New insights into tip supporting structures. Consequences for nasal surgery*

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Abstract

Background: Knowledge of tip supporting structures is crucial for successful rhinoplastic surgery. The aim of this study was to provide detailed anatomical and histological descriptions of the tip supporting structures.

Methods: Serial coronal sections of the entire external noses from seven cadavers were studied after staining by Mallory-Cason and Verhoeff-Van Gieson procedures.

Results and conclusions: We found no histological evidence of ligaments between the cartilaginous- and bony parts of the nasal skeleton, and between the skin and the nasal skeleton. Instead, we found a perichondrial-periosteal lining within the soft tissue envelope. The main tip supporting and shaping structures are: septal and lobular cartilages, premaxillae, and the soft tissue envelope including the periosteal-perichondrial envelope/membrane. These findings may have clinical relevance in functional and aesthetic rhinoplasties.

Key words: tip, perichondrium, periosteum, rhinoplasty, septum

Introduction

The nasal tip is one of the most prominent parts of the nose. It consists of two lobular cartilages (also named lower lateral cartilages), interdomal connective tissue, overlying skin with subcutaneous connective tissue and vestibular epithelial lining. Functionally, the nasal tip influences breathing as it is closely related to the nasal valve region and it provides a flexible transition between the outer world and the skull. Aesthetically, the shape and position of the nasal tip contribute to the appearance of the nose and rest of the face.

The lobular cartilages are connected to the anterior nasal spine, the septal cartilage, the triangular cartilages (also named upper lateral cartilages) and the overlying soft tissue envelope. Probably all these structures are involved in the stability, the position and shape of the nasal tip and therefore of great importance in rhinoplastic surgery. If tip support fails due to trauma, aging or surgery, in most cases the tip will de-project en de-rotate. This will have a negative effect on both the function of the nose and aesthetics. Therefore, precise knowledge of tip supporting structures is crucial. However, despite several studies in the past, the exact mechanisms are still not fully understood. Several anatomical studies identified tip supporting structures.

Janeke and Wright [(1)] identified: 1) the scroll junction between upper lateral cartilages (ULCs) and lower lateral cartilages (LLCs); 2) the lateral sesamoid cartilage complex; 3) the junction between medial crura and caudal septum; and 4) the interdomal sling.

Tardy et al. [(2)], distinguished: major tip support, i.e. 1) the intrinsic integrity of the alar cartilages; 2) attachement of the medial crural footplates to the caudal septum; and 3) the scroll junction between the upper lateral and lower alar cartilages; and minor tip support, i.e. 1) the interdomal sling, 2) sesamoid attachment to the piriform aperture. Additionally, more recently, among mi-

