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EFFECT OF SARCOPENIA AND DYNAPENIA ON PATIENT CANDIDATE TO TOTAL KNEE ARTHROPLASTY: EVALUATION WITH SEGMENTATION ON MAGNETIC RESONANCE IMAGING COMPARED TO HEALTHY POPULATION.

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ABSTRACT

Introduction

The manuscript initially provides an overview of sarcopenia and its potential implications in traumatology and orthopaedic surgery. With advancements in medicine and personal care leading to increased life expectancy, the relevance of frailty, of which sarcopenia is a key factor, has grown. Sarcopenia, characterized by loss of muscle mass and/or function, has gained progressively increasing interest, necessitating early diagnosis, multidisciplinary assessment, and targeted interventions to mitigate its adverse effects on patient outcomes. However, challenges remain in standardizing diagnostic thresholds, particularly due to diverse ethnic backgrounds and recent growth in the field. Therefore, research efforts should concentrate on establishing standardized imaging thresholds for sarcopenia diagnosis to enable less invasive, quicker, and more certain diagnostic methods.

Materials and Methods

The study recruited 20 healthy adult volunteers (HA) and patients candidate to total knee arthroplasty (TKA) meeting specific inclusion and exclusion criteria. All subjects underwent MRI scans, dynamometric testing, and surface electromyography for muscle assessment. Muscle measurements, including maximum cross-sectional area (CSA) and volume, were obtained from MRI scans using specialized software.

Results

MRI-scan segmentation allowed for evaluation of total lower limb muscle volume and side-to-side differences. Analyses focused on four muscle groups of interest: knee flexors, knee extensors, iliopsoas, and gluteal muscles, revealing statistically significant mean volume differences between TKA and HA subjects. TKA subjects exhibited overall volumetric reduction, particularly in muscles groups like knee extensors, and greater variability between right and left sides compared to HA subjects.

Discussion and Conclusion

The study highlights the impact of arthritic disease on muscle morphology. TKA patients demonstrated clear imbalances towards the healthy side, indicating deconditioning. These findings underscore the importance of early diagnosis and targeted interventions for sarcopenia management. Standard diagnostic criteria, more accessible tools and therapeutic protocols are essential to limit the adverse effects of sarcopenia on elderly patient and improve outcomes.

INTRODUCTION

Advancements in medicine knowledge, treatments and personal care led to a notable increase in life expectancy and a subsequent aging of the population. Thus led to a pivotal role of research dealing with age-related diseases. Some of them were already know, such as cachexia, frailty, and osteoporosis. Among them sarcopenia, which had a medical definition later, had a fast raise in interest in a limited amount of year and is currently evolving as one of the most relevant, wide, and interdisciplinary field of research in medical literature. By searching the term “sarcopenia” on PubMed, approximately 21.500 papers are retrieved, and approximately 19.500 have been published since 2013 (Tab.1).

Resulting from the union of the Greek words “σάρξ” (sarx, flesh) and "πενία” (penia, loss), sarcopenia was originally defined by Rosenberg in 1989[1] as the loss of muscle mass; however, growing interest on sarcopenia rapidly led to the intensification of studies and to the necessity of a Consensus, performed by the European Working Group on Sarcopenia in Older People (EWGSOP) in 2010[2] and an updated one in 2018[3]. As result of the consensus, the role of muscle function, before considered as a separate entity under the name of dynapenia, is now integrated in the definition of sarcopenia. This condition is more frequently found in the elderly population, with the prevalence increasing with age. Eventually, impact of sarcopenia extends beyond its effect on physical health: sarcopenia is estimated to be increasingly relevant in the future from a clinical, social, and economic point of view, because of the progressive aging of population worldwide.

Eventually, sarcopenia is relevant also in orthopaedic and traumatology clinical practice, since aged population will deal with increased number of fractures, functional limitation, and impairment due to loss of strength and muscle mass.

Aim of this research project is to compare HA and potentially sarcopenic patient candidate to TKA, a major joint replacement surgery, by performing 3Tesla MRI scans, through which 2D and 3D reconstructions are executed.

The following thesis will be articulated in 3 sections. First section provides an overview of sarcopenia, its epidemiology and etiopathology, clinical and imaging diagnosis and its limits and current orientation on treatment. Second section outlies the potential role of sarcopenia in traumatology and orthopaedic surgery, with special consideration for major joint replacement such as TKA and total hip arthroplasty (THA). Last section presents material and methods, preliminary results, discussion, and conclusions of the manuscript. The tables and images are attached subsequently to the text of the manuscript for easier consultation.

SARCOPENIA

a. DEFINITION AND EPIDEMIOLOGY OF SARCOPENIA

Sarcopenia is defined as a generalized loss of muscle mass and strength which is mainly age-related; however other conditions, such as malnutrition, obesity, chronic inflammation, neoplasms, can influence and worsen the course of sarcopenia.

The prevalence of sarcopenia is reported ranging from 3% to 27% in population older than 65 years[4]. Age is considered the key factor in developing sarcopenia, since the prevalence of sarcopenia increases with age, equally affecting men and women. It is estimated that individuals over the age of 50 have an average annual muscle loss rate of 0,37% in females and 0,45% in males, almost doubled after the age of 70[5]. However, some studies report that muscle mass and strength can start declining as early as 40 years old, with middle-aged patient failed to be detected due to lack of attention by physicians in its early stages, when intervention measures could be more effective in slowing down or reverse disease progression.

b. ETIOPATHOGENESIS

Other morbid conditions, including obesity, malnutrition, cachexia, osteoporosis, and frailty have been showed to overlap and directly influence the development and evolution of sarcopenia. Contributing factors to sarcopenia include hormonal changes, reduced physical activity, inadequate nutrition, and underlying chronic diseases. Emerging evidence indicates that sarcopenia is associated with adverse metabolic effects, such as insulin resistance and glucose intolerance.

Sarcopenic patients have a higher level of functional impairment either on mobility or cognition: sarcopenic patients have lower scores on the Functional Independence Measure (FIM), which measures a patient's ability to perform daily activities. Specifically, sarcopenia is associated with lower scores in tasks such as transferring between bed/chair/wheelchair, using the toilet, locomotion, climbing stairs, comprehension, and social interaction.

Aging leads to metabolic changes in muscle size and quality, with a progressive imbalance between anabolic and catabolic activities. This is due mainly to a gradual reduction in protein production that leads to a quantitative and qualitative reduction of muscle fibers, mainly type II, which are the fastest type. Additionally, fat infiltration between and inside

muscles fibers occurs. In this setting, fat infiltration can be even more relevant, since the loss of muscle strength happens 2- to 5-fold faster respect to the loss of muscle mass[5].

Sarcopenic muscle also shows a decrease in the number of satellite cells, which are responsible for replacing and repairing damaged muscle fibers. This reduction is caused by changes in the concentration of circulating factors controlling the activity and differentiation of satellite cells, such as transforming growth factor-β (TGF-β), and myogenin. Chronic inflammation and production of reactive oxygen species (ROS) contribute to muscle atrophy by determining dysfunction of the neuromuscular junction, a decrease in the number of motor units, inflammation, insulin resistance, mitochondrial dysfunction, and oxidative stress. There is a correlation among increase ROS levels and decrease in handgrip strength[5] and elevated levels of C-reactive protein, interleukin-6 (IL-6), and tumour necrosis factor-α (TNFα) and declines in muscle mass and muscle strength[6].

The relationship between sarcopenia and other age-related conditions is significant. The prevalence of these conditions, alone or more frequently paired, has been rising due to changes in the socio-demographic and epidemiological profile of the population.

Obesity and sarcopenia combined have been associated with worse outcomes and survival rates compared to obese individuals without sarcopenia[7]. In obese patients, sarcopenic obesity, characterized by decreased skeletal muscle mass in individuals with a body mass index (BMI) of 30 kg/m² or higher, represents a significant orthopaedic comorbidity. Obesity can further exacerbate sarcopenia through the release of pro-inflammatory mediators from adipose tissue, leading to myosteatosis, the ectopic accumulation of fat within skeletal muscles[8].

Malnutrition, often observed in older adults, further contributes to the development and progression of sarcopenia and frailty[9]. The loss of muscle mass can lead to declines in basal metabolic rate, making weight management more challenging for older individuals.

Cachexia, which is a multifactorial condition found in systemic diseases such as cancer, chronic infections, chronic heart failure, share several features with sarcopenia from the clinical manifestations of muscle loss and dysfunctions to the imbalance in molecular mechanisms for homeostasis of soft tissues; main difference is represented by the fact that cachexia has a clear hypercatabolic state due to inflammation, while in

sarcopenia prevail the role of anabolic resistance which manifest as a decrease in the rate of protein synthesis[10].

Sarcopenia and osteoporosis are both age-related and has been associated with a higher incidence of adverse outcomes. Muscles and bones are biologically and functionally connected, and their deterioration with age increases the risk of fractures in the elderly due to falls and reduced bone resistance. Sarcopenia and osteoporosis, characterized by low bone mineral density (BMD), limited mobility, and reduced muscle mass and strength, are major contributors to the increased risk of fractures in the elderly population.

Frailty is a condition that makes older people more susceptible to stressors and limits their ability to maintain homeostasis. Frail individuals have reduced autonomy and increased vulnerability. Most Authors consider sarcopenia as a key factor in the frailty syndrome[9,11–13]. Loss of muscle mass affects the well-being of the elderly population and favors frailty, which is associated with falls, disability, reduction of independency, cognitive impairment, and depression, which in most cases can occur together as a consequence of a vicious circle.

There is a relevant overlap among these conditions, and this makes more difficult also the identification of sarcopenia, with malnutrition, cachexia and frailty representing the main differential diagnosis[1,9,14,15].

c. DIAGNOSIS

EWGSOP highlighted the importance of early and prompt diagnosis and treatment of sarcopenic conditions[3]. In the second update, muscle mass and function are considered equally relevant in the diagnosis of sarcopenia[3]. Since 2016, sarcopenia has a classified definition[16], which means that it is considered a disease, and it is defined as a progressive and generalized skeletal muscle disorder characterized by accelerated loss of muscle strength, muscle mass, and motor function. Various assessment methods, including muscle strength measurements, imaging techniques, and functional tests, help identify patient at risk for sarcopenia. Combining these assessments with routine screenings during healthcare visits can aid in early detection and personalized treatment planning. However, current literature disagrees on which is the best diagnostic tool for imaging of the sarcopenic patient and there is a lack of standardized cut-off parameters to diagnose sarcopenia.

EWGSOP proposed a diagnostic flowchart[3], which is based on a stepwise approach including a detection, assessment, confirmation of the diagnosis, and evaluation of severity. This is performed through clinical suspicion, questionnaire, diagnostic imaging evaluation and physical tests.

The physician should be aware of sarcopenia and its prevalence in aged patient in order to begin the clinical steps to diagnose it. First step recommended by EGWSOP is SARC-F questionnaire[17], a 5-item self-evaluation administered to patient, which is characterized by low-to-moderate sensitivity and very high specificity[18], therefore avoiding the potential risk of false negative results in severe cases. If SARC-F results negative, screening is interrupted, and the patient should be rescreened subsequently.

After detection of possible sarcopenic condition, muscle strength should be assessed with simple, not invasive, and inexpensive tests such has hand grip dynamometer and chair stand test. These simple tests are cheap and can be administered in every setting, from the hospital to the general practitioner office. Grip strength has a correlation with strength in other districts[19], therefore is useful as an initial tool before proceeding with more complicated and expensive diagnoses; moreover the finding of low grip strength is already predictive of low patient outcome[19]; chair stand test assess strength of lower limbs by measuring how much time is needed to stand form seated position 5 times without using arms (or how many times a patient can stand from seated position in 30 seconds without using arms)[20,21]. If these tests result normal screening is interrupted, and the patient should be rescreened subsequently.

With probable sarcopenic condition, muscle quantity and quality should be assessed. This is the most debated step in diagnosis for sarcopenia: various methods such as dual-energy X-ray absorptiometry (DXA), bioimpedance analysis (BIA), computed tomography (CT), ultrasound (US) and magnetic resonance imaging (MRI) are available. However, the lack of standardized cut-offs hinders comparisons between studies and populations.

DXA is actually considered the gold standard for diagnostic imaging [22], allowing to effectively measure the lean mass of the studied body segment. However, it involves radiation exposure, is expensive and is not easily retrieved in all clinical settings. Moreover, it is not able to assess

intramuscular fat tissue[22,23], which is currently considered one of the most relevant features of sarcopenia[24].

BIA was introduced early as a technique to estimate body mass composition[25–27], and is still widely used in clinical settings since it is relatively inexpensive, non-invasive and easy to use[22]. BIA is based on evaluation of differences in resistance, "impedance", to electrical passage among different tissues (i.e. water and electrolyte-rich tissues are less resistant compared to fat tissues)[28]. Unfortunately, many factors condition BIA reliability and make it not ideal to evaluate lean mass: instrument variability, technician variability and patient- and ambient-related factors such as position, overnight fast or empty bladder, body temperature, skin conductibility, room temperature. Therefore, BIA has a large potential predictor error, with an overall underestimation of lean body mass[29].

