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Orbital Anatomy:

Optic Nerve and Retrobulbar Circulation

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Resumo

Introdução: A anatomia imagiológica do compartimento retrobulbar da órbita, nomeadamente do complexo bainha-nervo óptico e da artéria oftálmica, permite avaliar a dinâmica de fluidos do sistema nervoso central, o que pode ser útil no diagnóstico de patologias como o glaucoma ou a hipertensão intracraniana. A ultrassonografia é um método imagiológico com muitas vantagens, mas a sua aplicação ao estudo da anatomia retrobulbar no cadáver humano e comparação direta com dissecção anatómica nunca foi realizada.

Objetivo: Fazer uma revisão da literatura sobre a anatomia retrobulbar, seguida da caracterização das estruturas neurovasculares em disseção anatómica. Estudar ecograficamente a anatomia retrobulbar em cadáver, para correlação com os achados da disseção anatómica e aferição da precisão da ecografia na avaliação do compartimento retrobulbar.

Materiais e métodos: Efetuamos uma revisão das estruturas anatómicas presentes no compartimento retrobulbar, de modo a determinar as características fundamentais do nervo óptico e da artéria oftálmica. Procedemos à realização de duas disseções em cadáveres humanos, com o objetivo de integrar os achados com a anatomia macroscópica observada nas dissecções. Aplicamos, ainda, a técnica ecográfica em cadáver, com o intuito de estudar o compartimento retrobulbar.

Resultados: Os nervos ópticos apresentaram um trajeto posteromedial ao longo da órbita, desde o globo ocular até à entrada no canal óptico. Os segmentos retrobulbares intra-orbitais dos nervos encontravam-se envolvidos por uma bainha meníngea, com 5mm de diâmetro, quando medidos a uma distância de 3mm posteriormente ao globo ocular. A artéria oftálmica apresentou-se inferior e lateralmente ao nervo óptico na porção proximal da órbita, antes de cruzar o nervo superiormente. Ao longo do seu trajeto, observaram-se vários ramos colaterais da artéria, entre os quais, a artéria central da retina. A artéria central da retina perfurou a bainha do nervo óptico a 5mm do globo ocular, acompanhando a trajetória do nervo até à retina. O estudo ecográfico não permitiu a obtenção de imagens de leitura ou medições da bainha do nervo óptico.

Conclusão: Uma melhor compreensão da anatomia neurovascular do espaço retrobulbar poderá contribuir para a otimização de métodos de diagnóstico que permitem a avaliação da dinâmica de fluidos do sistema nervoso central.

Palavras-chave: anatomia; nervo óptico; circulação retrobulbar; ecografia.

Abstract

Introduction: The imagological anatomy of the retrobulbar compartment of the orbit, namely of the complex sheath-optic nerve and ophthalmic artery, allows to evaluate central nervous system fluid dynamics, which can be useful in the diagnosis of conditions such as glaucoma or intracranial hypertension. Ultrasonography is an imaging method with numerous advantages, but its application to study the retrobulbar anatomy in human cadaver and directly compare it with anatomical dissection has never been performed.

Objectives: Review of the literature on the retrobulbar anatomy, followed by a characterization of the neurovascular structures in anatomic dissection. Ultrasonographic study of the retrobulbar anatomy in cadaver, to correlate with the dissection findings and assess the accuracy of ultrasound in the evaluation of the retrobulbar compartment.

Materials and methods: We revised the anatomical structures in the retrobulbar compartment in order to establish the foundation characteristics of the optic nerve and ophthalmic artery. We also performed two human cadaver dissections to integrate these findings with the macroscopic anatomy observed at dissection. We applied the ultrasonographic technique on cadaver, to study the retrobulbar compartment.

Results: The optic nerves had a posteromedial course in the orbit, from the eyeball until reaching the optic canal. Their intra-orbital retrobulbar segment were surrounded by a meningeal sheath, which at a distance of 3mm posterior to the globe had a diameter of 5mm. The ophthalmic artery was located on the inferolateral aspect of the optic nerve in the proximal part of the orbit, before crossing the optic nerve superiorly. Throughout the artery's trajectory, numerous branches of the ophthalmic artery arouse, among which the central retinal artery. The central retinal artery perforated the optic nerve sheath at a depth of 5mm behind the globe and accompanied the optic nerve's trajectory to the retina. The sonographic study did not allow the obtention of readable images nor measurements of the optic nerve sheath.

