over the 3-week follow-up period (body weight, skeletal muscle mass, percentage body fat, visceral fat, total body water, and InBody Score). Additionally, the impact of BCAA, a dietary supplement that protects muscles and promotes muscle synthesis, was assessed.

Our study aligns with existing literature on tonsillectomy and body weight, showing no novel findings. We observed a 2.67 kg weight loss in the control group and 2.15 kg in the study group, similar to the reported 2.27 kg loss in adults following tonsillectomy (Rozycki et al, 2015)

However, solely focusing on body weight can be generally misleading; body composition data support the significance of our findings.

We briefly summarize the most significant results of our study as follows:

Despite the low-impact lifestyle, patients in the study group showed a continuous increase in muscle mass (from an average of 30.3 to 30.5 kg) and a parallel decrease in body weight (from an average of 73,55 to 71,40 kg), with a consequential decrease in fat percentage (from 26.69% to 25.15%). Patients in the control group showed a continuous decrease in muscle mass (from 30.3 to 28.5 kg) and body weight (from 74,02 kg to 71,35 kg), with a consequential increase in fat percentage (from 27.06% to 28.13%) in both subgroups.

In the active study group, the average muscle mass practically did not decrease, whereas the muscle mass of the inactive study group increased. Although this group also lost body weight, its muscle mass was maintained such that this group met the body's energy requirements mainly from fat. The same explanation accounts for the changes in visceral fat observed in our study.

In the nutritional point of view, muscle mass represents the qualitative aspect of "body weight," being the key of fitness status of the human body (Wall BT et al, 2015).

Our results indicated that the BCAA dose used in this study effectively protected muscle mass in the active group with relatively higher muscle mass and promoted muscle synthesis in the inactive group with lower initial muscle mass. In contrast, the muscle mass of the control group decreased in the absence of the dietary supplement. In this case, patients' energy needs were primarily covered by muscle breakdown.

The literature has indicated that the skeletal muscle mass-to-body water ratio in body composition tests is directly proportional (Sagayama et al, 2023). The physiological explanation for this finding lies in the ability of muscle mass to bind water. Therefore, when a loss of muscle mass occurs, a consequent decrease in body water percentage can also be observed.

Conversely, an increase in muscle mass is also expected to result in an increase in body water.

Consistent with these data in our study, the percentage of body water, which is similar to muscle mass, increased in the study group, whereas it decreased in the control group.

The InBody Score, also termed the fitness score, integrates various metrics, including muscle mass, body fat percentage, and body water. A higher muscle mass is frequently correlated with improved body composition and reduced fat percentage, positively influencing the InBody Score (Fritz P et al ,2022).

In our study, the changes in the InBody Score for each group matched the changes in muscle mass and body fat.

No significant changes were observed in liver or kidney function or ion levels, confirming the safety of BCAA supplementation.

Our study suggests that BCAA is beneficial during tonsillectomy recovery, preventing muscle loss and supporting a quicker return to normal activity.

Nowadays, patient satisfaction and quality of life play an increasingly significant role in patient care. Based on the results of our study, recovery with BCAA supplementation is associated with a higher state of fitness, thereby warranting its inclusion in postoperative treatment and care protocols.

This study had some limitations that should be acknowledged. First, stronger results may be achieved with a larger sample size. To mitigate this limitation, we not only examined changes in individual body composition components over time but also their ratios to current body weight. Second, the differences would have been more pronounced if we had examined the differences between professional athletes and average individuals as a measure of physical activity; this could be the goal of a future research.

For future perspectives, BCAA supplementation could be beneficial for patients with more serious pharyngeal diseases, such as cancer. Maintaining optimal general health is crucial for responding to treatments and mitigating the side effects of oncological therapies in these patients.

8. Conclusions

In recent decades studies have examined body weight changes following tonsillectomy. Nutrition science has shifted its focus from body mass index to body composition analysis, but no studies have explored body composition changes post-tonsillectomy. In oncology and digestive surgeries, the potential benefits of branched-chain amino acids (BCAAs) have been investigated; however, their effects on pharyngeal surgery remain unknown. Therefore, the aim of the present study was to investigate the body composition changes after tonsillectomy and to explore the potential benefits of branched-chain amino acids. Research focused on health promotion and prevention has led to a large number of studies aimed at maintaining health at an optimal level in the long term (Fritz R et al, 2024).

This prospective interventional controlled study enrolled 48 patients who were randomly assigned to a control group (CG) and an experimental group (EG). These groups were further divided into active and inactive subgroups on the basis of their activity levels. The EG consumed 2×4 mg of BCAA daily. Body composition was measured using bioimpedance (InBody 270) on the day of surgery and again on days 7 and 21 postoperatively.

Both groups experienced similar weight loss; however, significant differences in body composition emerged. The CG showed significant muscle mass loss (from 30,29 to 28,51 kg), whereas active EG members maintained muscle mass (from 35,33 to 35,40 kg); inactive EG members increased muscle mass (from 26,70 to 27,56 kg) and reduced body fat percentage (from 31.94% to 29.87%). The general health status (InBody score) remained stable or improved in the EG (from 75,13 to 75,96); however, it decreased in the CG (from 75,42 to 72,67).

The negative effects of tonsillectomy on body composition are mitigated by BCAA supplementation. Based on our results, a targeted dietary recommendation can be made for patients preparing for a similar intervention, in order to avoid negative body composition changes.

Finally, but not at least, my answers to hypotheses:

- **H₀: A loss of muscle mass can be verified during measurements in the postoperative period.**

Partially fulfilled: since in the case of the inactive experimental group, an increase in muscle mass can be observed.

In the case of the control group, the hypothesis was confirmed.

- **H₁: Significant fat loss cannot be verified during measurements in the postoperative period.**

Partially fulfilled. In case of the control group the hypothesis was confirmed.

In the experimental group fat mass loss was proven.

- **H₂: In the case of the study group, the loss of muscle mass will be less significant.**

Absolutely fulfilled.

9. Declaration of Thanks

Thank you very much to everyone who supported me along the way.

To the patients, without whose cooperation and willingness this research would not have been possible.

To the nurses, who helped all the way with the blood collection in the morning rush.

To the medical scribe ladies who helped with the administration.

To my medical colleagues, with whom we were able to coordinate the dates of control examinations, body composition measurements and blood draws.

Professor Rovó for making it possible for the research to be carried out in the institution he leads.

Special thanks to Associate Professor Dr. Zsófia Bere, who helped me all along with her good advice, practical and local experience.

And finally, but not least, I am very grateful to my husband, Dr. Péter Fritz, who is my support, my background, my partner in life and in my professional endeavors. Thank you for dreaming up and implementing this research.

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