CT has high accuracy in quantification of skeletal muscle by determining the coefficient of X-ray absorption of different tissues[30] and allows 3D reconstruction. This can be achieved either by manual segmentation either with automated software, and very low measurement errors are reported[31]. Moreover, the most recent CT machines allows to remove the already limited error connected to possible patient motion during CT scans acquisition. However, the main drawbacks related to CT are the limited availability, the high costs and, above all, the significant higher radiation dose when compared to DXA[22].

Since the ideal diagnostic tool would be inexpensive, non-invasive and without radiation exposure, reliable, easy to use and with high specificity and sensibility, focus should be oriented on the two instruments that do not use ionizing radiation, US[32] and MRI[33], which appear the most interesting tools in the next future for diagnosis of sarcopenia.

US shows several appealing features to evaluate sarcopenia, especially considering the diagnostic issues in a population of aged patients: it is inexpensive, easily disposable, portable and extremely safe and reliable in soft tissue imaging[34]. However, its effectiveness still relies on the experience of the operator. This aspect and the absence of a standardized protocol probably led the EWGSOP to exclude US from the diagnostic chart.

MRI represent the natural evolution of CT analyses and, allowing 3D reconstruction and a better evaluation of soft tissues[30], could be the most specific tool to diagnose sarcopenia. However, MRI, in particular if

equipped with enough resolution power, is often available only in advanced care settings, it is an expensive exam and it requires high technical expertise to perform the exam. It is also a slower exam compared to CT, therefore more easily leading to errors due to movements during acquisition. Moreover, there is a lack of standardized protocol to obtain MRI scan for the muscle mass[35].

d. TREATMENT

Considering the relatively recent outgrow of the research field, the lack of certain thresholds for diagnosis and the need for specific randomized controlled trials focused on therapies, at the moment effective treatment for sarcopenia is not well defined and it is widely debated. However, considering the pathophysiology of sarcopenia, both non-pharmacological and pharmacological approaches have been and are currently under evaluation.

Among non-pharmacological interventions, lifestyle modifications, and more precisely enhancement of physical activity, received strong recommendations as primary treatment for sarcopenia[36]. Many papers investigated the role of resistance training, showing benefits either for muscle mass[37] and for muscle strength[38]. The role of physical exercise has been highlighted also for sarcopenic obesity[39]. Physical exercise acts by improving all aspects related to aging, reducing cardiovascular risk, insulin resistance, and mortality, and by reducing lipotoxicity through increased beta-oxidation of fatty acids, resulting in an enhancement of the anabolic properties of muscle cells[40,41]. However, at the moment there is not a consensus on specific exercises or a defined protocol that can conclusively determine the slowing down or improvement of sarcopenia. There are doubts regarding the actual ability and the compliance of elderly patients to engage and persist in consistent exercise.

Interest is raising on dietary changes. Studies have demonstrated the potential benefits of specific dietary habits, including adequate daily protein intake, which is recommended to be raised from 0.8 g/kg/day to 1.2 g/kg/day in population aged over 65 years[42], vitamin D[43] and long-chain polyunsaturated fatty acids[44], which reduce lipotoxicity, insuline resistance and has anabolic effect on muscles. The combined use of leucine-enriched whey proteins, vitamin D and polyunsaturated fatty acids showed increased postprandial protein anabolism, muscle mass[45]

and muscle function[46]. However, even if there are evidences of the contribution of dietary interventions on the enhancement of the effects of resistance training on skeletal muscle mass[47–50], the eventual effect of sole nutritional therapy on sarcopenia is less clear[51,52].

Although no specific drug has received official approval for the treatment of sarcopenia[1], several drugs have been investigated with mixed results[53]: vitamin D suppletion, several hormonal therapies (estrogen-progesterone, growth hormone, testosterone, insulin-like growth factor 1…), biotherapies to reduce chronic inflammation (TNFα antagonist or IL-6 antagonist), metformin, angiotensin-converting enzyme (ACE) inhibitors, myostatin inhibitors to enhance anabolism in muscle cells.

SARCOPENIA IN ORTHOPAEDICS PATIENTS

While the role of sarcopenia in trauma is easily understandable, with the increased risk of falls and fractures that can lead to trauma (and in fact, most orthopaedic manuscripts related to sarcopenia deal with trauma), the eventual effect of sarcopenia on patients candidate to elective surgery for degenerative diseases such total joint replacement must not be underestimated[54], mainly because the age limit for this procedures is constantly raised thanks to the excellent results in terms of pain removal and functional recovery.

As mentioned before, there is considerable overlap between sarcopenia and several other chronic disease such as obesity[7,24], type 2 diabetes[55], malnutrition[9], chronic cardiovascular, respiratory and kidney disease[56], and neoplasms[57] that lead to frailty syndrome[11].

Among chronic conditions of the frailty syndrome, one of the strongest correlation is between sarcopenia and osteoporosis[58], a condition called osteosarcopenia[59]. The role of low BMD as an established risk factor for fracture is widely known[60], the action of muscle strength on the bone, which can effectively contribute to the maintenance of bone structure and strength[61,62], should always be taken into consideration. Hence, both low muscle strength and low BMD in older adults may not adequately stimulate osteogenesis thereby increasing fracture risk in the event of a fall. The two components of low muscle strength and low BMD determine a vicious circle in which each cooperate in reinforce the other, until the final event that is a fracture. The typical fracture of osteosarcopenic patients is a fragility fractures, defined as fractures that occur as a result of minimal or low-energy trauma, typically falls from a standing height or less, or even with no identifiable trauma[63–65].

The type of fracture depends on the mechanism of fall and the reactivity of the patient[66]: a osteosarcopenic patient could show slowness of reflexes and impaired stability due to muscle loss[67–69]. Most frequent fragility fractures are femoral neck and proximal epiphysis fracture[70], followed by wrist, homerus, ankle and knee fractures. Also vertebral fractures, usually compression and amielic fractures, are frequent in elderly patient, often without specific trauma. However, given the reduced reactivity and the eventual incapacity to protect the face with the upper limbs, a osteosarcopenic patient could have craniofacial fractures, which are the most dangerous and related with higher mortality risk[71,72].

In literature, a considerable overlap between osteoporosis and sarcopenia is reported: in example, patients sustaining a hip fracture, have both in 45% of the cases, in 28% sarcopenia alone and only 14% have neither[73]. However, since the vast majority of fragility fractures are caused by falls, risk of falling is a better predictor of fractures than BMD, even if low BMD increase the likelihood of a fracture[74]. This highlight the central role of sarcopenia in frailty syndrome, to the extent that identifying individuals at increased risk of falls, rather than osteoporosis diagnosis, has been indicated as a primary goal in the prevention of fragility fractures[75].

In this context, the current tendencies by healthcare systems for the prevention and treatment of fragility fractures should be incorporated: considering the expected rise in elderly population [76], the parallel increase of fragility fractures, and particularly hip fractures, will not only be relevant for patients and families, which experience a decrease in independence and quality of life and an increase in disability and mortality, but also on healthcare services which will face an increased economic burden.

To achieve better prevention to fractures, epidemiology has to be taken into consideration: in particular, there are substantial gender differences. Male fractures are more frequent during young and early adulthood, and are connected to high energy trauma; on the contrary, the average hip fragility fracture is a woman aged over 80. Reported incidence for fractures at 15-24 years of age is 200 per 10.000 males versus 40 per 10.000 females while over 85 years old there is an incidence of 350 per 10.000 males versus 450 per 10.000 females[77]. Other studies performed in different periods report similar rates of fractures[78,79]. Moreover, also interesting is a gender gap among frailty patients: fragility fractures start to manifest and rapidly increase after 60 years, but females aged 85 years have an annual incidence of hip fracture of 4% compared to 2% of males of the same age[79]. Naturally, also men experience osteosarcopenia and fragility fractures; however, those manifestations appear at an older age compared to women, with a temporal lag of approximately 10 years.

Sarcopenia and its consequences must be considered even in the case of elective surgery. Several papers show how the presence of osteoarthritis contribute substantially to worsening of sarcopenia and vice versa. Total joint replacements, and particularly TKA and THA, are among the most

common practiced orthopaedic surgeries. In recent decades, the age range of patients for whom the intervention has been recommended has progressively widened, including both very young and very elderly patients. This is possible thanks to various factor like reduced invasivity of the procedures, the improvement in geriatric and perioperative care of the patients but also in the higher functional request of elderly patients. However, as mentioned before the muscle loss can begin already in after the age of 40, with an average muscle loss rate of 0,37% in females and 0,45% in males, that result almost doubled after the age of 70[5].In a systematic review on women patients awaiting THA, sarcopenia had an incidence three times higher compared to general population, very similar to the incidence of patient who sustain a hip fracture[80]. Other studies show similar results[54,81–83]. This highlights the role of inactivity, in this case due to pain and limited articular function, in deconditioning the muscle and determine reduction of muscle mass and strength.

Moreover, the same studies show how after THA there is a substantial improvement of muscle mass[83] and gait speed of patients with sarcopenia, even compared to non-sarcopenic patients[80]. A retrospective study which analyzed CT scans showed similar reduction of mass and quality of psoas and paravertebral muscles in patient with THA compared to contralateral; similar reduction was found in case of bilateral THA. Moreover, in case of complications of THA, the same reduction were appreciated[84].

Sarcopenia also affect the risk of complications after total joint replacement and lead to longer postoperative hospital stay, more hospital costs and lower functional scores and patient reported outcome measures. In the case of THA, all the main complications can be enhanced by sarcopenia, and particularly dislocation and periprosthetic fracture, due to the reduced activity of the muscle in maintaining the stability of the hip[85] and to the aforementioned reported higher risk of fall.

In case of TKA, even if not complicated and without necessity of reinterventions, patients with sarcopenia need longer hospital stays, and had a higher risk of 90-day medical problems. Moreover, the number of 2-year implant-related problems, falls, lower extremity fractures, and reoperations is higher in sarcopenic patients[86].

The reduction of muscle mass, and in particular low Psoas Lumbar Vertebral Index in both THA and TKA patients has been found to represents a significant independent predictor of higher risk of

infections[87], which is known to be the most complicated to treat and debilitating complication after total joint replacement.
Eventually, several reports show how the forced inactivity after a major surgical procedure could plays a major role in developing sarcopenia: reported muscle mass loss after 10 days bed rest is reported up to 1 kg[88], while quadriceps strength decrease has been reported up to 9% after just 5 days bed rest[89]. Six days of hospitalization following THA could determine substantial leg muscle atrophy in older patients[90].
Therefore, the focus in the orthopaedic field should be firstly on primary prevention of fragility fracture, that should begin with the general practitioner, whose role is to identify patients at risk and refer them to a multidisciplinary assessment and treatment of all aspects of the frailty syndrome, minimizing the need for orthopaedic intervention. It must be avoided, as unfortunately frequently happen, that the orthopaedic would be the first and sometimes the only physician that deal with a patient with a fragility fracture. If orthopedic surgery, particularly on the lower limbs and, above all, on the femoral neck, becomes necessary, it should be performed promptly to minimize bed rest time within the constraints of the patient's overall condition[91,92]. Even in the case of elective procedures, in which patients are usually healthier, the role of sarcopenia should not be underestimated. Whenever possible, the preference should be for minimally invasive approaches such as direct anterior approach for THA[93,94], which reduce surgical trauma and, ultimately, may facilitate postoperative recovery.
From what has been presented, it is evident that sarcopenia is a vast and multidisciplinary topic that however requires significant developments to be effectively addressed across different disciplines.
Aim of this research project is to compare HA and potentially sarcopenic patient candidate to TKA, a major joint replacement surgery, by performing 3Tesla MRI scans, through which 2D and 3D reconstructions are executed. Any differences found will then be clinically compared later on with isometric test and electromyography stimulation.

EXPERIMENTAL SECTION

a. MATERIALS AND METHODS

Clinical collection followed two steps. For both steps, positive feedback was received from the regional ethical committee following the submission of two separate applications. The collection of the HA volunteers, named Forceloss I and numbered 216/2020/Sper/IOR was evaluated by the local Ethical Committee, which provided a favorable opinion during the session on April 23, 2020, with approval for conduct granted by the Extraordinary Committee of Rizzoli Orthopaedic Institute, P.G. 0006402, on May 5, 2020. The collection of the TKA patients, named Forceloss II and numbered 30/2021/Sper/IOR was evaluated by the local Ethical Committee, which provided a favorable opinion during the session on January 21, 2021, with approval for conduct granted by the Extraordinary Committee of Rizzoli Orthopaedic Institute, P.G. 0002015, on February 8, 2021.