Conclusion: A better understanding of the neurovascular anatomy of the retrobulbar space could contribute to the optimization of the diagnostic methods that allow the evaluation of fluid dynamics in the central nervous system.

Keywords: anatomy; optic nerve; retrobulbar circulation; ultrasound.

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Introduction

The retrobulbar space is the area within the orbit that lies posterior to the globe (Salgado-López, Campos-Leonel, Pinheiro-Neto, & Peris-Celda, 2020). It contains important neurovascular structures, therefore requiring a thorough comprehension of its anatomy.

The optic nerve is responsible for the transmission of visual information. It carries sensory nerve impulses from the retina through afferent fibers. After emerging from the posterior surface of the eye, the nerve follows its course in the posterior portion of the orbit and exits it through the optic canal. Intracranially, the optic nerve from each eye comes together forming the optic chiasm, from where the nerve fibers travel in optic tracts to the visual centres in the brain (Salazar, et al., 2018).

The main vascular structure of the region is the ophthalmic artery, which provides blood supply to the orbit. It is an intracranial branch of the internal carotid artery, which enters the orbit through the optic foramen, transversing through the optic canal alongside the optic nerve. In the retrobulbar space, the ophthalmic artery gives off several ocular and orbital branches (Michalinos, Zogana, Kotsiomitis, & Maz, 2015).

The assessment of the retrobulbar circulation and the optic nerve is useful to evaluate fluid dynamics in the central nervous system (CNS), extrapolating information about intracranial pressure. It can be used to assist in the diagnosis of diseases, such as glaucoma (Pinto, Vandewalle, Willekens, Marques-Neves, & Stalmans, 2014) or intracranial hypertension (Golshani, Zadeh, Farajzadegan, & Khorvash, 2015).
Magnetic Resonance (MR) and Computed Tomography are good imaging methods to evaluate the anatomy of the optic nerve sheath and retrobulbar circulation, however they are expensive, not always available and have some contraindications. Ultrasonography (US) is an alternative and easily accessible technique, that can be performed at the bedside of the patient and have no major drawbacks. Therefore, imaging tests providing an accurate evaluation of structures in the retrobulbar compartment, such as ultrasonography with Doppler waveform may be relevant to

clinical practice (Munawar , et al., 2019). However, it is not known if the measurements performed by US are directly comparable to the ones measured by MR or classic anatomical techniques.

The present work aims to characterize the anatomy of the retrobulbar space in the cadaver and compare it with the anatomy evaluated by US in the same specimen.

This work is the first part of a larger and comprehensive project aiming to assess the reliability and validity of retrobulbar compartment ultrasound as a method to evaluate intracranial pressure in vivo.

Objectives

- Bibliographic review of retrobulbar anatomy.
- Orbital dissection with anatomical characterization of the optic nerve and retrobulbar circulation.
- Assessment of the ultrasound accuracy in the evaluation of retrobulbar structures in the same specimen.
- Correlation of cadaver anatomical findings with literature review.

Material and Methods

Material

Two frozen cadaver heads from normal adults, without history of vascular or neurologic disease were dissected. The human cadavers were donated to the Anatomy Department for scientific research, according to ethical and Portuguese law requirements.

Equipment

- Dissection instruments: dissection tray, dissecting scissors, scalpel handle, scalpel blade, electric bone saw, dissecting forceps, bone retractor.
- Measuring instruments: caliper, ruler
- GE Healthcare LOGIQ compact ultrasound system
- Digital photography camera
- Computer with software appropriate to storage and processing of the digital images

Methods

i) Revision of retrobulbar anatomy

- A bibliographic search in PubMed was conducted for studies on optic nerve and ophthalmic artery anatomy. Terms used were “optic nerve”, “optic nerve sheath diameter”, “optic nerve sheath diameter ultrasound”, “ophthalmic artery” and “doppler waveform ocular blood flow”. Results were selected based on relevance, used methodologies and publication date. Moreover, we complemented our bibliographic search by resorting to a neuroanatomy medical book.
- The retrobulbar anatomy and key neurovascular structures were characterized, by describing the optic nerve sheath and retrobulbar circulation (ophthalmic, central retinal and posterior ciliary arteries).