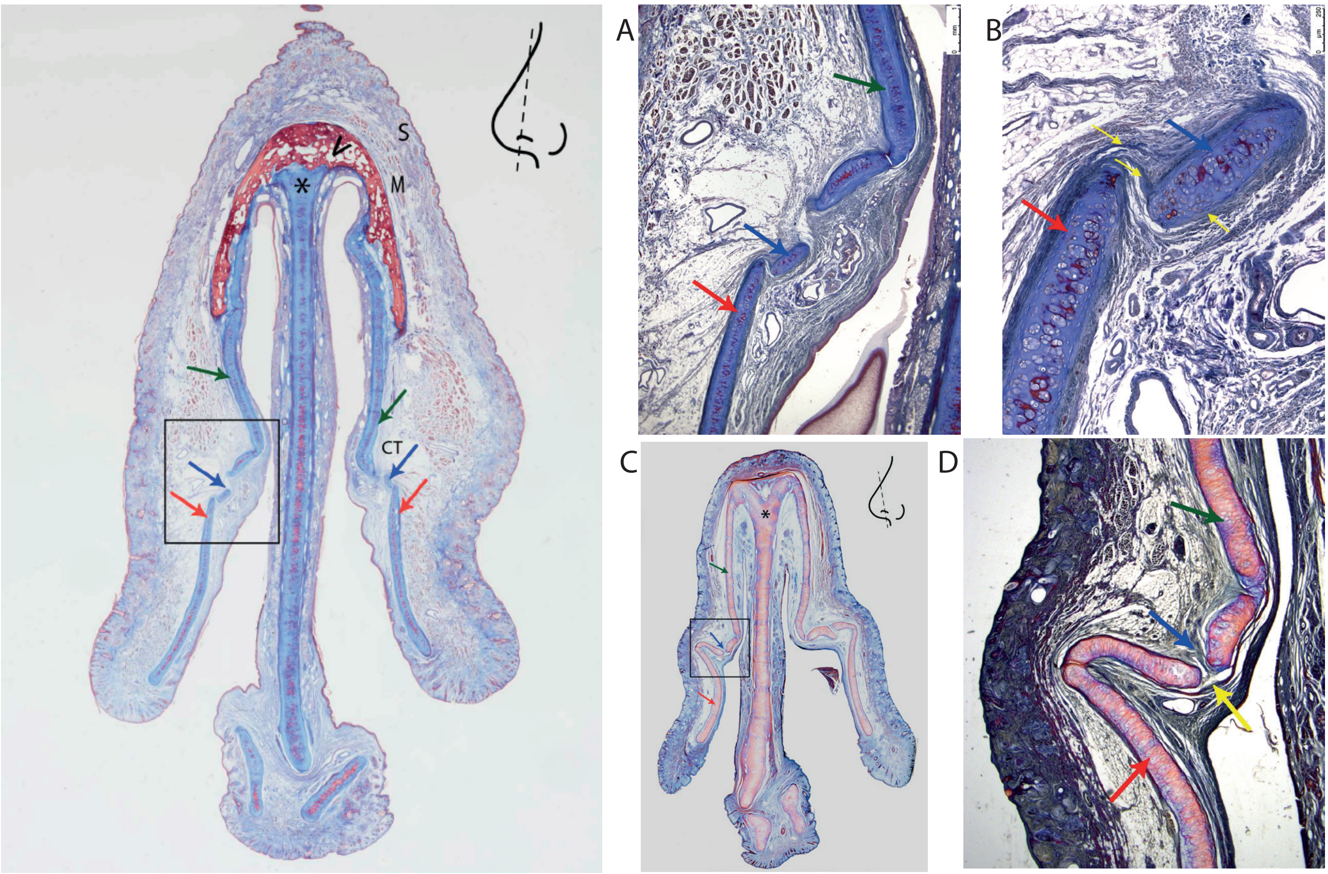

Figure 1. Overview of the external nasal pyramid (cranially) at the K-stone area, showing a connection between triangular cartilage and the lobular cartilage (rectangle), bony nasal vault (arrowhead), the septolateral cartilage (asterisk), triangular cartilage (green arrow), accessory cartilage at the scroll area (blue arrow), lobular cartilage, lateral crus (red arrow), and soft tissue envelope: S – skin, M – muscles, CT – loose connective tissue (specimen 1, Mallory-Cason staining). A) Higher magnification of Figure 1 (rectangle) showing the connection between triangular (green arrow), and lobular cartilage (red arrow) with an accessory cartilage (blue arrow). There is no additional ligament conneting these structures (1,25x). B) Higher magnification of A) showing the scroll area with an accessory cartilage (blue arrow) and lobular cartilage (red arrow) surrounded by perichondrial envelope (yellow arrow) (5x). C) Overview of the external nasal pyramid (caudally) showing the connection between triangular and lobular cartilage (blue arrow in the rectangle), the septolateral cartilage (asterisk), triangular cartilage (green arrow), lobular cartilage (red arrow), (specimen 2, Mallory-Cason staining). D) Higher magnification of Figure 1c with the scroll area (the black rectangle) and its overlying continuous perichondrium (yellow arrow), triangular cartilage (green arrow), lobular cartilage (red arrow). There are no ligaments between the triangular and lobular cartilages in the connection between triangular and lobular cartilage (1,25x).

nor supporting mechanisms, Nolst Trenité et al. also named: the strong ligamentous attachment of the skin to the interdomal region, the cartilaginous and membranous nasal septum, dorsal septum, the sesamoid complex extending the support of the lateral crura to the piriform aperture, the anterior nasal spine [3].

Above mentioned descriptions are based on gross anatomical dissections and experiences during surgery. Further studies [4,5] emphasized the consequences of these findings for rhinoplasty, including ligamentous suture techniques [6-10]. However, histological descriptions of tip supporting structures are limited [11,12].

In a previous article, we have reported on our microscopic studies of nasal cartilages and bones, their perichondrial-periosteal envelope, adjacent structures and consequences for nasal surgery [13]. Our present study, combined with rhinoplasty experiences, revise concepts based on numerous previous anatomical studies regarding structures that contribute to the stability of the nose and might thus be relevant for nasal surgery. The previous view on nasal tip support is not in line with our clinical observations during surgery. There is much emphasis put on the ligamentous structures that are difficult to identify intraoperatively, however claimed to support the tip [7-12]. Therefore, in order to obtain more predictable results in rhinoplasty and less complications, we need to redefine concepts in rhinoplasty that exist over the last two decades. Thus, the aim of our study was to provide precise and comprehensive anatomical and histological descriptions of the tip supporting structures.