Firstly, 20 volunteers HA were collected . Inclusion criteria were: age between 20 and 40 years, BMI between 5 and 30 kg/m^2. Exclusion criteria were: neurological diseases, rheumatic diseases, neoplasms, conditions of incompatibility with MRI or electromyography (pacemaker, epilepsy, severe venous insufficiency of the lower limbs, pregnancy), previous trauma or surgery to articulation of the lower limbs.

Secondly, patient candidate to TKA with potential sarcopenic condition were collected. Inclusion criteria were: patient with diagnosis of primary knee osteoarthritis, age between 65 and 80 years, BMI between 18.5 and 30 kg/m^2, American Society of Anesthesiologists (ASA) Classification 2 or lower. Exclusion criteria were: neurological or neuromuscular diseases, rheumatic diseases currently in treatment with steroid or immunosuppression therapies, neoplasms, conditions of incompatibility with MRI or electromyography (pace-maker, epilepsy, severe venous insufficiency of the lower limbs), previous trauma or surgery to articulation of the lower limbs, dementia, inguinal or abdominal hernia, type I or II diabetes, severe (Grade 3) hypertension, severe cardiopulmonary insufficiency, chronic steroid therapy in last 12 months, osteonecrosis of articulation of the lower limbs.

Given limitation in obtaining necessary instrumentation (mainly dynamometer) both HA and TKA patient enrollment experienced a slowdown. Moreover, clinical case enrollment was necessarily scheduled after HA examinations and was further limited after Covid-19 pandemics.

As a result, 3 patients candidate to TKA were collected and fully examined before surgery, while other 12 have been enrolled and are waiting for examination to be performed. Therefore, clinical results proposed subsequently must be considered preliminary.
Both HA and patient underwent MRI, dynamometric testing, and surface electromyography.

Radiological analyses

MRI was acquired using 3T General Electric Co. (Boston, Massachusetts, USA) MRI Scanner, employing T1-weighted and Dixon sequences with parameters previously optimized to facilitate the identification, segmentation, and separation of various leg muscles. MRI scans acquired the entire lower limbs, starting from the L4 vertebra down to the feet in the axial plane. Software used to perform analyses on RM scans was Mimics (Materialise, Leuven, BE). Patient names were anonymized using Mimics, associating each patient with an identification code. Volunteers were subsequently coded as HA and TKA patients were coded as TKA; each subject were subsequently given a progressive number from 1 to 20. For each muscle of the leg, 2D (maximum cross-sectional area, CSA, cm^2) and 3D (volume, cm^3) measurements were extrapolated from the Digital Imaging and Communications in Medicine (DICOM) files of individual patients imported into the Mimics software. As reported in literature[95], and already validated in previous studies[83,96], lower-limb muscles were segmented, initially using the automated muscle segmentation toolbox followed by manual adjustments when necessary.
CSA is a well-known and validated assessment parameter[97], while 3D volumetric reconstructions are a less commonly used study method due to their high costs and extended production times.

Statistical analyses

All statistical tests were performed using Microsoft Excel software (version 16.78; Microsoft Corporation©, Redmond, Washington, USA). $P<0.05$ was regarded as significant difference. Confidence Interval was 95%.

b. RESULTS

For each subject, a maximum of 39 muscles per side were segmented, resulting in a total of 78 acquisitions. The complete scans were used to

calculate the total volume of lower limb muscles and side-to-side and HA to TKA differences. For the remaining analyses, only the muscles belonging to the four muscle groups of interest were considered: knee flexors (biceps femoris long and short head, gracilis, popliteus, sartorius, semimembranosus, semitendinosus), knee extensors (including rectus femoris, vastus lateralis, intermedius, and medialis), iliopsoas (segmented separately into iliacus and psoas muscles), and gluteal muscles (including gluteus maximus, medius, and minimus). The gastrocnemius muscle (including medial and lateral heads), conventionally considered a knee flexor, was excluded because its primary motor contribution is plantar flexion, while its function related to the knee is mainly stabilization[98].

Three scans (HA4, HA13, HA14) were found to be corrupted, and modeling was not possible; therefore, the subjects have been excluded from the current preliminary results and will be rescheduled for the final analysis.

For HA2, it was possible to reconstruct a reduced number of muscles (24 per side, 48 in total); however, the only missing muscle in the 4 analyzed muscle groups was the popliteus, whose volumetric value is extremely low. Moreover, acquisition of left side iliopsoas was corrupted. Therefore, HA2 was excluded from the assessment of the total volume, but evaluations related to the muscle groups of interest except for iliopsoas muscle were carried out.

In the remaining cases, 13 muscles were not reconstructed in the MRI scans. However, in all cases, these were muscles with lower volumetric importance and in muscle groups not included in the analysis (in 5 cases, gemellus superior muscle; in 3 cases, gemellus inferior muscle; in 2 cases external obturator muscle, in 1 case peroneus brevis muscle, flexor digitorum longus muscle, plantar muscle). Thus, the missing muscle pair and its contralateral counterpart were only excluded from the total volume assessment.

Subjects demographics data are reported in Table 2. Even if there is not a side preference in selection of the patients, at the moment all the TKA subjects are candidate to right TKA.

The total volumes of the subjects and the comparison between the right and left sides are graphically represented in Figures 1 and 2. The percentage difference between the right and left sides never exceeded 10% in both HA and TKA, with the sole exception of HA12, where the total volume of the right lower limb was 23% lower than the left.

The average total volume in HA was 12,210.33 cm^3, while in TKA, the average volume was 8,852.56 cm^3, with a statistically significant mean volume difference of 3,347.77 cm^3 ($p=0.02$) and a percentage difference of 27% which did not reach statistical significance ($p>0.05$).
For each evaluated muscle, the mean volume and mean CSA max were calculated either in HA or TKA subjects. Moreover, mean volume and mean maximum CSA were calculated for the muscle groups of interest.
A test of agreement between the detected volumes and CSA max was conducted. For each segmented muscle, the percentage difference in volumes and CSA max between the right and left sides was calculated, both in HA and TKA subjects. The result is presented graphically in Figure 3 and shows an overall concordance among the two measurements. The same procedure was performed for the studied muscle groups, and the result is presented graphically in Figure 4.
Figure 5 shows the comparison between average volume for each muscle analyzed between HA and TKA subjects. The spikes observed in the graph demonstrate that the muscles with the highest volumetric representation are the gluteus maximus, gluteus medius, and the complex of knee extensors, either in HA or in TKA subjects. However, TKA subjects exhibit an overall volumetric reduction compared to HA subjects, which is more pronounced particularly in the case of the larger muscles. A similar trend is found in Figure 6, which shows the comparison between average CSA max for each muscle analyzed between HA and TKA subjects. In particular, the knee extensor muscles are the only muscle group in which the difference between the mean volume and CSA max is statistically significant in almost all cases: the left rectus femoris has a mean volume difference between HA and TKA of 107.63 cm^3 (49%, $p=0.02$) and a mean CSA max difference of 510.92 cm^2 (44%, $p=0.01$); the right rectus femoris 116.45 cm^3 (51%, $p=0.03$) and 571.34 cm^2 (47%, $p=0.03$); the left vastus intermedius 201.74 cm^3 (50%, $p=0.01$) and 821.89 cm^2 (43%, $p=0.03$); the right vastus intermedius 222.09 cm^3 (53%, $p=0.01$) and 1015.71 cm^2 (52%, $p=0.004$); the left vastus lateralis 268.05 cm^3 (45%, $p=0.03$) and 1182.39 cm^2 (41%, $p=0.02$); the right vastus lateralis 286.01 cm^3 (48%, $p=0.02$) and 1320.97 cm^2 (45%, $p=0.02$); the left vastus medialis 202.39 cm^3 (50%, $p=0.01$) and 806.86 cm^2 (36%, $p=0.02$); the right vastus medialis, the only extensor not reaching statistical significance, 204.73 cm^3 (54%, $p=0.01$) and 737.76 cm^2 (34%, $p=0.07$). Some other mean differences reach statistical significance: the

left semitendinosus has a mean volume difference between HA and TKA of 72.08 cm^3 (39%, p=0.053); the right semitendinosus 74.62 cm^3 (40%, p=0.052); the left gluteus minimus 38.42 cm^3 (51%, p=0.002); the right iliacus 65.06 cm^3 (42%, p=0.03). Additionally, the right gluteus minimus has a mean CSA max difference of 277.57 cm^2 (33%, p=0.02) in favor of TKA patients. All the other mean differences, despite showing a similar trend, do not reach statistical significance.

The same analysis was then performed on the four major muscle groups: the trend was similar, with an average volume difference of 335.63 cm^3, 21%, in knee flexors, 464.22 cm^3, 19%, in gluteal muscles, 291.47 cm^3, 40%, in the iliopsoas, and 1609.09 cm^3, 50%, in knee extensors; the mean CSA max difference was 1171.37 cm^2, 11%, in knee flexors, 932.79 cm^2, 5%, in gluteal muscles, 1984.82 cm^2, 32%, in iliopsoas, and 16,967.85 cm^2, 42%, in knee extensors. The results are graphically presented in Figures 7 and 8.

The subsequent analyses investigated the variation in mean volumes and mean CSA max between the right and left sides, in individual muscles and muscle groups. Due to the significant difference in sample size in these preliminary results, statistical significance was not achieved.

However, TKA subjects exhibited a wider range of variability on each side in individual muscles, with differences ranging from 1% to 37% in volume and 1% to 31% in CSA max, compared to HA subjects who showed a range between 0% and 13% in volume and 1% and 12% in CSA max. In agreement between volume and CSA max, the individual muscles showing the greatest variation for absolute value in TKA patients were the iliacus (26.68 cm^3, 285.18 cm^2), the vastus lateralis (24.45 cm^3, 77.62 cm^2) and the vastus medialis (15.54 cm^3, 29.93 cm^2). The gluteus minimus muscle also showed a relevant volumetric variation (21.46 cm^3) and CSA max (343.06 cm^2), and it was the muscle showing the greatest percentage change (37% volume, 31% CSA max). However, this change was in the direction of the operated side (right). For HA subjects, the muscle with the most side-to-side variation was the gluteus maximus (38.24 cm^3, 216.85 cm^2); percentagewise, the greatest variation was seen in the sartorius (13% volume, 12% CSA max). The results are graphically presented in Figures 9 and 10.

Eventually, Figures 11 and 12 show the analysis of side-to-side variability in volume and CSA max of muscle groups. Similarly to individual muscles, TKA patients exhibited greater variability in both absolute and

percentage values (range 0-10% compared to 0-2% in volume and 2-15% compared to 1-4% in CSA max of HA subjects). In TKA patients, the flexors showed the greatest volume variability in absolute value (41.66 cm^3), while the iliopsoas showed the highest percentage variation (10%). HA subjects exhibited the highest volume variability in the gluteal muscles (29.35 cm^3, 2%). Regarding CSA max, the gluteal muscles showed the greatest absolute variability in TKA patients, favoring the operated side (300.35 cm^2, 3%). However, the iliopsoas was numerically almost equivalent to the gluteal muscles (295.40 cm^2) but had a higher percentage variation (15%), favoring the healthy side. In HA subjects, the results were similar, with smaller variations: gluteal muscles 192.81 cm^2, 2%; iliopsoas 132.74 cm^2, 4%.

c. DISCUSSION

This study conducted a comparison at various levels of muscle masses and their respective variations in HA subjects and patients candidate to TKA surgery. The comparisons were performed using 3D parameters (volume) and 2D parameters (CSA max), which were acquired in a partially automated manner through 3T MRI scans performed on the whole lower limbs both in HA and in TKA patients.

As shown in Figure 1, the total volume for TKA subjects is similar, and in some cases even higher, than HA subjects with lower values. However, when examining the biometric data, it can be noted that HA subjects with similar values have lower height, weight, and/or BMI compared to TKA subjects. Since muscle mass grows in proportion to height and weight[99], this analogy could be considered in this context.

In Figure 2, the volumes divided by side show a substantial agreement both for HA subjects and TKA patients. A slight prevalence in terms of volume can be identified on the right side in HA subjects, possibly reflecting a greater recruitment of the right hemisphere, which is dominant in a higher percentage of individuals in the healthy population[100]. Conversely, in TKA patients, all of whom are candidates for surgery on the right side, a minimal predominance of left-sided volumes can be observed. However, these preliminary results seem to demonstrate that there is no substantial loss of lower limb volume in patients undergoing TKA, as previously highlighted in a study of patients subsequently undergoing THA[83]. However, it should be noted that the number of

subjects is limited, and there is a possibility that they may have contralateral arthritic pathology.

The agreement test between volume and CSA max was conducted by comparing the percentage differences between the two values in the individual muscles and muscle groups under examination. The graphs shown in Figures 3 and 4 demonstrate substantial agreement between volume and CSA max, both for individual muscles and muscle groups. The greater difference visible in muscle groups should be attributed to the smaller magnitude of the percentage difference. Furthermore, it can be observed in an approximate manner that the differences for TKA patients exhibit a more pronounced trend compared to HA subjects, indicating greater variability in both volumes and CSA max.