ii) Dissection of the orbit

- The frozen cadaver heads were prepared and positioned in vertical position at 90º degrees. Then the dissection was conducted by opening the skulls through a transverse craniectomy. The orbital roof was exposed and then removed, enabling the visualization of the orbit and its structures. In the course of the dissection, the optic nerve and the ophthalmic, central retinal and posterior ciliary arteries were identified and their anatomy was carefully noted. Then, measurements of the optic nerve sheath diameter at a depth of 3mm behind the eye globe were performed. The findings were recorded by a digital camera.

iii) Comparison of cadaver anatomical findings with literature description

- Anatomical findings from the cadaver dissection were compared with the literature description. The images obtained in the dissection were cross-reviewed with the content selected in section i in order to substantiate and illustrate the neuroanatomy of the retrobulbar compartment.

iv) Assessment of the ultrasound accuracy in the evaluation of retrobulbar structures

- Ultrasonography was performed in the second cadaver, with a GE Healthcare LOGIQ compact ultrasound system, following a similar protocol to previous studies on retrobulbar ultrasonography (Stalmans, et al., 2011). The optic nerve sheath diameter was assessed in B-scan mode and measured 3mm behind the eye globe.

Results

• Revision of retrobulbar anatomy

a) Optic Nerve

The optic nerve, second of twelve paired cranial nerves, is formed as over one million axons of ganglion cells exit the retina through the optic disc.

The nerve is an extension of the central nervous system and it is sheathed by the meningeal layers and, therefore, by the cerebrospinal fluid that circulates in the subarachnoid space (Hayreh S. S., 1984). Measurements of the optic nerve sheath diameter are widely variable in the literature, ranging between 3.57-4.7 and 4.6-6.4mm, measured 3mm posterior to the globe by ultrasonography (Chen, et al., 2019; Bäuerle, et al., 2013).

Based on its trajectory, the optic nerve can be divided in four segments:

<u>Intraocular segment</u>

The short intraocular course of the optic nerve (1mm) extends from the optic disc to the posterior margins of the sclera (Salazar, et al., 2018). In this portion, the nerve fibers are unmyelinated.

<u>Intraorbital segment</u>

The intraorbital optic nerve extends from the posterior part of the eye to the optic canal (25-30mm), taking a posteromedial course (Salazar, et al., 2018). When the nerve pierces the lamina cribrosa and enters the orbit, its nerve fibers become myelinated. Additionally, this portion of the nerve also becomes surrounded by the three meningeal layers, forming its sheath (Hayreh S. S., 2011). As the nerve approaches the optic canal, it relates to the tendinous annulus of Zinn, oculomotor, abducent and nasociliary nerves and ophthalmic artery.

Intracanalicular segment

The optic nerve enters the optic canal and runs alongside the ophthalmic artery throughout its intracanalicular course (4-10mm) (Salazar, et al., 2018). This portion of the nerve maintains its three-layer meningeal sheath.

Intracranial segment

The optic nerve passes through the optic foramen to follow its intracranial course (10mm) (Salazar, et al., 2018). It runs posteromedially, reaching the suprasellar space in the middle cranial fossa, where it merges with the contralateral optic nerve to form the optic chiasma. In this segment, the optic nerve lies superomedial to the ophthalmic artery, medial to the internal carotid artery and inferior to the anterior cerebral artery. The pia mater is the only meningeal layer sheathing the optic nerve in the cranial cavity.

In the optic chiasma, the nerve fibers from the nasal field of each retina cross the midline and enter the contralateral optic tract, while the fibers from the temporal field of each retina do not decussate and continue in the ipsilateral optic tract.

The optic tracts emerge from the optic chiasma and pass posterolaterally around the cerebral peduncle. Most of these fibers will continue to the lateral geniculate body of the thalamus, to synapse on the dorsal lateral geniculate nucleus. A small portion of these fibers will terminate in the pretectal nucleus and the superior colliculus.

The fibers that leave the lateral geniculate body form the optic radiation (geniculocalcarine tract), which subsequently terminate in the visual cortex (Brodmann area 17), in the occipital lobes (Snell, 2010).

b) Ophthalmic Artery

The ophthalmic artery is the first major branch of the internal carotid artery, which arises after the latter pierces the dura and emerges from the cavernous sinus, medial to the anterior clinoid process. It usually originates from the superomedial or anteromedial walls of the internal carotid artery (Michalinos, Zogana, Kotsiomitis, & Maz, 2015), with a diameter between 0.7 and 1.4mm (Hayreh S. S., 1963).