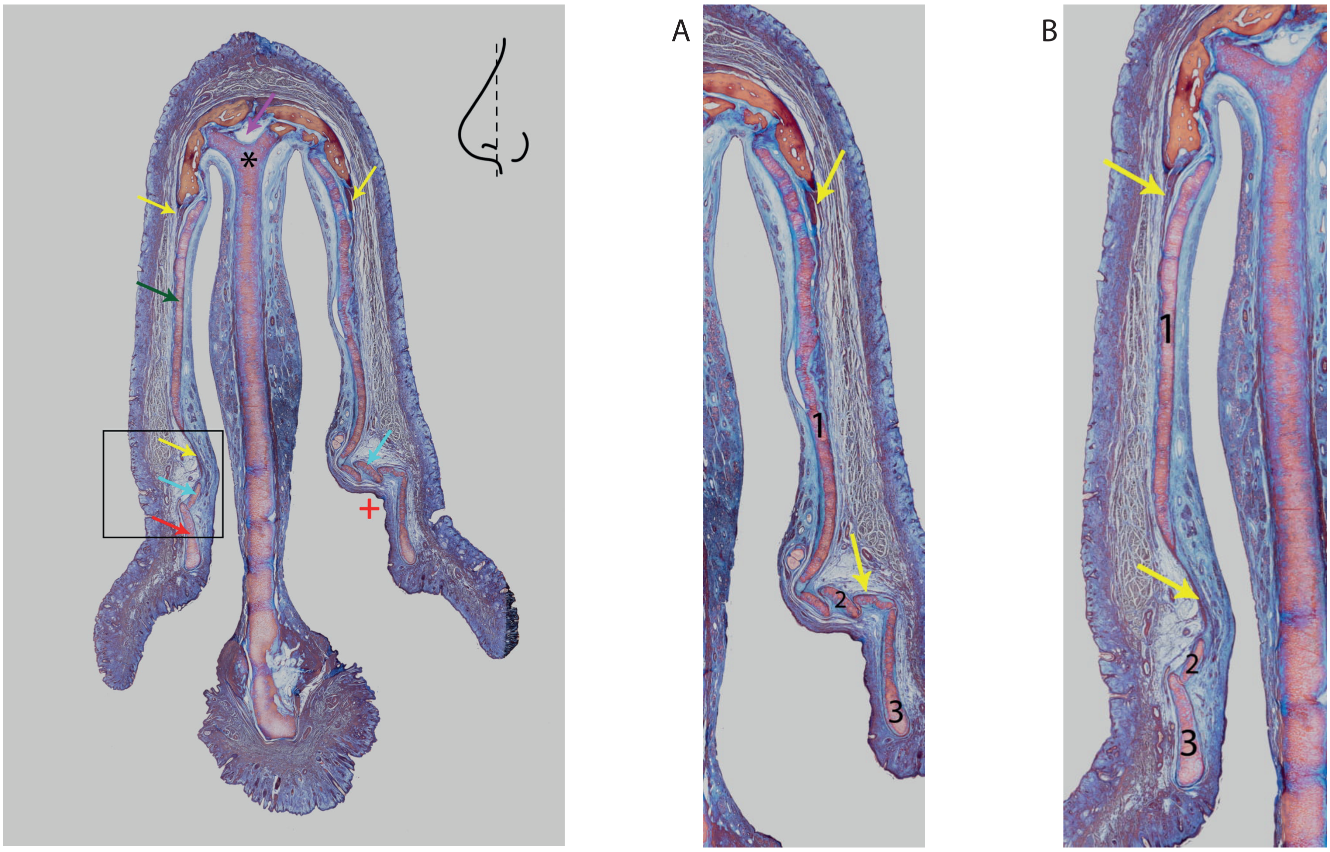

Figure 2. Overview of the external nasal pyramid with its periosteal-perichondrial covering (yellow arrows) of the bony and cartilaginous nasal vault. Note the underlay of the triangular cartilage (green arrow) under the nasal bones and the frontal processes of the maxilla, the subnasal triangular space (pink arrow), the septal cartilage having the shape of an Y-beam (asterisk), the sesamoid cartilages (blue arrow) in the hinge area (the black rectangle), and "a cul-de-sac" (red cross) (specimen 3, Mallory-Cason staining). A) B) Detail of Figure 2 demonstrating the thick periosteum (yellow arrow) of the nasal bones and frontal processes of the maxilla. The periosteum is continuous with the perichondrium (yellow arrow) of the triangular (number 1), sesamoid cartilages (number 2), and alar cartilage (number 3) (specimen 3, Mallory-Cason staining).

Material and methods

The external nose from seven male cadavers of Caucasian origin aged 58, 68, 75, 75, 80, 87, and 89 years was studied. On inspection, there were no signs of deformities of the external noses. Specific medical history, however, was unknown due to the patients' privacy policy. The specimens were preserved and fixed in 4% buffered formaldehyde, decalcified with sodium formiat solution, and then dehydrated in increasing concentrations of alcohol and embedded in paraffin. Serial sections of 10, 15, 20, 25µm thickness, depending on the amount of the bone in the particular section, were cut in the coronal plane at intervals of 200 and 400µm with Reichert-Jung Leica Tetrander: Large Section Microtome (Germany) and then mounted on glass slides and stained by:

1. Mallory-Cason trichrome staining which colors bone: orange; cartilage: varying shades of blue; muscle fibers: brownish-red; collagen: intense blue, orange; elastin: pale pink, pale yellow, or unstained.
2. Verhoeff-Van Gieson stain to distinguish between collagen and elastin fibers. With this staining collagen fibers stain pink to red, whereas elastin fibers stain intensely blue, grey to black.

Results

Our findings demonstrate the following components of tip supporting structures:

Lobular cartilages

Our findings depict lobular cartilages that consist of the medial crura, domes, and lateral crura (Figures 1-5). The triangular cartilage, lateral crura of the lobular cartilages, and accessory cartilage are connected by the periosteal-perichondrial envelope/membrane (Figures 1, 2). There is no scroll ligament inbetween. Furthermore, there is neither a junction between medial crura and caudal septum (Figures 3, 3a) nor an interdomal ligament (Figures 4, 4a) or an intercrural ligament (Figure 6). Likewise, the thin layer of periosteal-perichondrial envelope/membrane connects the lobular cartilage with the piriform aperture at the hinge area. There is no additional attachment of the lobular

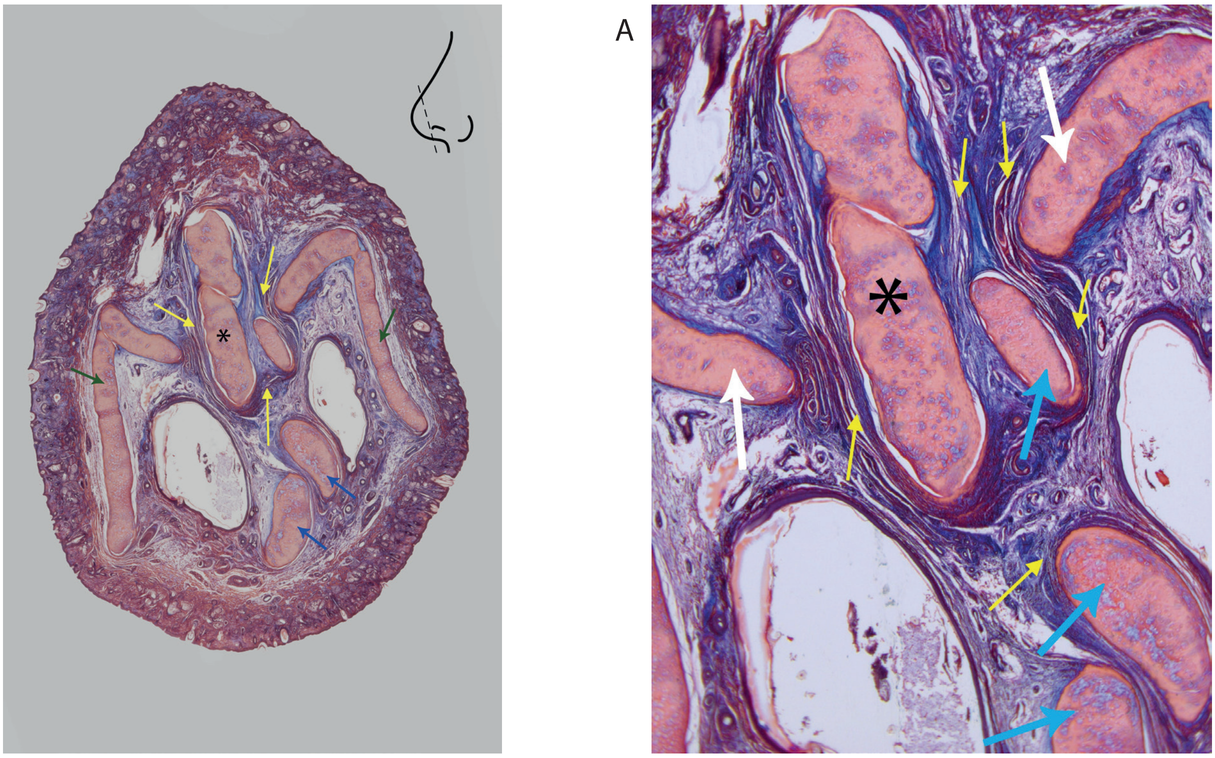

Figure 3. Overview of the nasal tip (at the supratip break) with lobular cartilages, its medial crura (blue arrow), lateral crura (green arrow), caudal septum (asterisk), and gliding planes of perichondrium (yellow arrow) (specimen 4, Mallory-Cason staining). A) Higher magnification of Figure 3 showing the area between the medial crura of the lobular cartilages and the caudal septum. Note the gliding planes of the perichondrium (yellow arrow) surrounding the individual cartilage, i.e. the septal cartilage (asterisk), the lobular cartilage: medial crura (blue arrow), domes (white arrow) (1,25x) (specimen 4, Mallory-Cason staining).

