·文献综述·

眼眶减压术治疗甲状腺相关眼病的研究进展

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摘要
甲状腺相关眼病(TAO)是成人最常见的慢性眼眶疾病,严重影响患者的生活质量和身心健康。目前眼眶减压手术已成为减少 TAO 患者眼球突出度、缓解视神经压迫的重要治疗手段,且制定个性化手术方案是该术式发展的趋势。但对于眼科医生来说眼眶减压的手术方式、减压范围的选择仍是比较棘手的问题。文章系统综述了近年来眼眶减压手术治疗 TAO 的研究进展,探讨了包括眼眶脂肪减压手术、眶壁减压手术及多壁联合减压手术等不同术式的疗效、适应证及操作要点,并综述了影响眼眶减压手术效果的关键因素以及新兴技术在眼眶减压手术中的应用。以期加深对眼眶减压手术的认识,为眼科医师制定个性化的减压手术方案提供新思路。
关键词:甲状腺相关眼病;眼眶减压术;精准治疗
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Research progress on orbital decompression surgery for thyroid-associated ophthalmopathy

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Abstract

• Thyroid-associated ophthalmopathy (TAO) represents the most prevalent chronic orbital disease in adults, significantly compromising patients' quality of life and physical and psychological well-being. Orbital decompression surgery has now emerged as a critical therapeutic intervention for reducing proptosis and alleviating optic nerve compression in TAO patients, with the development of tailored surgical regimens reflecting a key trend. Nonetheless, ophthalmologists encounter persistent hurdles in navigating the selection of optimal surgical techniques and quantifying the necessary extent of decompression. This review systematically synthesizes recent research advances in orbital decompression surgery for TAO. It examines the efficacy, indications, and key technical considerations of various surgical techniques, including orbital fat decompression, orbital wall decompression, and multi-wall decompression. Furthermore, the review summarizes critical factors influencing surgical outcomes and the application of various emerging techniques in orbital decompression procedures. This study aims to enhance the understanding of orbital decompression surgery and provide novel perspectives for ophthalmologists in formulating personalized surgical decompression strategies.
• KEYWORDS: thyroid-associated ophthalmopathy; orbital decompression surgery; precision medicine

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0 引言

甲状腺相关眼病(thyroid-associated ophthalmopathy, TAO)又称 Graves 眼病,与甲状腺功能异常密切相关,是一种器官特异性的自身免疫性疾病[1]。具体发病机制不详,目前认为其发病机制可能与免疫、遗传和环境等因素有关[2]。脂肪增生、糖胺聚糖沉积、以及肌肉增粗导致的眼眶内容物体积膨大是其主要病理表现[3]。由于眶骨的限制,眼眶内容物的体积膨大会逐渐导致眼球突出。且由于眼眶组织的免疫与炎症反应,患者可由轻至重出现一系列临床症状,从轻微的眼睑症状到出现复视及眼球运动障碍等功能异常,甚至发展为暴露性角膜炎和甲状腺功能障碍性视神经病变(dysthyroid optic neuropathy, DON)导致失明,该疾病可对患者的生活质量和身心健康造成严重影响[4-5]。TAO 的常规治疗方式包括糖皮质激素、生物制剂、免疫抑制剂、眼眶放射治疗以及手术治疗[6]。目前糖皮质激素是活动期患者的一线治疗方案,但当非活动期患

者突眼影响美观或严重暴露性角膜炎及 DON 保守治疗无效时,眼眶减压手术已成为目前最有效的干预手段。眼眶减压手术旨在减轻视神经压迫和改善眼球突出,通过切除骨壁或去除眶内脂肪组织来减少及重新分配眼眶内容物实现减压,其对恢复视功能、减少眼球突出度和提高患者生活质量有重要意义[6-8]。自 1911 年 Dollinger 首次对 TAO 患者进行眼眶减压手术以来,眼眶减压手术的手术方法和手术技术在不断改进,以获得更好的减压效果及减少并发症的发生。近年来国内外针对眼眶减压手术的研究繁多,本文将对目前眼眶减压手术治疗 TAO 的研究现状进行综述,探讨分析不同术式的疗效、适应证及操作要点,并展望精准化、个体化治疗的发展方向,以期增加对眼眶减压手术的认识从而更好地为患者制定减压方案。