Origin variations of the ophthalmic artery have been described, the most common being the medial meningeal artery and the cavernous segment of the internal carotid artery (Toma, 2016).

Based on its course, the ophthalmic artery can be divided in three segments:

Intracranial segment

The ophthalmic artery follows a short intracranial course (0.5-9.5mm) (Michalinos, Zogana, Kotsiomitis, & Maz, 2015), from its origin until it enters the optic canal. This portion of the artery usually lies in the subdural space (Hayreh S. S., 2006) and closely relates to the internal carotid artery and the inferior aspect of the optic nerve.

Intracanalicular segment

The ophthalmic artery enters the optic canal, usually inferior to the optic nerve. During the intracanalicular course (5-7mm) (Michalinos, Zogana, Kotsiomitis, & Maz, 2015), the artery pierces the outer dura layer of the sheath surrounding the optic nerve and reaches the distal part of the optic canal situated inferolateral the optic nerve, lying between the dural layers. The intracanalicular ophthalmic artery sends small branches to the intracanalicular optic nerve through fibrous bands connecting the dural sheath to the optic nerve (Hayreh S. S., 2006).

Intraorbital segment

The ophthalmic artery enters the orbit, lying inferolateral to the optic nerve in its proximal segment. Afterwards, it crosses the optic nerve superiorly (83%) or inferiorly (17%) (Hayreh & Dass, 1962) and proceeds along the medial side of the orbit. The intraorbital course of the ophthalmic artery (13-20mm) ends near the upper medial edge of the orbit, as the artery divides into its terminal branches (Michalinos, Zogana, Kotsiomitis, & Maz, 2015).

Throughout its intraorbital path, the ophthalmic artery gives off numerous branches: central retinal artery, posterior ciliary arteries, lacrimal artery, muscular branches, ethmoidal arteries, palpebral arteries, supraorbital artery, dorsal nasal artery, and frontal artery. Branching patterns of the intraorbital ophthalmic artery are, however, extremely variable.

The main retrobulbar branches of the ophthalmic artery are the central retinal artery and the posterior ciliary arteries.

The central retinal artery is usually the first branch of the ophthalmic artery. It runs along the inferior aspect of the optic nerve, before piercing the optic sheath (5-15mm behind the globe) and proceeding to the center of the nerve (Semmer, McLoon, & Lee, 2010). During its course, the artery supplies blood to the surrounding nerve and runs anteriorly to enter the retina, where it divides into terminal branches to supply the retina.

The posterior ciliary arteries exist in variable number and, according to their position, are termed medial or lateral. There are two long ciliary arteries, lateral and medial, that run along either side of the globe to supply the ciliary muscle, iris, and the choroid. And multiple short ciliary arteries, usually arising from the division of two to three bigger trunks, that pierce the sclera to supply the choroid and the optic nerve head (Semmer, McLoon, & Lee, 2010).

Ultrasonography is currently one of the standard methods used to approach the retrobulbar region. Being a non-invasive, radiation-free, portable and easily affordable tool, it can be significantly advantageous in the clinical practice. Orbital ultrasounds allow the evaluation of the optic nerve and several studies have suggested that sonographic optic nerve sheath diameter measurements correlate with elevated intracranial pressure (Munawar , et al., 2019; Blaivas, et al., 2003). Additionally, Doppler waveform allows evaluation of blood flow through vessels, contributing to the diagnosis of diseases such as glaucoma and diabetic retinopathy (Stalmans, et al., 2011; Pinto, et al., 2014).

There is, nonetheless, a lack of studies correlating retrobulbar anatomic details with ultrasound findings. Two previous studies performed ultrasound evaluations of the optic nerve sheath in cadavers, however they either lacked dissection confirmation of sonographic studies (Steinborn, et al., 2011) or directly assessed extracted specimens of the nerve, instead of applying a transbulbar approach in integral skulls, which entailed significant manipulation of the optic nerve (Hansen & Helmke, 1996).

- **<u>Dissection of the orbits</u>**

The dissections were carried out in two stages.

i) First dissection stage:

The first session was performed in a frozen cadaver head, in which the real anatomy of the intraorbital part of the optic nerve was studied. From the point where it pierced the posterior aspect of the eye and entered the retrobulbar space, the optic nerve, enveloped by its sheath, followed a posterior and medial course until reaching the optic canal (Figure 1).