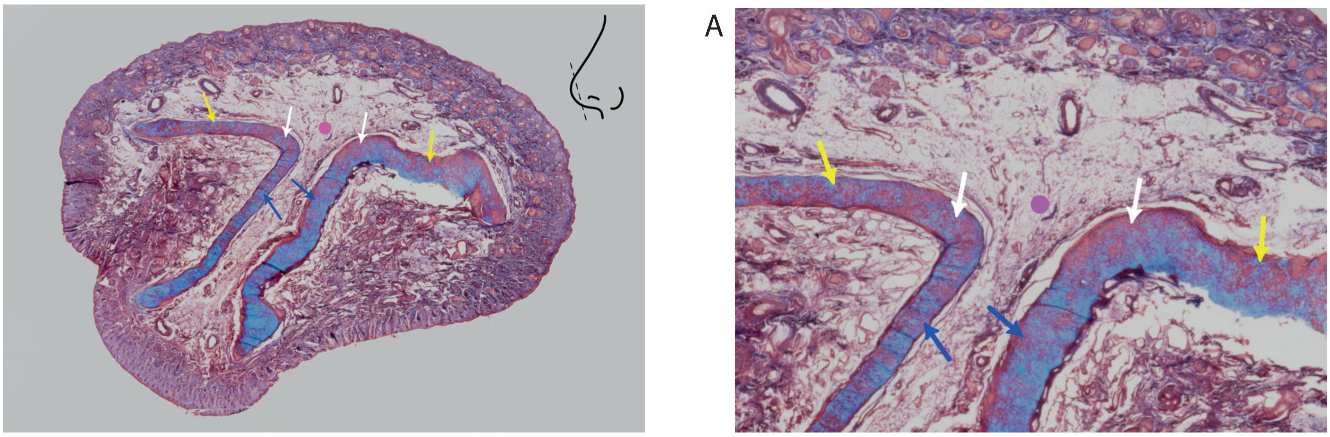

Figure 4. Overview of the nasal tip with the medial crura (blue arrow), domes (white arrow), lateral crura (yellow arrow) of the lobular cartilages, interdomal area (pink dot). There is no interdomal ligament, as has been suggested in the literature (specimen 5, Mallory-Cason staining). A) Detail of Figure 4 demonstrating the interdomal area (pink dot) filled with loose connective tissue, the medial crura (blue arrow), domes (white arrow), lateral crura (yellow arrow) of the lobular cartilages. There are no transverse fibers between the cartilages, no interdomal ligament (specimen 5, Mallory-Cason staining).

cartilage to the piriform aperture (Figures 5, and 5a-5e).

Soft tissue envelope and periosteal-perichondrial envelope/ membrane

Our study reveals the existence of a soft tissue envelope that consists of skin, muscles, and connective tissue (Figures 1-8). The soft tissue envelope overlies the bony and cartilaginous nasal vault that is covered by the periosteal-perichondrial envelope/ membrane (Figures 1, 2, and 5). The connective tissue between the muscles and the periosteal-perichondrial envelope/membrane is loose and therefore serves as a gliding plane (Figures 1, 2, and 4), whereas at the level of caudal margin of the septum it