This trend of greater variability appears to be confirmed by the analysis of volumes for individual muscles in HA subjects compared to TKA patients. Figure 5 shows that the volumes between HA and TKA follow a similar pattern; however, there is an overall reduction in volumes in TKA patients, which is more pronounced with larger muscle volumes (e.g., gluteus maximus, rectus femoris, vastus intermedius, vastus lateralis, and vastus medialis.) The same pattern with the same differences can be observed regarding CSA max, further demonstrating the concordance between the two values. Furthermore, as previously reported, the complex of knee extensor muscles, including rectus femoris, vastus intermedius, vastus lateralis, and vastus medialis, which converge in the quadriceps muscle complex, is basically the only muscle group in which a statistically significant difference in mean values was found, despite the small number of TKA patients and the preliminary nature of the results reported. This highlights the central role of extensor muscles in knee biomechanics and how this muscle complex can be the first to be affected when knee arthritis restricts its function. This is in accordance with recent literature reporting that knee extensors and in particular rectus femoris is often the most atrophying muscle[101]. The presence of some smaller muscles in terms of volume, where TKA patients have a slightly higher value (e.g., short head of the biceps femoris, gracilis, popliteus, and sartorius), may suggest a compensatory mechanism by surrounding muscles or an opposing effect due to the antagonistic position of these muscles.

The same analysis was performed for muscle groups, with the results depicted graphically in Figures 7 and 8. In this case as well, a common trend can be observed for both volume and CSA max, with similar values

but an overall reduction in TKA patients compared to HA subjects. Again, the difference becomes more pronounced when considering the knee extensor compartment, while it is more subtle for the other muscle groups. When considered as a whole, however, the compensatory effect seen in some of the smaller knee flexor muscles is lost and these muscles groups are always smaller both in volume and CSA max in TKA patients compared to HA subjects.

The last analysis performed on the volume and CSA max of individual muscles and muscle groups is the difference in mean values between the two sides in HA subjects and TKA patients. This analysis is particularly interesting as it allows to assess any changes that occur in TKA patients and also consider the variability that may be present in HA. For example, as depicted in Figures 9 and 10, the gluteus maximus muscle represents the muscle with the greatest volumetric and CSA max variability in HA subjects, favoring the right side. This may again indicate right-sided dominance; however, it should be noted that the gluteus maximus is one of the largest muscles in the entire lower limb, and its greater variability in absolute terms is not matched by the percentage value, for which the greater variability is observed, either for volume and for CSA max, in the sartorius, one of the muscles that exhibited the smallest absolute variation between the right and left sides.

The substantial loss of muscle mass in TKA patients can be particularly identified in the iliopsoas, vastus lateralis, and vastus medialis muscles, which are characterized by the greatest average volumetric difference in favor of the unaffected side (all TKA patients are candidates for right-side surgery). This further confirms the central role of extensor muscles, which, in the case of knee arthrosis pathology, experience deconditioning, similar to what has been reported for patients undergoing THA[83]. Furthermore, a significant volumetric variation is observed in muscles that do not belong to the extensor category: the gluteus minimus and psoas muscles. This variation (to be framed in the right perspective, given the small size of the muscle heads, especially the gluteus minimus), unlike the extensor muscles, is in the direction of the side to be operated and could likely be attributed to the previously mentioned adaptation of the lower limb musculature to a deconditioned state, which primarily affects the extensor muscle group. It is reasonable to hypothesize that by extending the analysis to the entire musculature of the lower limb, other individual muscles, likely of smaller size, may exhibit a similar trend. This may

partially explain the finding of substantial balance in overall volumetric differences between the two sides in TKA patients.

Regarding the CSA max shown in Figure 10, some differences are observed in the case of TKA patients: the absolute value that shows the greatest differential between the right and left sides is in the iliopsoas muscle, towards the healthy side, and again in the gluteus minimus muscle towards the affected side. The extensor musculature, although still showing variability towards the healthy side, exhibits absolute area differences comparable to those of other muscles such as the gluteus maximus and gluteus medius. This likely indicates lower reliability of CSA max in this specific assessment.

Lastly, the assessment of volumetric and CSA max differences per side applied to the examined muscle groups allows for a clearer evaluation of trends in both HA and TKA. Figure 11 analyzes the volumetric difference, showing a distinct division with the variation in HA muscle groups all trending towards the right side, and the greater variability exhibited by the gluteal musculature, possibly again reflecting the predominance of the right side in the overall population.

Conversely, TKA patients show a clear imbalance in all muscle groups towards the healthy side, demonstrating deconditioning caused by reduced mobility resulting from arthritic pathology in this case. The muscle group that displays the greatest absolute variability is once again represented by knee extensors, followed by the iliopsoas. The latter, in particular, is often involved in arthritic processes even when not directly related to its function, serving as an indicator of overall patient mobility and well-being[83]. Again, there is variability in the assessment of CSA max compared to the values shown by volumetric variations. Figure 12 shows an opposite trend between knee extensors and iliopsoas, which, in agreement with the volumetric analysis, vary in favor of the healthy side, and knee flexors and gluteal muscles, which, conversely, vary in favor of the affected side in TKA patients. In HA subjects, the variations are smaller, and, compared to the volumetric analysis, only iliopsoas changes sides. Several observations can be made regarding these variations.

Firstly, CSA max loses validity as a parameter compared to overall volume, which is further justified by the measurement of CSA max in individual muscles and subsequent summation. For a more indicative value, it would likely be necessary to recalculate CSA max based on the overall volume of the analyzed muscles. Additionally, it should be noted

that the percentage variations in CSA max in the knee extensors and iliopsoas muscle groups are more significant and in line with percentage volumetric variations (5% variation in both volume and CSA max in knee extensors, 10% in volume and 15% in CSA max in iliopsoas) compared to the percentage variations in muscle groups showing an opposite trend (0% in volume and 2% in CSA max in knee flexors, 1% in volume and 3% in CSA max in gluteal muscles). Similarly, both absolute and percentage variations (range 0-2% in volume, 1-4% in CSA max) are reduced in HA subjects.

These findings are consistent with the literature reporting the atrophy that affects the musculature of joints involved in arthritic processes[81,82,102],other forms of immobilization[103] or simply aging-related sarcopenia[101]. In these studies, measurements were performed either by MRI[82] or CT scans[81,102].

The quantitative assessment of lower limb muscle variations allows for comparisons between HA and TKA patients and between the healthy and affected sides. However, the validity of quantitative analysis alone is debated in the literature[104]. Furthermore, it is reported that for a better assessment of the effect of fatty degeneration, closely linked to sarcopenia, qualitative clinical correlation is necessary[105]. Therefore, correlation with functional parameters will be necessary. The analyses had already begun by recording of maximum strength of knee extensors and flexors produced under isometric conditions. Subjects were positioned on a dynamometer and secured in a seated position with safety belts across the chest and the analyzed limb to minimize movement during the test. The analyzed limb is fixed at three different joint angles: 30°, 60° and 90°, recording the maximum force in flexion and extension. To achieve maximal voluntary isometric contraction, the subjects were stimulated verbally by examinators to exert the maximum force as quickly as possible and maintain the peak value for at least three seconds. Subjects were able to see the force exerted in real-time on a computer screen, and the maximum recorded value during the test will be highlighted on the screen. Three trials were performed for each joint angle. A break after each trial were applied to the participants to prevent the onset of fatigue. For each joint angle, the corresponding force curve for the trial with the highest force value was analyzed. Before performing the maximal contractions, a warm-up was conducted following previous literature on arthritic patients[106].

The activation of the muscles involved in the force measurements on the dynamometer was recorded through surface electromyography. Surface electrodes were applied to the major flexor and extensor muscles of the knee joint, in the area between the muscle's motor point and its distal insertion, following the orientation of the muscle fibers of each muscle, in accordance with SENIAM recommendations[107].
The electromyographic signals were displayed in real-time during the tests to monitor signal quality and subsequently filtered and analyzed to quantify the activation of each individual muscle and the co-activations between agonist and antagonist muscles.
While HA had no problems in completing the dynamometric test, patients showed physical or psychological difficulties in completing the whole test, and were not forced over their availability, especially in case of test performed in close proximity to the surgery.
To complete the evaluation, only the patients filled out the Western Ontario and McMaster Universities Arthritis Index (WOMAC) questionnaire and the Knee Society Score (KSS) to quantify knee function and pain. The WOMAC scale is a self-assessment questionnaire consisting of 24 items divided into three subscales that respectively evaluate knee pain, joint stiffness, and functionality during common daily life activities. The KSS scale, in addition to recording the perceived pain and joint function, objectively assesses joint mobility and knee alignment.
This leads to the main limitation of the study, which is the small sample size of the TKA patient group, due to administrative and bureaucratic delays in recruitment over the 3 years of the project. The results presented and discussed should be considered necessarily preliminary, and while it was possible to provide quantitative analysis, the qualitative analysis requires the completion of recruitment and analysis on all TKA patients. However, initial indications from the analysis of isometric tests show significant variability between the TKA patient group and the HA subjects. The completion of the study will allow for a more comprehensive assessment, taking into account potential confounding factors such as pain-induced reduction in strength and the psychophysical condition of TKA patients performing the dynamometric test a few days before surgery, circumstances that can influence performance, even on a psychological basis.

d. CONCLUSION

In conclusion, the advancements in medicine and personal care have resulted in an increase in life expectancy, leading to changes in patient demographics and the increasing significance of the frailty syndrome within the healthcare service setting. Sarcopenia, a key factor of frailty syndrome, and its association with osteoporosis, obesity and chronic diseases pose significant challenges in the geriatric population. Early diagnosis, multidisciplinary assessment and targeted interventions are necessary to address sarcopenia and mitigate its adverse effects on patients' quality of life and outcomes. Research efforts should focus on finding standardized thresholds for the imaging of sarcopenia that enables a less invasive, quicker, and more certain diagnosis. Additionally, well-defined conservative therapy protocols should be established to modulate or improve sarcopenia, taking into account the specific features of the frailty patients undergoing such interventions.

The preliminary results obtained allow the identification of a pattern, which will need to be confirmed with the completion of the study. In alignment with scientific literature, the extensor component undergoes the most significant modifications in terms of mass reduction and functionality. This is countered by a potential compensatory effect of antagonist muscles that could partially mask the decline in mass of the extensor component, resulting in a loss of mass and function in extensors that is not accompanied by an absolute mass loss. This study opens the possibility of improving both the diagnostic capability and the potential treatment of sarcopenic conditions. The goal is to identify well-defined values using advanced instruments such as MRI, which allows to identify also mild sarcopenic conditions, with the future prospect of subsequently transfer and automatize diagnostic processes on more widely available tools for mass use, such as ultrasound examinations.

LIST OF ABBREVIATIONS

EWGSOP: European Working Group on Sarcopenia in Older People
HA: healthy adults
TKA: Total knee arthroplasty
MRI: Magnetic resonance imaging
CSA: cross sectional area
THA: Total hip arthroplasty
FIM: Functional Independence Measure
TGF-β: Transforming growth factor-β
ROS: Reactive oxygen species
IL-6: interleukin-6
TNFα: tumour necrosis factor-α
BMI: Body mass index
BMD: Bone mineral density
DXA: Dual-energy X-ray absorptiometry
BIA: Bioimpedance analysis
CT: Computed tomography
US: Ultrasound
ACE: Angiotensin-converting enzyme
ASA: American Society of Anesthesiologists
DICOM: Digital Imaging and Communications in Medicine
WOMAC: Western Ontario and McMaster Universities Arthritis Index
KSS: Knee Society Score

TABLES AND FIGURES

Tab. 1 – “Sarcopenia” PubMed Timeline Results per Year

2023	1957
2022	3347
2021	3160
2020	2574
2019	2033
2018	1701
2017	1345
2016	1112
2015	915
2014	729
2013	591
2012	447
2011	327
2010	241
2009	181
2008	142
2007	98
2006	98
2005	93
2004	61
2003	65
2002	51
2001	28
2000	40
1999	18
1998	12
1997	21
1996	2
1995	19
1994	1
1993	4

Tab. 2 – Subject demographics data

ID	Demographics				
	Height	Mass	BMI	Age	Sex
HA01	1,7	56	19,38	27,36	F
HA02	1,78	85	26,83	31,23	M
HA03	1,7	59	20,42	27,4	M
HA05	1,58	52,5	21,03	26,93	F
HA06	1,77	85	27,13	33,55	M
HA07	1,67	53	19	39,51	F
HA08	1,66	63	22,86	38,36	F
HA09	1,78	98	30,93	31,28	M
HA10	1,55	50	20,81	33,73	F
HA11	1,81	78	23,81	21,6	M
HA12	1,58	55	22,03	28,69	F
HA15	1,7	60	20,76	40,73	M
HA16	1,7	75	25,95	29,11	M
HA17	1,6	50	19,53	29,48	F
HA18	1,65	49	18	26,75	F
HA19	1,58	52	20,83	25,98	F
HA20	1,63	57	21,45	36,4	F
TKA01	1,65	73	26,81	70,96	F
TKA02	1,65	67	24,61	80,1	F
TKA03	1,67	80	28,69	75,91	F