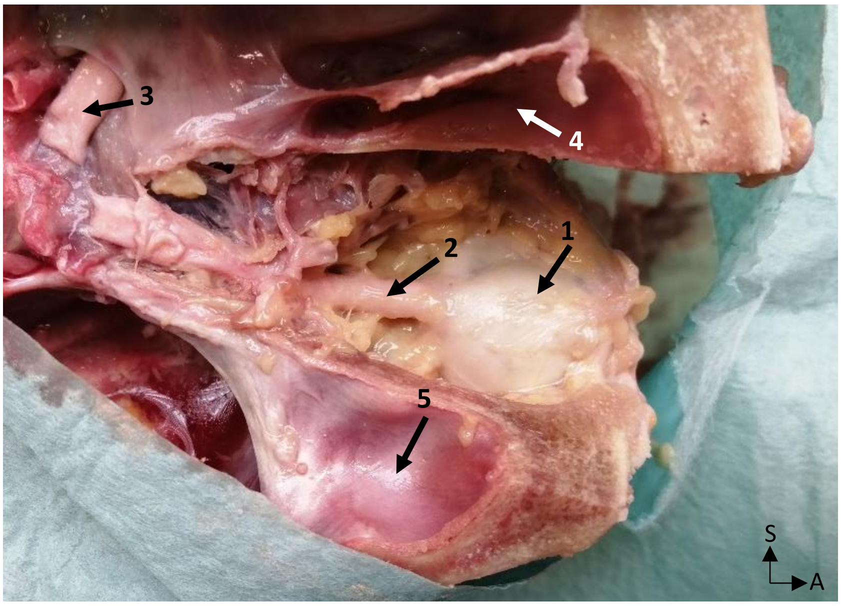

Figure 1 – Superior view of the right orbit. 1 - eye globe; 2 – intraorbital optic nerve; 3 – optic nerve (contralateral); 4 – orbital roof; 5 – maxillary sinus

ii) Second dissection stage:

The second session was performed in a second frozen cadaver head, in which the intraorbital ophthalmic artery and its branches were studied. The ophthalmic artery entered the orbit inferior and laterally to the optic nerve and followed a short anterior course until superiorly crossing the nerve and proceeding its trajectory anteromedially throughout the orbit (Figure 2). The central retina artery was identified, following a course inferiorly to the optic nerve, piercing afterwards the optic nerve sheath 5mm behind the eyeball (Figure 3). Several branches of the ophthalmic artery were observed in the retrobulbar area, however due to the abundance of orbital fat, it was not possible to accurately identify them.

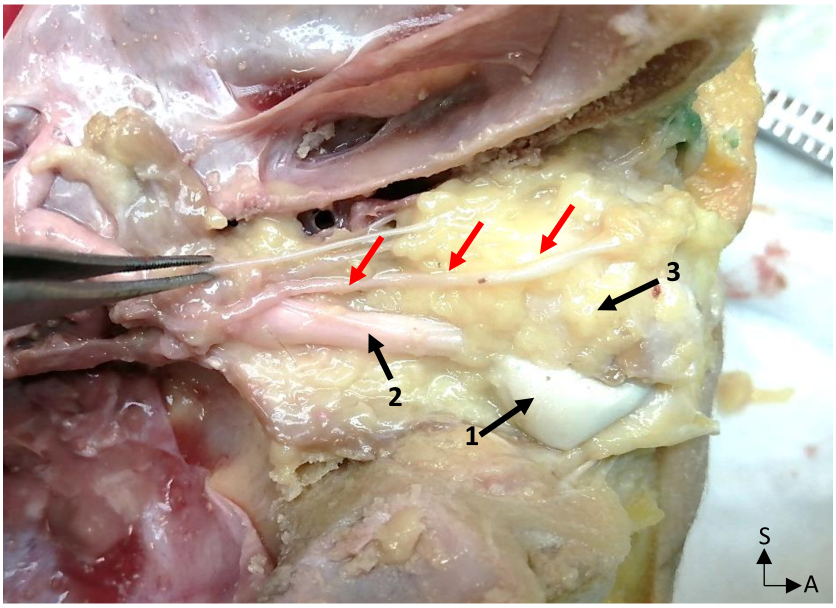

Figure 2 – Right intraorbital ophthalmic artery (red arrows). 1 - eye globe; 2 – intraorbital optic nerve; 3 – intraorbital fat