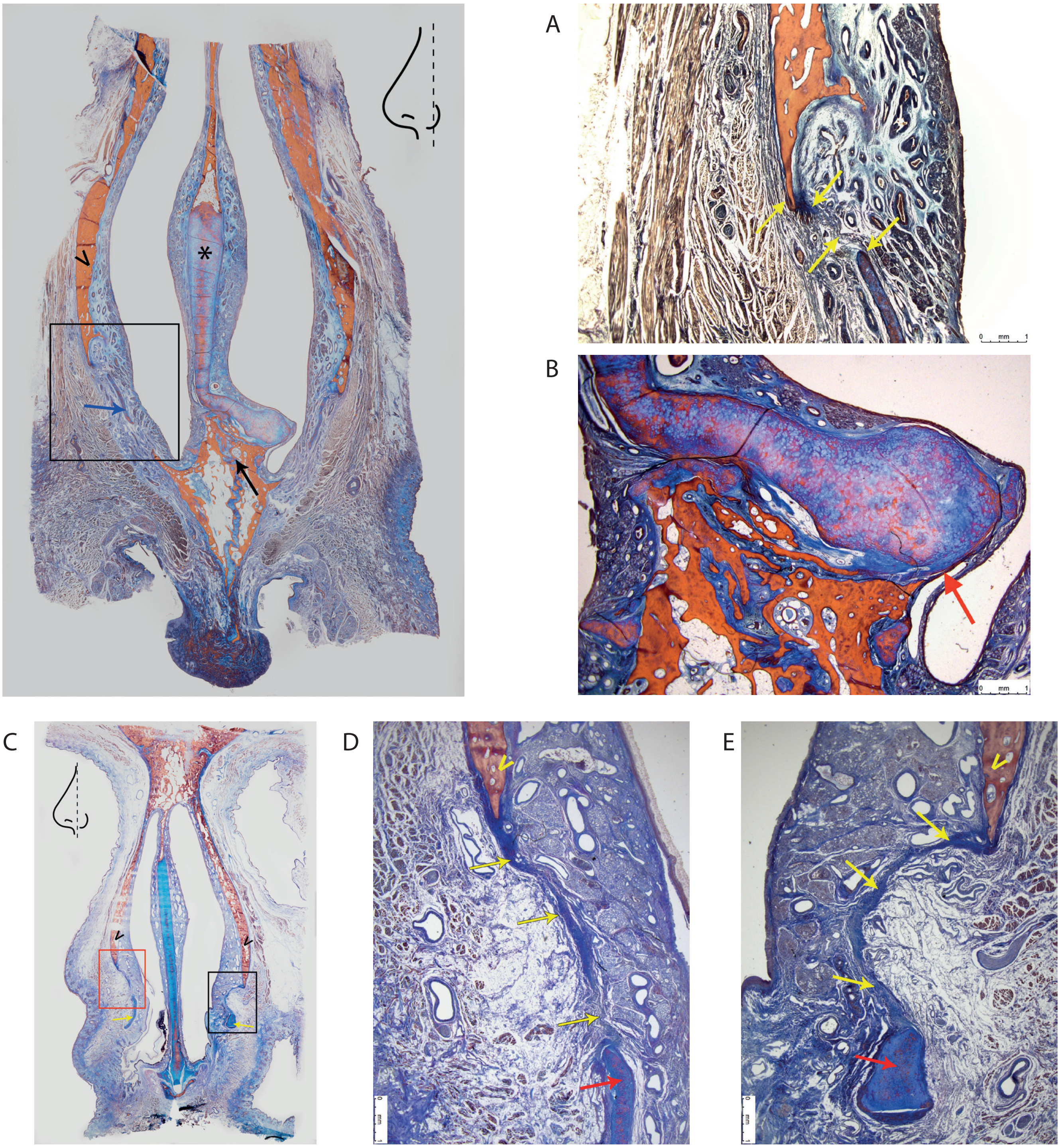

Figure 5. Overview of the pirifom aperture at the hinge area and the premaxilla (black arrow) (specimen 6, Mallory-Cason staining). A) Higher magnification of Figure 5 at the hinge area. Note the thin layer of periosteal-perichondrial envelope (yellow arrow) between the piriform aperture and lobular cartilage. There is no additional attachment of the lobular cartilage to the piriform aperture (1,25x) (specimen 6, Mallory-Cason staining). B) Higher magnification of Figure 5 at the premaxilla with an anterior nasal spine. Note the solid anterior nasal spine and the thin intact layer of periosteal-perichondrial envelope between the bone and cartilaginous septum (red arrow), despite the septal deviation (1,25x) (specimen 6, Mallory-Cason staining). C) Overview of the external cartilaginous and bony nasal pyramid at the hinge area (red and black rectangular) showing the relation between the piriform aperture (arrowhead) and the lateral crus of the lobular cartilage (yellow arrow) (specimen 1, Mallory-Cason staining). D) E) Higher magnification the hinge area (red rectangle 5d, black rectangle 5e) demonstrating, unlike in Figure 5a, a thick periosteal-perichondrial envelope (yellow arrow) connecting the piriform aperture (yellow arrowhead) and the lateral crus of the lobular cartilage (white arrow) (1,25x) (specimen 1, Mallory-Cason staining).

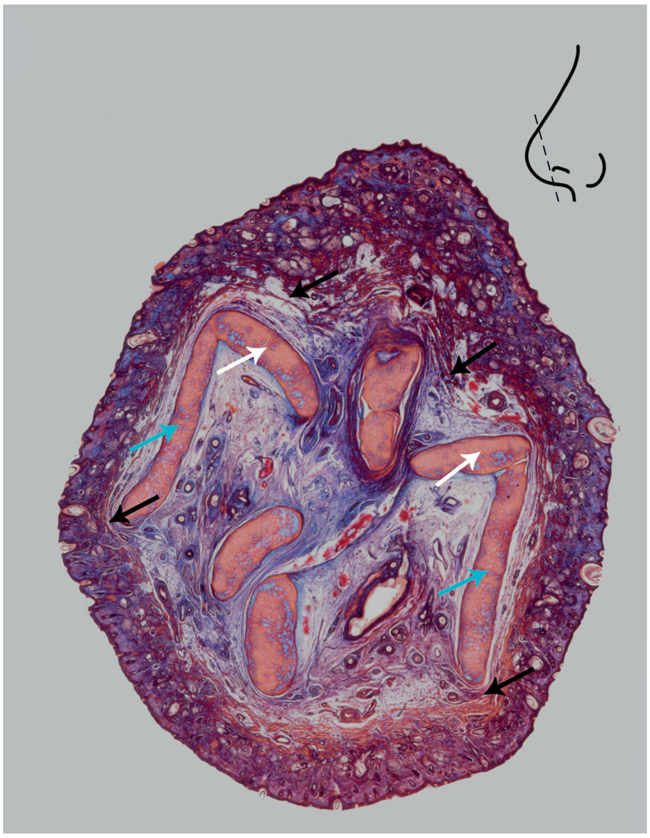

Figure 6. Overview of the external cartilaginous nasal pyramid at the supratip break showing the relation between the domes (white arrow) and the lateral crura of the lobular cartilages (blue arrow). There is no intercrural ligament, only a soft tissue envelope of skin and muscle fibers (black arrow) (specimen 2, Mallory-Cason staining).

becomes denser (Figures 3, 3a). Furthermore, there are no fibers that connect the dermis to cartilage or muscles (Figures 7-8).

Septum

Our study demonstrates that the cartilaginous septum is continuous with the triangular cartilages to form the septolateral cartilage. The septolateral cartilage is interconnected with lobular cartilages merely with the periosteal-perichondrial envelope/membrane (Figures 1-3, 5-8). There are no other ligaments between the above mentioned structures.

Premaxillae and anterior nasal spine

In our study we demonstrated that the premaxillae including the anterior nasal spine are directly connected to the septal cartilage to provide support for the tip. The thin intact layer of periosteal-perichondrial envelope overlies the bony premaxilla and the septal cartilage, even in this case of septal deviation (Figures 5, 5b, 8, and 8a).

Discussion

The main purpose of this anatomical and histological study was to redefine the structures that support the tip and discuss it with relevant literature. While several studies, aimed at anatomical dissection, proposed i.a. numerous ligaments that contribute to the nasal tip support, our clinical observations show that there are more important structures that contribute to shape and support of the nasal tip. In our present study, we focus on histology and the related functional anatomy by creating large sections and thus visualizing the entire external nose. This technique provides a more natural way to demonstrate anatomical structures and its course because it avoids the risk of creating non-existing structures by pulling and stretching the tissue as may happen during cadaver dissection. Therefore, tip supporting structures at macro- and microscopic levels may be defined more precisely.