Fig. 1

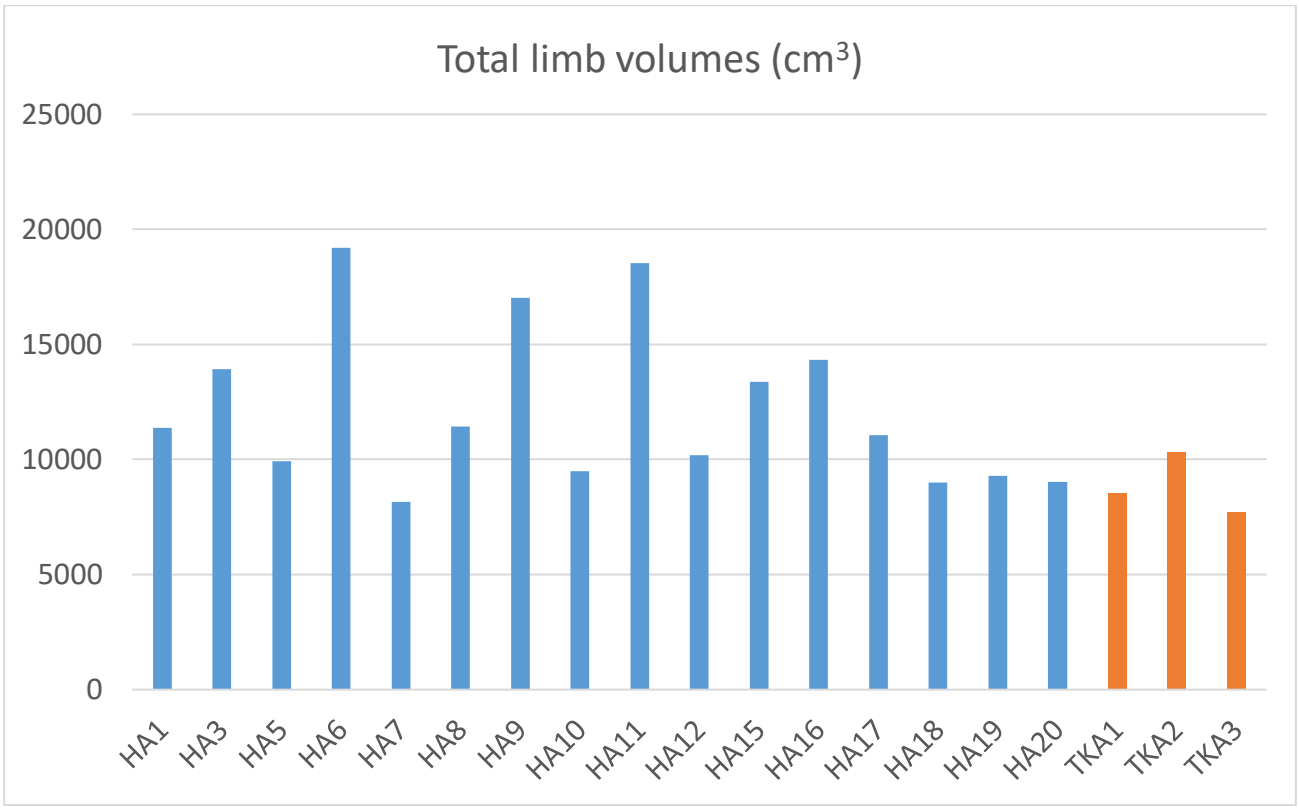

Total limb volumes (cm3)
25000
20000
15000
10000
5000
0
HA1
HA3
HA5
HA6
HA7
HA8
HA9
HA10
HA11
HA12
HA15
HA16
HA17
HA18
HA19
HA20
TKA1
TKA2
TKA3

Fig. 2

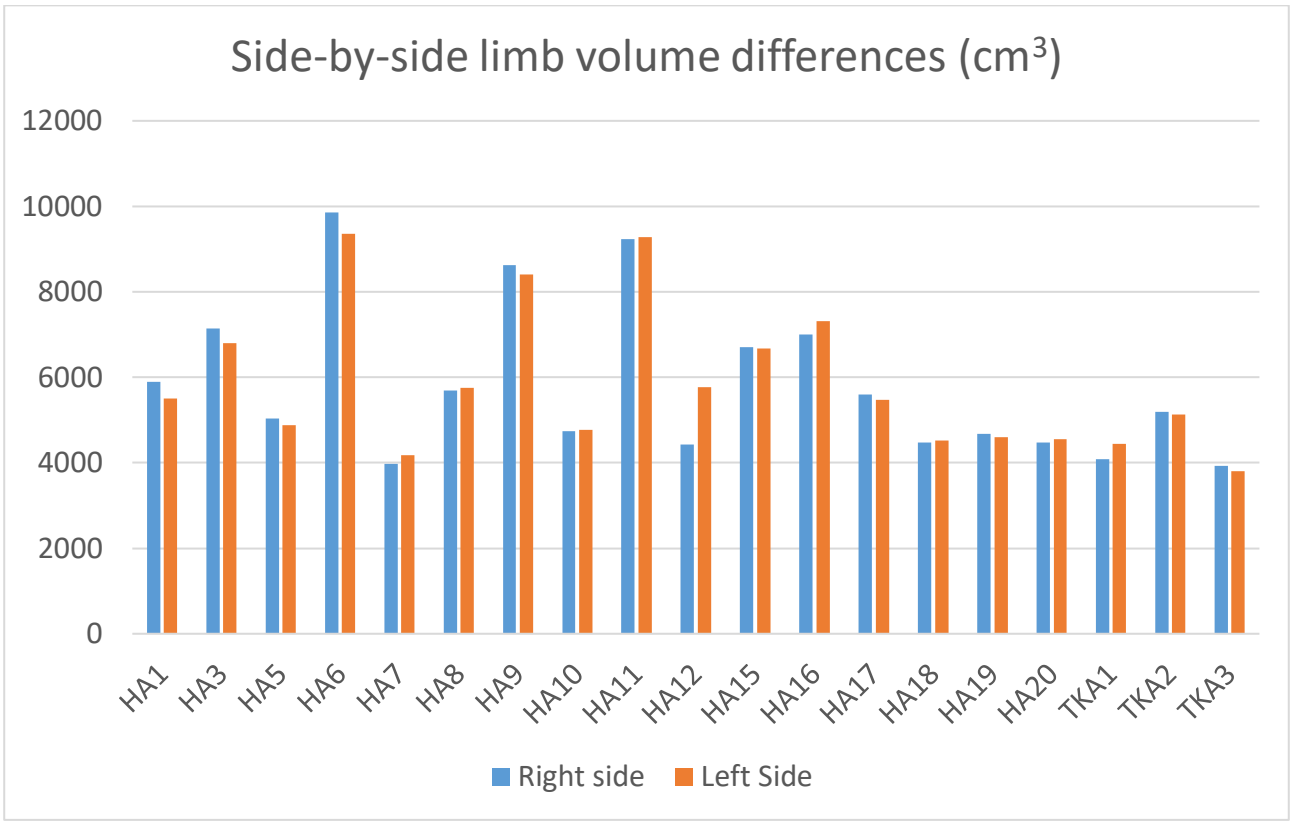
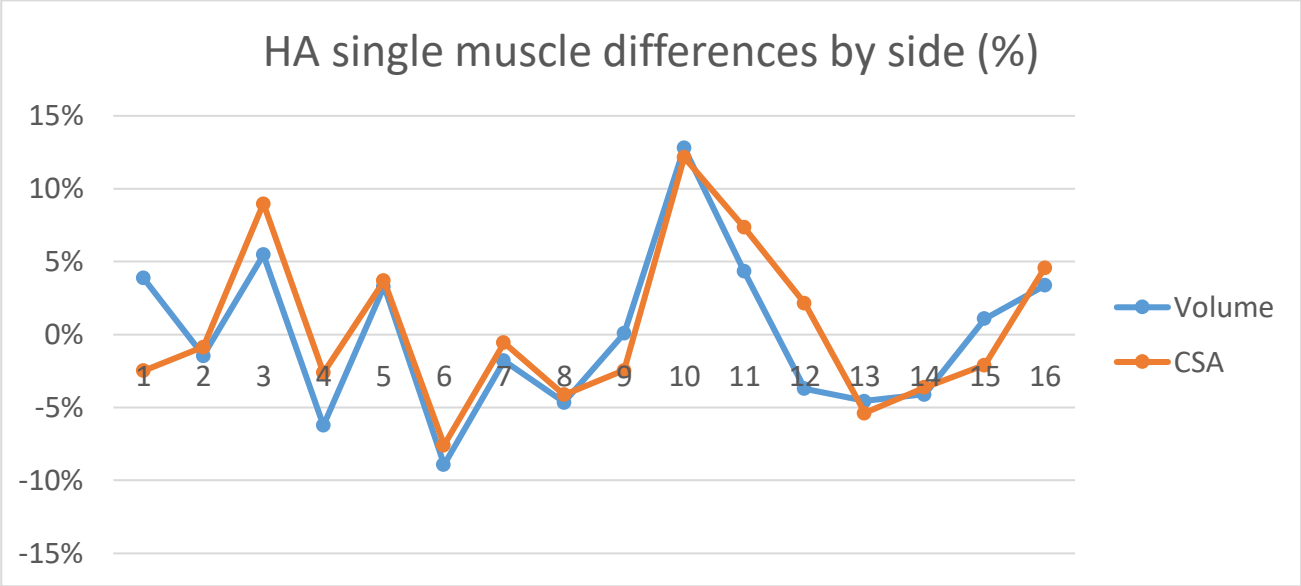
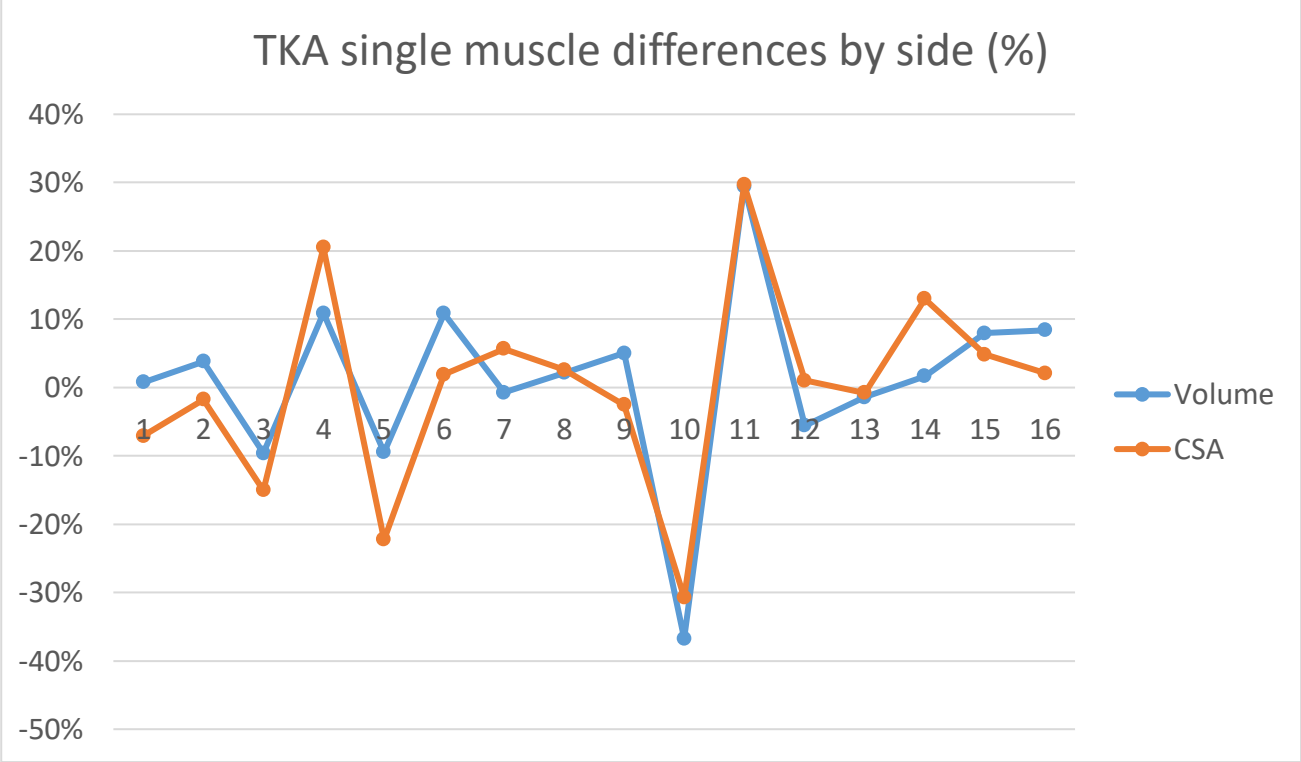