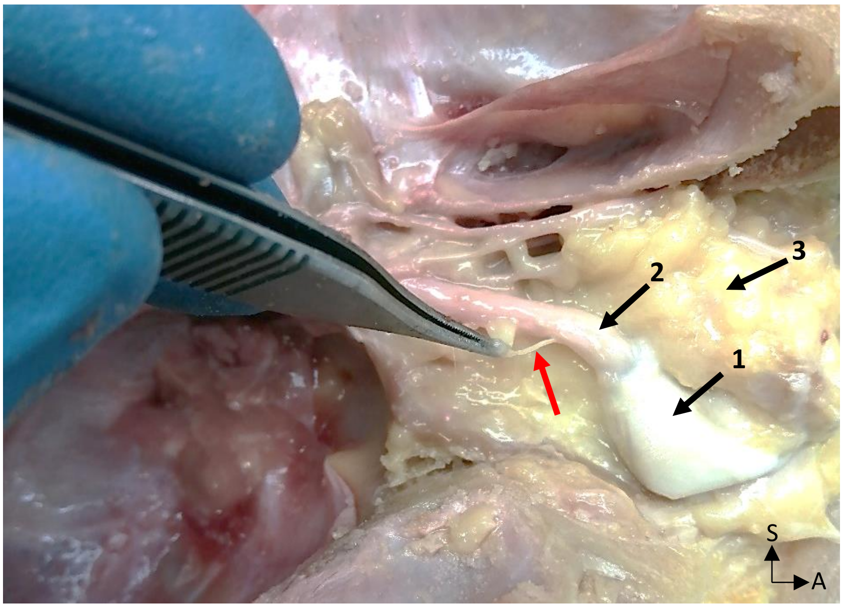

Figure 3 – Right central retinal artery (red arrow). 1 - eye globe; 2 – intraorbital optic nerve; 3 – intraorbital fat

Measurement of the optic nerve sheath diameter:

Optic nerve sheath diameter measurements were performed at a depth of 3 mm behind the eye globe. In both specimens the diameter values were 5mm (Figure 4).

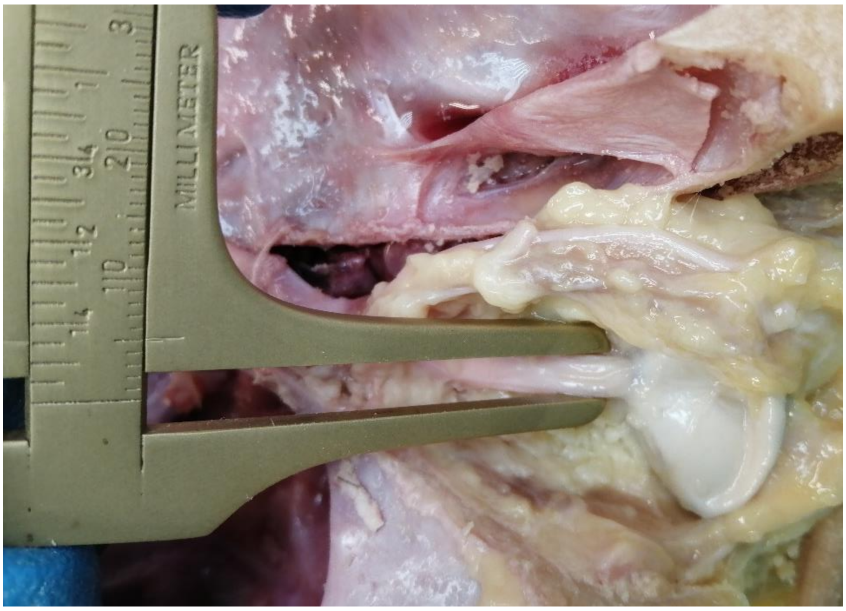

Figure 4 – Measurement of the optic nerve sheath diameter

- **<u>Orbital ultrasonography</u>**

The orbital ultrasonography was carried out through a transbulbar approach. The ultrasound probe was placed on the closed upper eyelid, using ultrasound gel, and different probe positions were attempted.

Acquisition of readable ultrasound imagens was not possible, presumably due to tissue dehydration and distortion of integrity, resultant to the cadaver conservation method.

This sonographic study was conducted under the restrictions associated to the COVID-19 pandemics, which limited the number of available specimens and extended the cadaver's conservation time. Analysis of fresher specimens could lead to a better preservation of tissue's characteristics and eventually allow the obtention of sonographic results.