According to our current findings the following structures contribute to the nasal tip: 1. lobular cartilages, 2. soft tissue envelope and periosteal-perichondrial envelope/membrane; 3. septum; 4. premaxillae and anterior nasal spine.

We identified lobular cartilages as an important component of the nasal tip. Mechanistically, it is obvious that the intrinsic integrity of the lobular cartilages provides the shape for the nasal tip, and due to their rather weak fixation to the surrounding tissues, the mobility on the tip is enabled. Our histological findings endorse clinical observations. We demonstrated that the lobular cartilages are connected with the triangular cartilage, and accessory cartilage by merely the periosteal-perichondrial envelope/membrane (Figures 1, 2) that unlike ligaments enable mobility and provide support to the tip. The existence of the scroll ligament between triangular and lobular cartilages, as suggested by Janeke, Tardy or Daniel [1,2,7] in their macroscopic dissection studies, could not be confirmed by us in histological sections. We speculate that in these studies the soft tissue envelope may have impressed as a ligamentous structure. Furthermore, we could not identify either a junction between medial crura and caudal septum (Figures 3, 3a), or an interdomal ligament (Figures 4, 4a), or an intercrural ligament (Figure 6), as has been proposed in the literature [1,7,14]. Likewise, the thin layer of periosteal-perichondrial envelope/membrane connects the lobular cartilage with the piriform aperture at the hinge area. Unlike Daniel et al. [7], we found no histological evidence of an additional attachment of the lobular cartilage to the piriform aperture (Figures 5, and 5a-5e).

Age- and gender-related changes in the human external nose have been addressed by Sforza et al. [15]. However, these findings relate to measurements of dimensions of the external nose and growth changes from childhood to old age, and not to qualitive and quantitative differences in the histology of the external nose. There is no evidence that histology of the external nose, including ligaments, differs in age and gender. Therefore, the

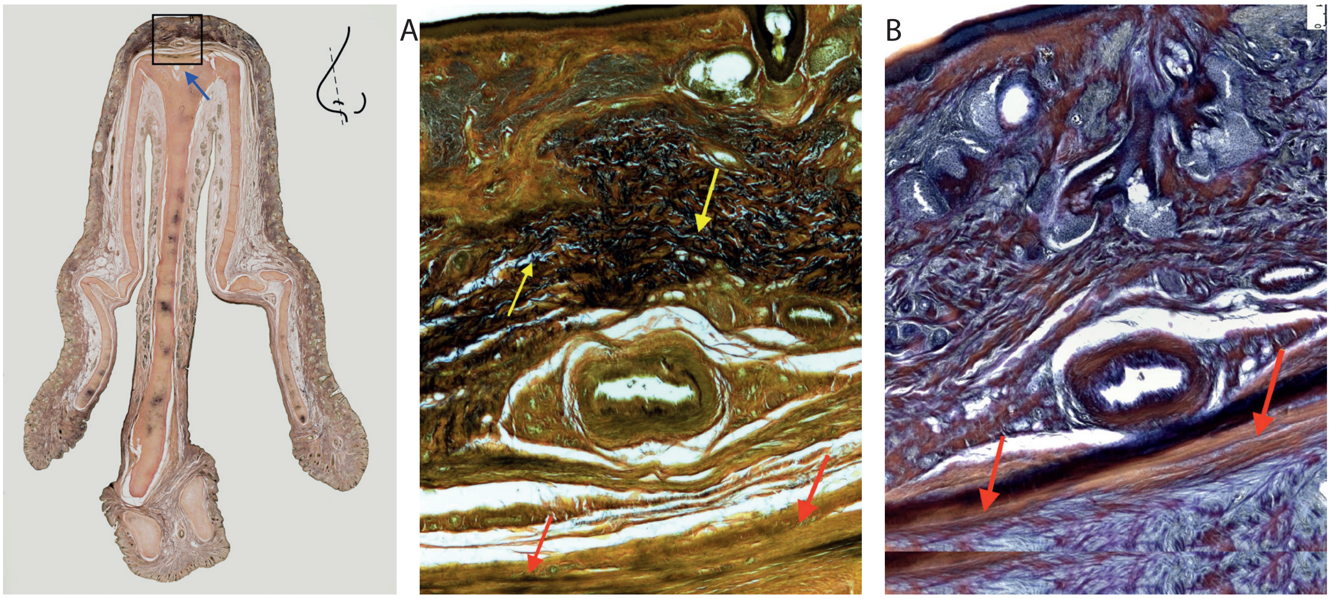

Figure 7. Overview of the external cartilaginous nasal pyramid demonstrating septolateral cartilage in a form of Y-beam, triangular subnasal space (blue arrow), overlaying parallel fibers of perichondrium, and a soft tissue envelope. There are no connecting fibers between the skin and the perichondrium (rectangle) (specimen 2, Verhoeff-Van Gieson staining). A) (Verhoeff-Van Gieson staining) and B) (Mallory-Cason staining). Higher magnification of Figure 7 at the dorsum (rectangle) demonstrating parallel collagen fibers of perichondrium (red arrow) and elastin fibers (yellow arrow) of the soft tissue envelope. There is no dermocartilaginous ligament in the region (5x).