Side-by-side limb volume differences (cm3)
12000
10000
8000
6000
4000
2000
0
HA1
HA3
HA5
HA6
HA7
HA8
HA9
HA10
HA11
HA12
HA15
HA16
HA17
HA18
HA19
HA20
TKA1
TKA2
TKA3
Right side
Left Side

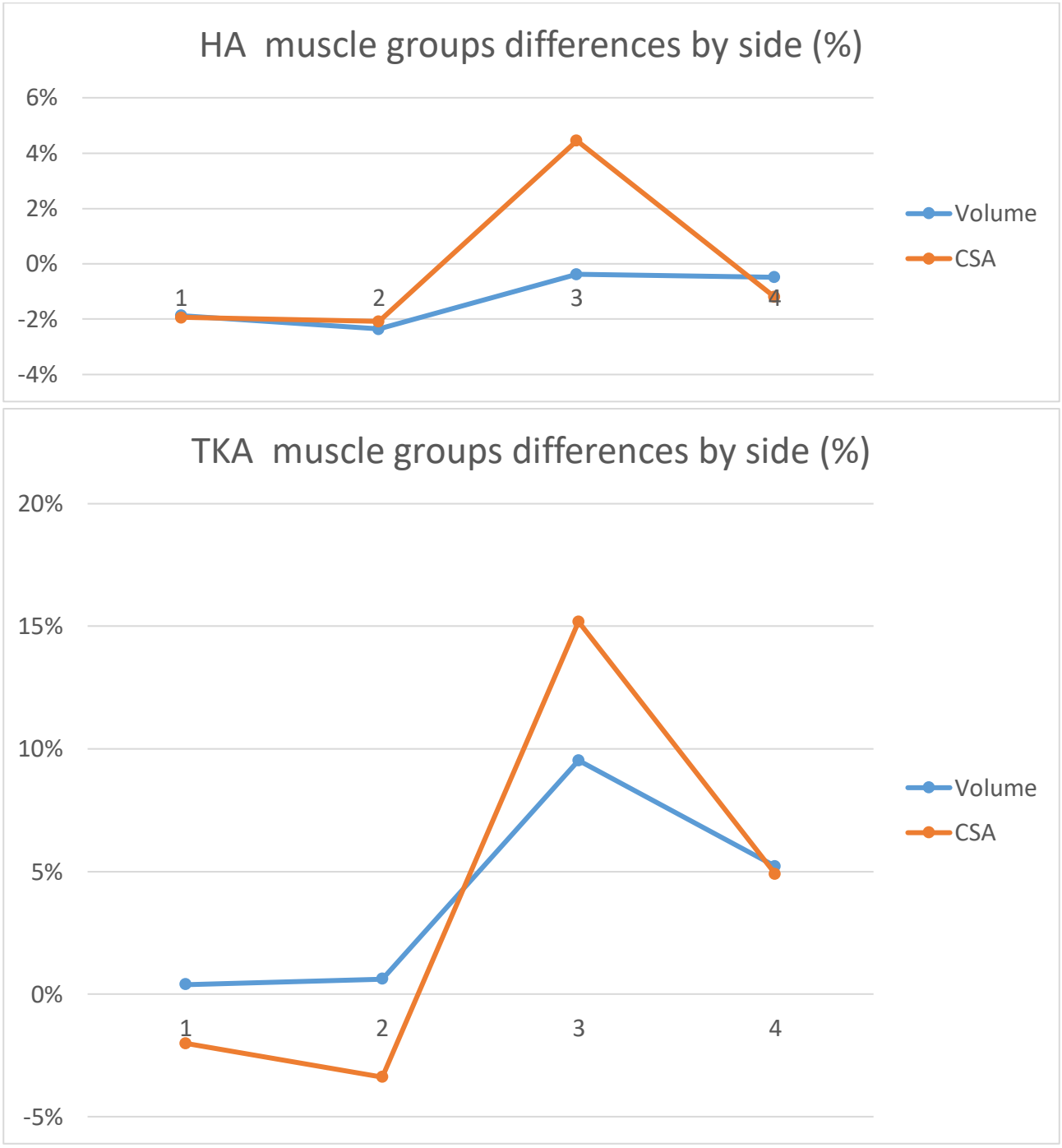
Fig. 3 – Agreement between Volume and CSA in single muscle differences by side





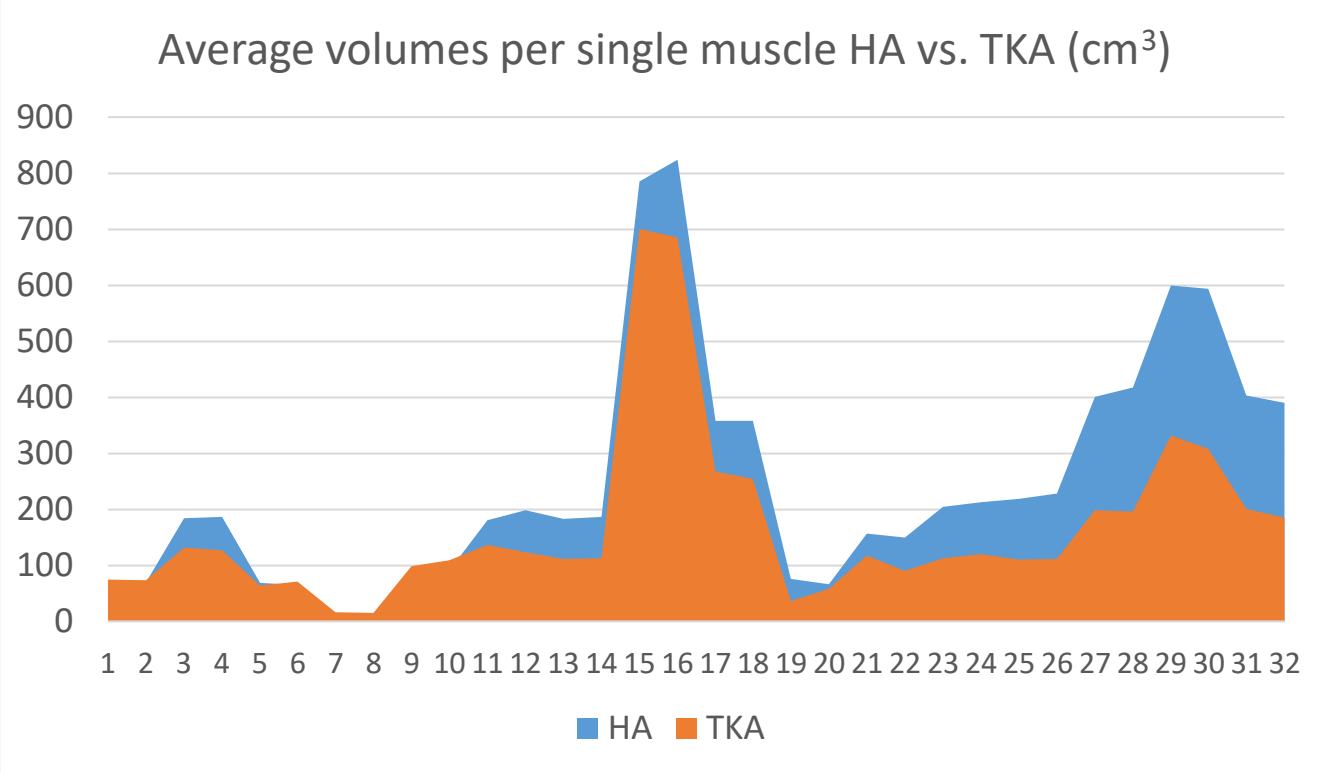
1. Biceps femoralis caput breve
2. Biceps femoralis caput longum
3. Gracilis
4. Popliteus
5. Sartorius
6. Semimembranosus
7. Semitendinosus
8. Gluteus maximus
9. Gluteus medius
10. Gluteus minimus
11. Iliacus
12. Psoas
13. Rectus femoris
14. Vastus intermedius
15. Vastus lateralis
16. Vastus medialis

Fig. 4 – Agreement between Volume and CSA in muscle groups differences by side



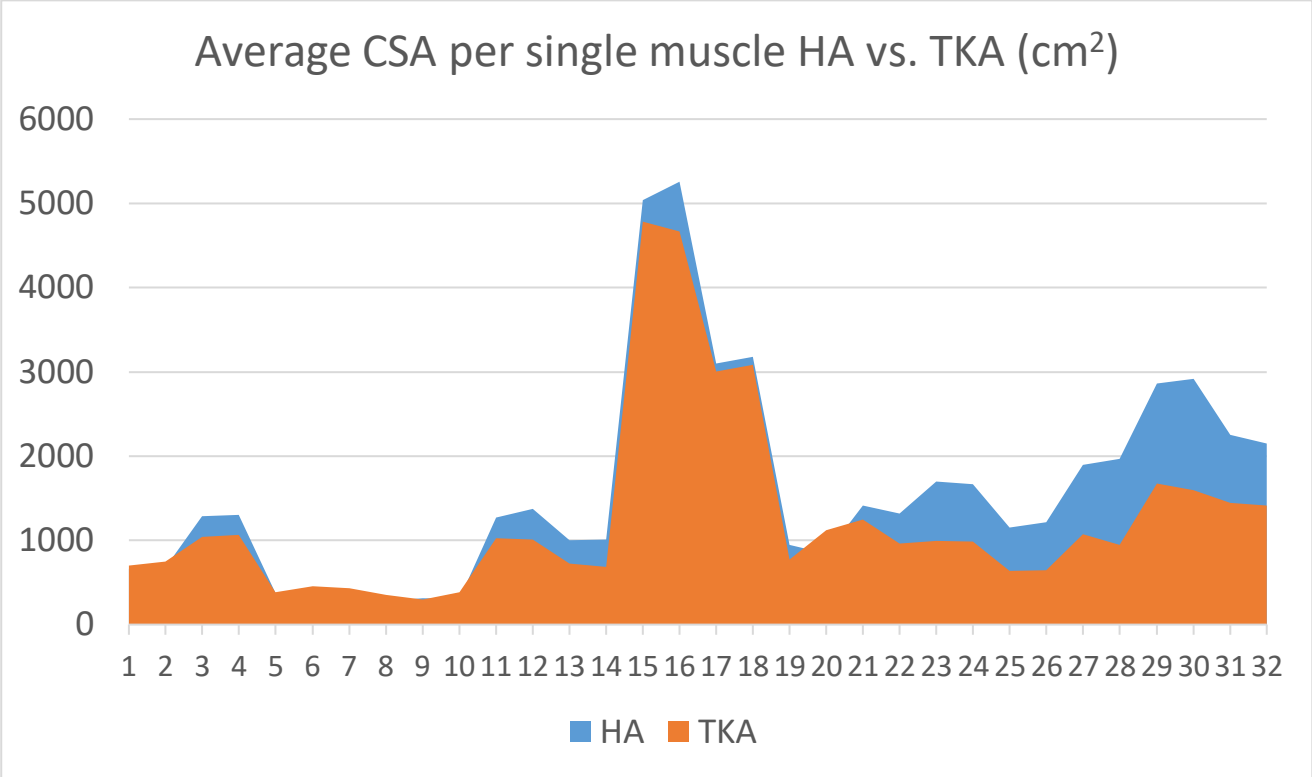
1. Knee flexors
2. Gluteal muscles
3. Iliopsoas
4. Knee extensors