Discussion

The optic nerve and the ophthalmic artery are the main neurovascular structures found in the retrobulbar space and their thorough anatomical knowledge is extremely relevant for the clinical approach of the several conditions.

Our exploratory dissection study allowed to establish a comparative analysis between the real anatomy observed in human cadaver and the literature. Assessing the optic nerves, we found a high correspondence with literature descriptions (Salazar, et al., 2018; Hayreh S. S., 2011), with the nerves emerging from the eye globe and following a posteromedial course until the optic canal. We also performed measurements of the optic nerve sheath diameters at a depth of 3mm behind the eye globes, which were found to measure 5mm in both specimens. It is, however, predictable that the obtained values are slightly inferior to the real ones (measured *in vivo*), considering the absence of cerebrospinal fluid circulation in the *post mortem*. Nevertheless, our results are within the range of values found in the literature, which varied between 3.57-4.7 and 4.6-6.4mm, in sonographic evaluations (Chen, et al., 2019; Bäuerle, et al., 2013).
Our results also corroborate previous studies of the ophthalmic artery's intraorbital course (Hayreh & Dass, 1962), with our findings showing the artery entering the orbit inferolateral to the optic nerve and then crossing it superiorly towards the medial wall of the orbit. Throughout its trajectory, numerous branches of the ophthalmic artery arouse, among which the central retinal artery. In our findings, the central retinal artery's course is also analogous to the literature, running along the inferior aspect of the optic nerve until penetrating the nerve's sheath, which occurred 5mm posterior to the globe.

We found insurmountable obstacles during the performance of the orbital ultrasound in the cadaver, that did not allow the assessment of the optic nerve and its sheath as initially proposed. The present study was affected by the contingency measures applied in the context of the COVID-19 pandemics, which delayed the practical procedures and resulted in an extended period of the cadaver head's conservation time before our analysis. These factors are presumably responsible for the anatomical distortion and tissue dehydration that interfered with the application of the ultrasonographic method. Moreover, for the same epidemiologic constraints, our sample size was very limited due to the restrictions in the process of body donation to the Anatomy Department, which also contributed to our lack of results. A larger sample size could allow the existence of fresh specimens in eligible conditions to our sonographic study.

Despite the faced obstacles and the limited outcomes, we consider that our study design would provide new valuable information. To our knowledge, no previous studies of ultrasound in cadaver to evaluate the retrobulbar neurovascular structures followed by direct confirmation through anatomical dissection were conducted, which could be useful to provide evidence of the ultrasound as a reliable method to assess the retrobulbar compartment. The validation of this technique in the cadaver is the first part of a larger ongoing study that aims to assess the reliability and validity of retrobulbar compartment ultrasound as a method to evaluate intracranial pressure in vivo.

Limitations of the study

Our study has some potential pitfalls. The anatomical study was conducted in frozen cadaver heads, which carry some limitations inherent to the specimen conservation process that have influenced tissue characteristics, leading to loss of anatomical fidelity. In particular, the removal of the brain and meninges during the dissection, compromises the integrity of the subarachnoid space and subsequently of the optic nerve-sheath measurement. We expect this may have underestimated our measurements and reduced our accuracy. Also, the conservation process may have been a contributing factor to our inability to perform ultrasonography of the optic nerve as initially proposed, which limited the outcomes of the study and anatomical-imaging correlation. Additionally, the low sample size does not provide the statistical power to independently draw our own conclusions about retrobulbar anatomy. Further studies conducted in specimens with a shorter period of elapsed time between death and the analysis, as well as larger samples sizes are necessary to confirm the obtained results and to provide the additional information that lacks in this study.

Conclusion

We have detailed the anatomy of the retrobulbar compartment and highlighted its relevance in clinical practice. Our results showed a high correspondence of real anatomy in the cadaver with literature, in particular regarding the optic nerve and the ophthalmic artery trajectory and relations. Our findings on the optic nerve sheath diameter, although probably underestimated due to the disruption of the subarachnoid space, also support the literature suggesting normal diameters around 5mm. We were, however, not able to demonstrate the adequacy of the ultrasound as a method to assess the retrobulbar compartment in our sample.

Considering the clinically relevant information that these neurovascular structures may relay about the fluid dynamic of the central nervous system and intracranial pressure, further studies are needed to optimize diagnostic methods based on their assessment, namely the normal cut-off values for optic nerve sheath diameter.

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