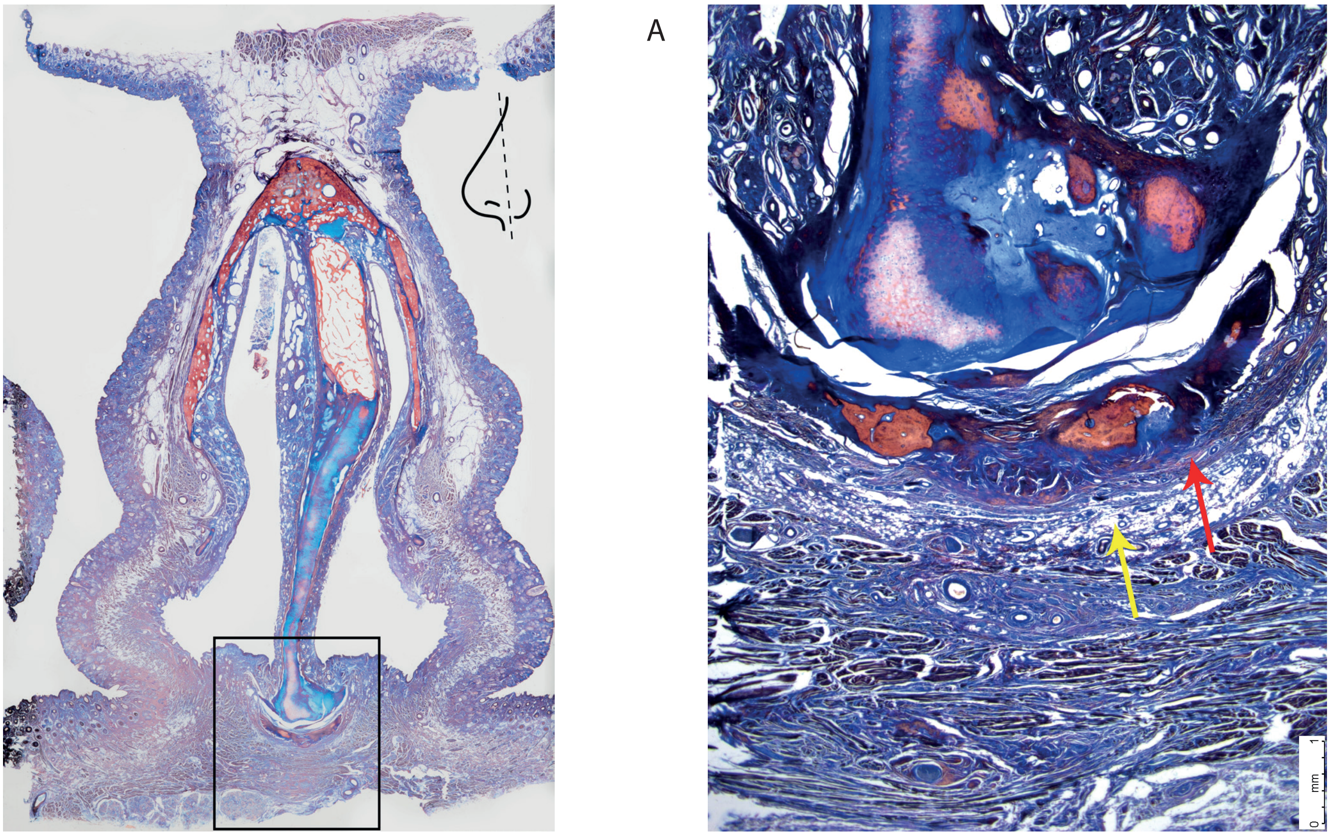

Figure 8. Overview of the external cartilaginous nasal pyramid demonstrating the external nasal pyramid, the premaxillae and anterior nasal spine (rectangle) (specimen 7, Mallory-Cason staining). A) Higher magnification of Figure 8 at the premaxillae and anterior nasal spine. There are parallel fibers of periosteum (red arrow) and the loose conective tissue (yellow arrow). There are no fibers running from the anterior nasal spine to the skin (1,25x).

Table 1. Previous and current concepts on the tip supporting structures.

Tip supporting structures		
Previous concept based on anatomical studies	**Current concept based on functional anatomy and histology**	**Figures**
The scroll junction between triangular and lobular cartilages [1,2] or vertical and longitudinal scroll ligament [7]	Periosteal-perichondrial envelope	1, 1a, 1b, 1c, 1d
The lateral sesamoid cartilage complex [1,2,9]	Periosteal-perichondrial envelope	2, 2a, 2b
The junction between medial crura and caudal septum [1,2]	Dense connective tissue	3, 3a
The interdomal ligament [1,2]	Loose connective tissue [9]	4, 4a
The intrinsic integrity of the lobular cartilages [2]	Lobular cartilages	1 - 5
Sesamoid attachment to the piriform aperture [2,9]	Periosteal-perichondrial envelope [10]	2
Lateral crural attachment to the piriform aperture [9]	Periosteal-perichondrial envelope [10]	2a, 2b, 5, 5a, 5c, 5d, 5e
The intercrural ligament [7,9]	Soft tissue envelope	6
Pitanguy's Midline Ligament [8,10]	Soft tissue envelope	7, 7a, 7b
Septum: cartilaginous and membranous septum [3]	Septal cartilage	1 - 3, 5 - 8
Anterior nasal spine [3]	Premaxillae with anterior nasal spine	5, 5b, 8, 8a
Soft tissue envelope; superficial aponeurotic muscular system - SMAS [3]	Soft tissue envelope: skin, muscles, and connective tissue	1 - 8

Table 2. Nasal tip components that provide shape and support.

Nasal tip	
Shape	**Support**
1. Lobular cartilages	1. Septal cartilage
2. Soft tissue envelope with periosteal-perichondrial envelope/membrane	2. Premaxillae and anterior nasal spine

homogeneity of our investigated cadavers is justified.

In addition, we would like to comment on the nomenclature of the connection between the triangular and lobular cartilage, and the lobular cartilage itself. As it was described by Huizing et al. [16], the most common relationship between the triangular cartilage and lobular cartilage are: overlap, end to end, scroll, and opposed scroll. Therefore, we suggest to not to name all variants "a scroll area".
Other factors that may determine the shape of the tip, such as the exact morphology and the age of the cartilage are beyond the scope of this study and therefore not discussed here.

Further, we prefer to adhere to the nomenclature proposed by Huizing et al. [16], i.e. lobular cartilage, whereas in North American the nomenclature of lower lateral cartilage is more popular. The reason for this is that the medial crura of the lobular cartilages are located in the median and paramedian plane, therefore naming the entire cartilage as lower lateral cartilage does not accord with the true topography.

Subsequently, to verify the structures that overly the bony and cartilaginous nasal vault, we found that the nasal pyramid is covered from outside to inside by: skin, varying thickness of superficial loose connective tissue, muscles, deep connective tissue of varying thickness and density (either loose or dense) containing the blood vessels and nerves (Figures 1-8), and the periosteal-perichondrial envelope/membrane that is attached to the bone and cartilage (Figures 1, 2, and 5). The connective tissue between the muscles and the periosteal-perichondrial envelope/membrane is loose and therefore may permit gliding movements of the overlying tissues (Figures 1, 2, and 4), whereas at the level of caudal margin of the septum it becomes denser providing more stability (Figures 3, 3a). Furthermore, there are no fibers which connect the dermis to cartilage or muscles in contrast to what was suggested in previous macroscopic studies (Figures 7-8) (Pitanguy ligament) [8-10]. Consistent with our findings, we suggest to not to address the non-existing structure in rhinoplasty.