Fig. 5



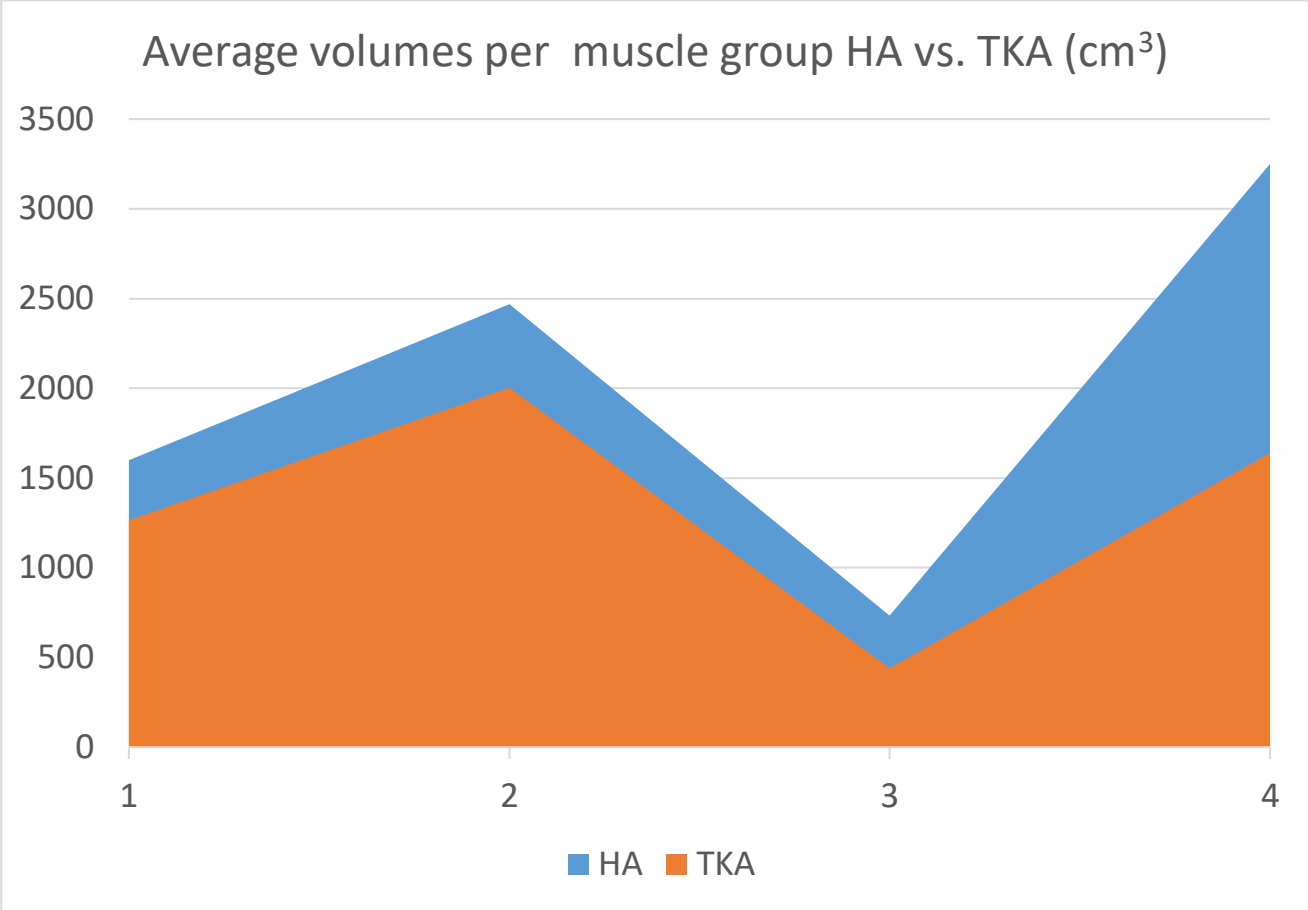
1. Biceps femoralis caput breve left
2. Biceps femoralis caput breve right
3. Biceps femoralis caput longum left
4. Biceps femoralis caput longum right
5. Gracilis left
6. Gracilis right
7. Popliteus left
8. Popliteus right
9. Sartorius left
10. Sartorius right
11. Semimembranosus left
12. Semimembranosus right
13. Semitendinosus left
14. Semitendinosus right
15. Gluteus maximus left
16. Gluteus maximus right
17. Gluteus medius left
18. Gluteus medius right
19. Gluteus minimus left
20. Gluteus minimus right
21. Iliacus left
22. Iliacus right
23. Psoas left
24. Psoas right
25. Rectus femoris left
26. Rectus femoris right
27. Vastus intermedius left
28. Vastus intermedius right
29. Vastus lateralis left
30. Vastus lateralis right
31. Vastus medialis left
32. Vastus medialis right

Fig. 6



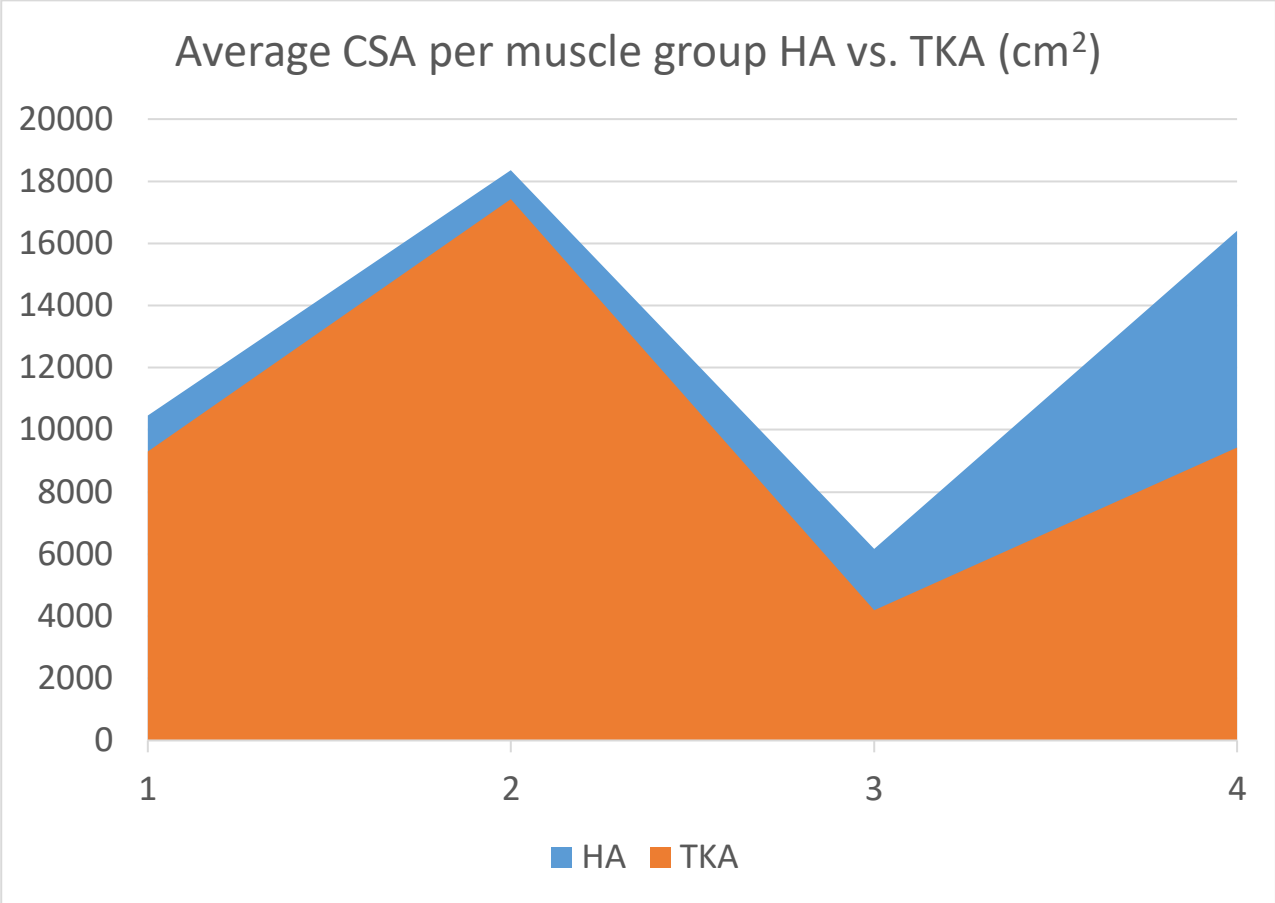
1. Biceps femoralis caput breve left
2. Biceps femoralis caput breve right
3. Biceps femoralis caput longum left
4. Biceps femoralis caput longum right
5. Gracilis left
6. Gracilis right
7. Popliteus left
8. Popliteus right
9. Sartorius left
10. Sartorius right
11. Semimembranosus left
12. Semimembranosus right
13. Semitendinosus left
14. Semitendinosus right
15. Gluteus maximus left
16. Gluteus maximus right
17. Gluteus medius left
18. Gluteus medius right
19. Gluteus minimus left
20. Gluteus minimus right
21. Iliacus left
22. Iliacus right
23. Psoas left
24. Psoas right
25. Rectus femoris left
26. Rectus femoris right
27. Vastus intermedius left
28. Vastus intermedius right
29. Vastus lateralis left
30. Vastus lateralis right
31. Vastus medialis left
32. Vastus medialis right

Fig. 7



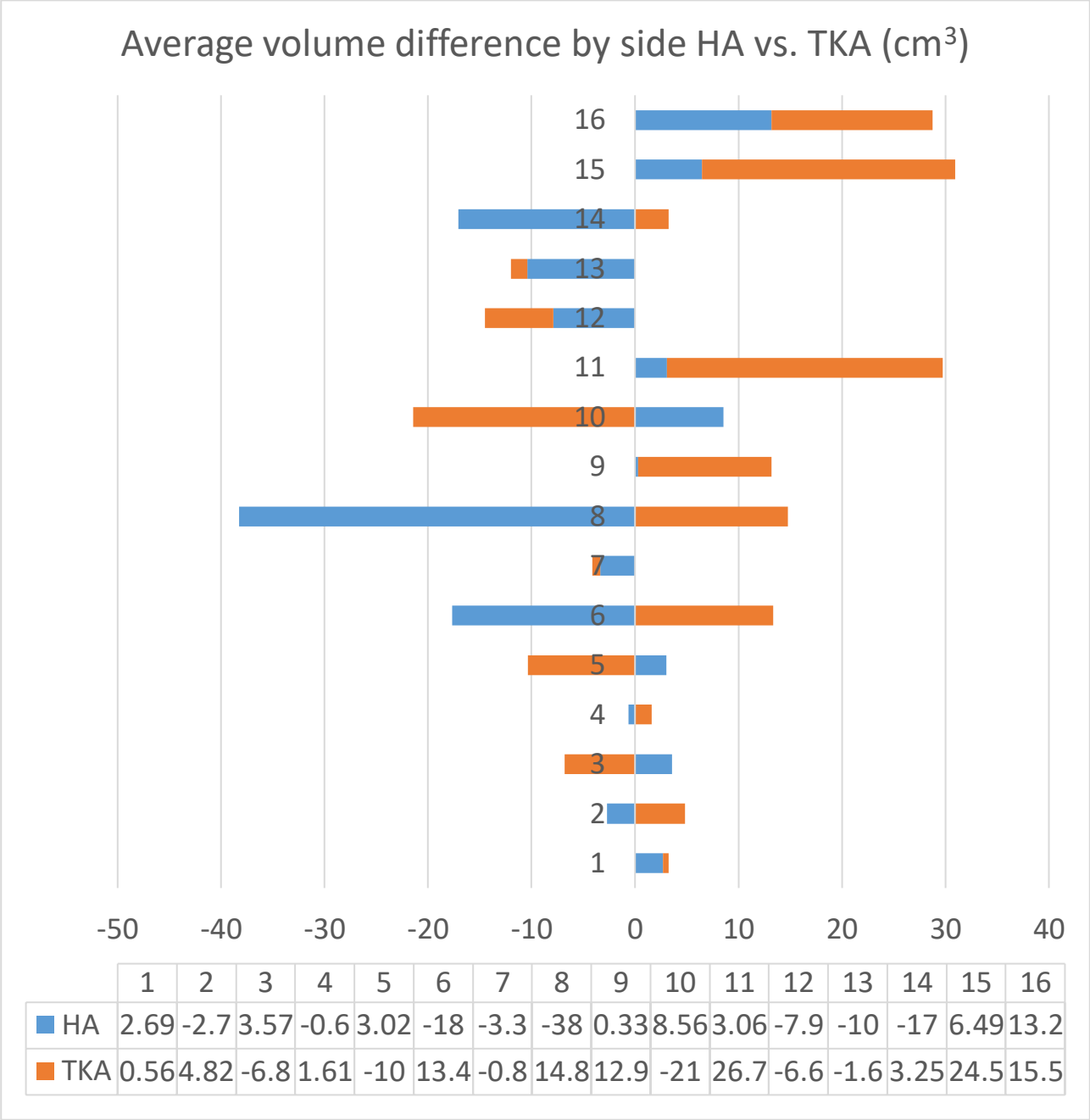
1. Knee flexors
2. Gluteal muscles
3. Iliopsoas
4. Knee extensors