In some literature the soft tissue envelope is named superficial musculoaponeurotic system (SMAS), consisting of a superficial fatty layer, a fibromuscular layer, a deep fatty layer, a longitudinal fibrous layer, and an intercrural ligament [17]. This arrangement of layers corresponds to our findings with the exception of the intercrural ligament, however, we agree with other authors [18-20] that the term SMAS should be reserved for a connective tissue layer containing a variable amount of muscle fibers that extends cranially from the platysma, covers the parotid gland and facial nerve branches, and stops at the level of the zygomatic arch. Anteriorly, the SMAS is continuous with orbicularis oculi and zygomaticus major. According to this definition the nasal region is not involved in the SMAS [20]. Above the zygomatic arch the temporoparietal fascia is a SMAS-like layer which is continuous with frontalis and galea aponeurotica.

To better understand the supportive role of septum in the external nose, we showed in details its relation to adjacent structures. The septum is a rigid, fixed structure and is continuous with the triangular cartilages to form the septolateral cartilage. Based on our study, the septolateral cartilage is interconnected with lobular cartilages merely with the periosteal-perichondrial envelope/membrane (Figures 1-3, 5-8). There is no histological evidence for other ligaments between the above mentioned structures. These data identify a well-balanced continuum "the septolateral cartilage-lobular cartilage", enabling the mobility of hanging down structures (triangular cartilages) and resulting in indirect shaping and positioning of the lobular cartilages. It is therefore suggestive that dysfunction within the septum may influence the position of lobular cartilages.

Finally, we explored the role of the premaxillae and anterior nasal spine. The anterior nasal spine is considered by some to be a unique human characteristic, however, it has been reported to occur in chimpanzees. Among human populations, the anterior nasal spine's size correlates with facial prognathism and timing of premaxillary-maxillary sutural fusion, which may have implications for midfacial growth. The more prominent the anterior nasal spine, the more orthognathic facial profiles, and more fused premaxillary-maxillary sutures [21].

The premaxillae and anterior nasal spine may be underestimated in rhinoplasty, however these are the structures of great importance as they determine the morphology of the lower third of the nose, and by far affect projection of the tip. Hyperplasia of the anterior nasal spine may contribute to a wide nasolabial angle and over-projection of the tip, whereas hypoplasia - an acute angle and under projection of the tip [22].

In our study we demonstrated that the premaxillae including the anterior nasal spine are providing a robust foundation for the septal cartilage, thus indirectly support the nasal tip. The thin intact layer of periosteal-perichondrial envelope overlies the bony premaxilla and the septal cartilage (Figures 5, 5b, 8, and 8a). In rhinoplasties it is recommended that after correction of the anterior nasal spine it is subsequently important to suture the periosteum to the septum [22-26]. Here, we demonstrate that the layer of the perichondrial-periosteal envelope might be not thick enough to fixate the suture. The perichondrial-periosteal envelope is part of the soft tissue envelope. Since the soft tissue envelope is dissected free from the cartilaginous- and bony skeleton including the perichondrial-periosteal envelope, it does not require separate reattachment to the skeleton. When there is a need for re-fixation of the caudal cartilaginous septum to the corrected anterior nasal spine area with a (permanent) suture, this can be achieved by drilling a hole in the remnants of the anterior nasal spine or maxilla. At the end of surgery, the soft tissue envelope is approximated to the skeleton in order to avoid dead space. This is performed with septal mattress sutures, internal packing, and dressing of the nose.

While multiple rhinoplasties techniques aim at restoring numerous structures that are believed to support the tip, good functional and aesthetic appearance of the tip continues to pose a serious challenge for long-term therapeutic efficacy. By focusing on the histology and functional anatomy study, we revised previous concepts of the tip support (Table 1). Further, based on the revised knowledge, we posited the new concept of distinguishing nasal tip components based on its function, thereby providing either shape or support (Table 2). However, it should be mentioned that it is somehow artificial to separate these functions completely because all structures interfere with each other. Structures which are listed in Table 2 as tip-supporting obviously also contribute to the shape of the tip by giving support.

In addition, all structures except premaxillae with anterior nasal spine, also determine mobility. Our data uncover the principles in the external nose anatomy, thus enables to avoid complex techniques in functional and aesthetic nasal surgery.

The strength of this study is that we made sections of the entire, undissected external nose. This approach enabled us to study the continuity of all anatomical structures. A drawback of this approach is that it is technically challenging and labour-intensive. As a consequence the number of studied specimens was limited to seven. However, given the consistency of the findings, there is no reason to believe that increasing the number of specimens would lead to different results. This is in line with the literature which shows that many descriptive anatomical studies are based on comparable numbers of specimens [27,28].

Conclusion

In contrast to previous dissection studies we found no histological evidence of ligaments between the cartilaginous and bony parts of the nasal skeleton. Instead, we found a perichondrial-periosteal lining within the soft tissue envelope. The main tip supporting and shaping structures are: septal and lobular cartilages, premaxillae and soft tissue envelope with periosteal-perichondrial envelope/membrane.

The goal of rhinoplasty is to achieve a successful functional and aesthetic long-term postoperative outcome. Based on our histological findings we suggest avoiding over-resection of the septal and lobular cartilages and preservation of the premaxillae, since these structures provide shape and support, respectively. Sometimes, especially in revision cases, there will be a need for septal and lobular cartilages reconstruction or stabilization with nasal grafts.

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Authorship contribution

Conceived and designed the experiments: MP, EHH, RLAWB. Performed the experiments: MP, SAMWVS, CM. Analyzed the data: MP, RLAWB, EHH, DJM. Contributed reagents/materials/analysis tools: RLAWB, SAMWVS, CM. Wrote the paper: MP, EHH, RLAWB, DJM.

Conflict of interest

The authors declare no conflict of interest.

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