Fig. 8



1. Knee flexors
2. Gluteal muscles
3. Iliopsoas
4. Knee extensors

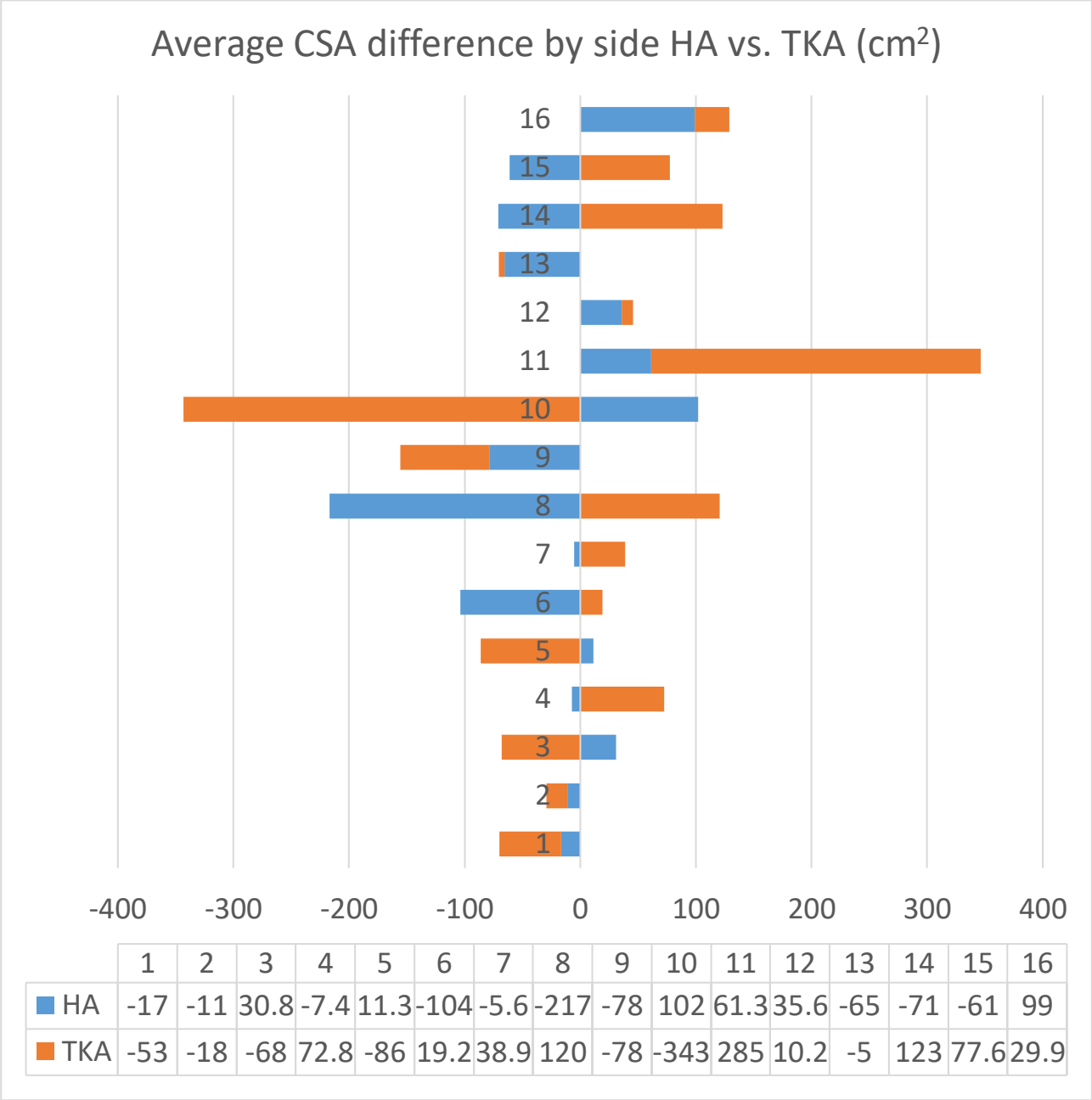
Fig. 9



	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
HA	2.69	-2.7	3.57	-0.6	3.02	-18	-3.3	-38	0.33	8.56	3.06	-7.9	-10	-17	6.49	13.2
TKA	0.56	4.82	-6.8	1.61	-10	13.4	-0.8	14.8	12.9	-21	26.7	-6.6	-1.6	3.25	24.5	15.5

1. Biceps femoralis caput breve
2. Biceps femoralis caput longum
3. Gracilis
4. Popliteus
5. Sartorius
6. Semimembranosus
7. Semitendinosus
8. Gluteus maximus
9. Gluteus medius
10. Gluteus minimus
11. Iliacus
12. Psoas
13. Rectus femoris
14. Vastus intermedius
15. Vastus lateralis
16. Vastus medialis

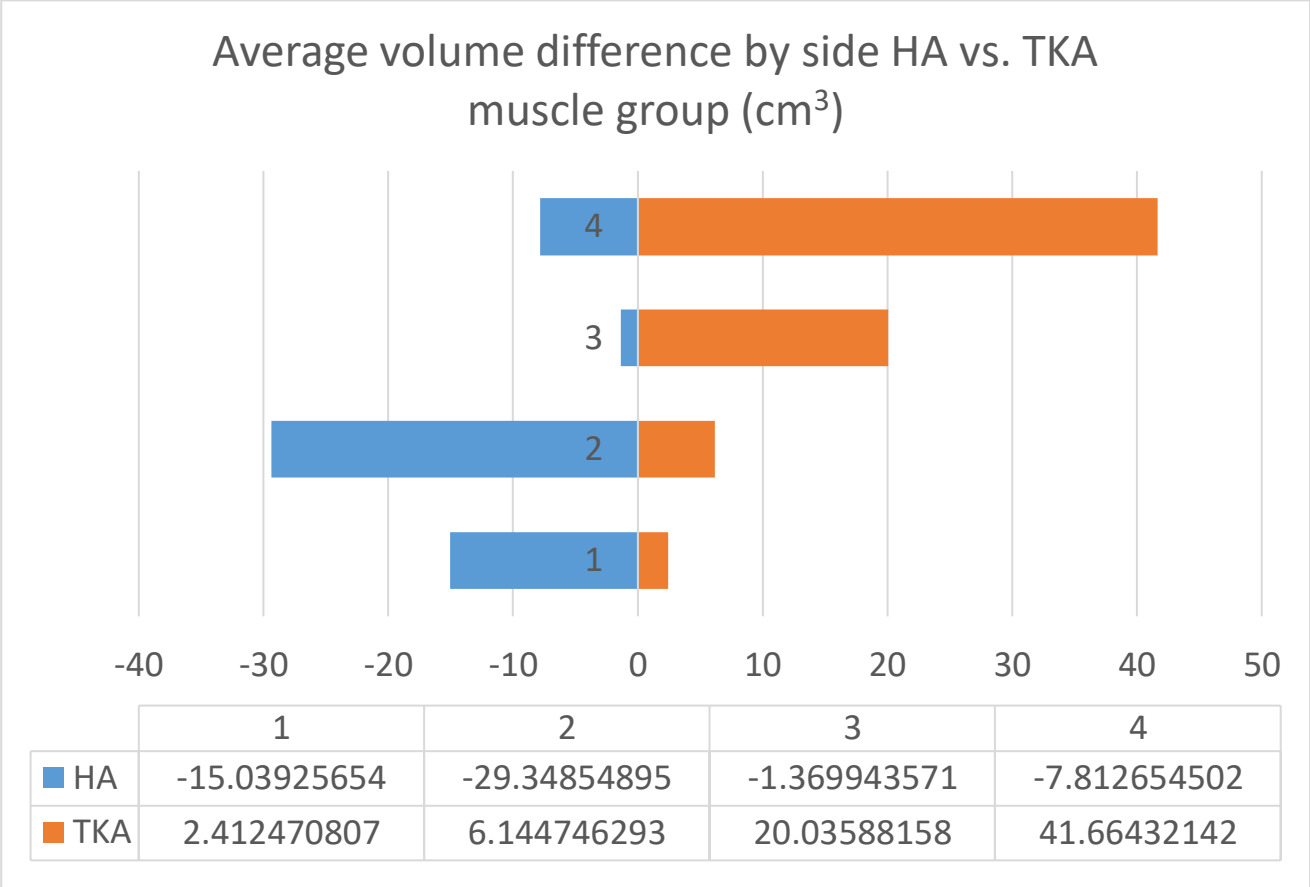
Fig. 10



	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
HA	-17	-11	30.8	-7.4	11.3	-104	-5.6	-217	-78	102	61.3	35.6	-65	-71	-61	99
TKA	-53	-18	-68	72.8	-86	19.2	38.9	120	-78	-343	285	10.2	-5	123	77.6	29.9

1. Biceps femoralis caput breve
2. Biceps femoralis caput longum
3. Gracilis
4. Popliteus
5. Sartorius
6. Semimembranosus
7. Semitendinosus
8. Gluteus maximus
9. Gluteus medius
10. Gluteus minimus
11. Iliacus
12. Psoas
13. Rectus femoris
14. Vastus intermedius
15. Vastus lateralis
16. Vastus medialis

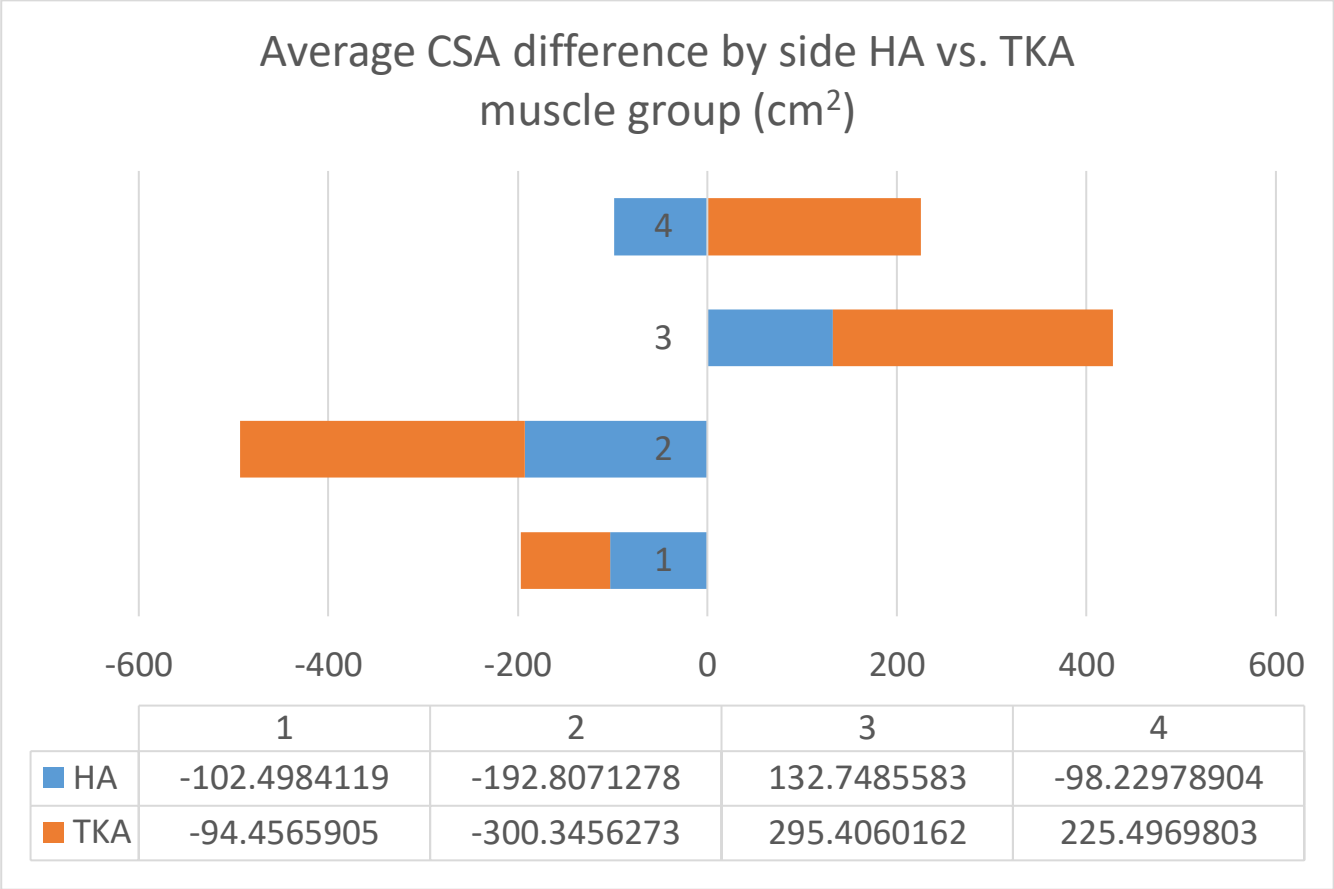
Fig. 11



	1	2	3	4
HA	-15.03925654	-29.34854895	-1.369943571	-7.812654502
TKA	2.412470807	6.144746293	20.03588158	41.66432142

1. Knee flexors
2. Gluteal muscles
3. Iliopsoas
4. Knee extensors

Fig. 12



	1	2	3	4
HA	-102.4984119	-192.8071278	132.7485583	-98.22978904
TKA	-94.4565905	-300.3456273	295.4060162	225.4969803

1. Knee flexors
2. Gluteal muscles
3. Iliopsoas
4. Knee extensors

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