1 常见的眼眶减压手术术式

1.1 眼眶脂肪减压术 眼眶脂肪减压术通过去除眶内增多的脂肪来起到减压效果,手术可经结膜入路或经眼睑皮肤切口入路进行,约可实现 3-5 mm 的眼球突出度减少[9]。Prat 等[10]行回顾性研究发现在接受眼眶脂肪减压手术的患者中,以脂肪增生为主临床亚型的眼球突出度减少值(3.27 mm)显著高于以肌肉增生为主者(2.83 mm)。因此该术式更适用于以脂肪增生为主的 TAO 患者。多项研究显示脂肪的切除量与眼球突出度减少程度之间存在较强的相关性,切除 1 mL 脂肪可减少约 0.6-0.8 mm 的眼球突出度,但切除的眼眶脂肪量越大诱发复视的可能性越高,切除脂肪量在 3-5 mL 左右比较合适[9,11-12]。切除的眶内脂肪可分为肌锥内和肌锥外,切除肌锥内的脂肪可使眼球直接回退,得到更佳的减压效果。但因为肌锥内血管及神经分布较多,操作时可能会增大眶内出血、神经损伤、斜视等并发症发生概率。因此,目前临床上切除眶周鼻下和颞下象限脂肪是普遍采用的方式。如需适量切除肌锥内脂肪以实现更大的减压效果,操作时需注意直视下操作、保护神经及血管。相较于去骨减压,单纯脂肪减压理论上可避免因去除眶壁导致的并发症,研究发现在接受眼眶脂肪减压手术的患者中脑膜炎、脑脊液漏、视力丧失等并发症的发生率接近于 0[13-14]。由于眼眶脂肪减压术具有良好的可预测性以及安全性,因此该术式可作为轻中度突眼患者的首选手段,或作为眶壁减压的辅助手段治疗重度眼球突出。

1.2 眶外侧壁减压术 眶外侧壁减压术是通过去除眶外侧壁来扩大眼眶容积,传统的骨性减压范围位于眶外侧壁前部,去除后眼眶扩大的容积有限[15]。自 1998 年有学者发现充分磨除蝶骨大翼的肥厚部可实现更大程度的眼眶容积扩张,减压范围随即由前部减压向深部减压演变[16]。为减少术后瘢痕影响美观,手术切口也由眶周皮肤切口逐渐向更微创的切口演变,如上睑皮肤皱褶切口、联合外眦切开的结膜切口以及发际切口等[17-18]。单独行深外侧壁减压术可实现 2.5-4.5 mm 的眼球突出度减少[15]。深外侧壁减压术的优点在于相较于其他骨壁减压其术后新发复视率低(3%, 95% *CI*:1%-6%)[19],可能原因是减压去除的骨壁范围几乎位于肌锥的后方从而眶内组织不易产生移位[20]。但由于深外侧壁骨质较深且蝶骨大翼后缘紧邻颅中窝,术中有可能出现硬脑膜损伤与脑脊液漏[21]。除此之外,此种术式并发症还包括硬膜下出血、眶周感觉异常、颞部凹陷、咀嚼振动幻觉、瘢痕形成等[22]。近年来眶外侧壁减压术的具体操作细节对手术疗效的影响得到了研究者们关注。研究发现在眶外侧壁减压术操作过程中注意保留颞肌上方的薄骨具有两方面益处:(1)有助于防止颞肌与外直肌间形成黏连;(2)能有效限制颞肌向内侧移位占据扩大的眼眶容积,从而改善术后减压效果[23-24]。然而目前关于眶外壁减压术中眶缘的处理方式仍存在争议,现在常见的处理眶缘方式包括保留眶缘、去除眶缘以及术后重建眶缘。Zhang 等[25]对比了保留与去除眶缘的减压效果,结果显示两组在眼球突出度减少程度上无显著差异($P>0.05$),但去除眶缘组患者颞部凹陷的发生率(5.8%)显著高于保留眶缘组(0),提示外侧眶缘在保护眼球和维持眼眶外部形状的方面发挥着重要作用。而在其他一些研究者的研究中发现即使保留或重建眶缘仍存在咀嚼振动幻觉、颞部凹陷等并发症,因此上述并发症可能不是由切除外侧眶缘本身引起的,而是由于术中损伤颞肌所致[26-27]。部分学者认为如果移除边缘则可以减少对颞肌的损伤,可避免上述并发症的发生[28]。基于现有研究,目前在临床实践中无论采取何种眶缘处理方式,均应强调对颞肌的保护。而未来研究应着力于术式优化与新技术的应用以提升颞肌保护效果,同时可通过前瞻性研究深入评估不同眶缘处理方式对患者长期预后的影响。

1.3 眶内侧壁减压术 眶内侧壁减压手术通过去除眶内壁使增生的脂肪及内直肌疝入至邻近的筛窦中以实现减压效果,其潜在减压空间相较于外侧壁减压术更大[29]。研究者测定了行不同眼眶减压术式后患者扩大的眼眶容积,结果显示行眶内侧壁减压术后扩大的眼眶容积(平均 2.1 cm^3)显著大于外侧壁减压术(平均 1.03 cm^3)[30]。且由于眶内壁最靠近眶尖部,因此去除眶内壁对缓解眶尖部的视神经压迫更有效,可作为治疗 DON 的首选术式。Currò 等[31]行眼眶内侧壁减压手术治疗 DON 患者,其术后最佳矫正视力、视野和色觉均显著改善($P<0.05$)。通常内侧壁减压术约可实现 3-4 mm 的眼球突出度减少,联合其他术式可实现更大程度的眼球突出度减少[22]。Wu 等[32]对脂肪增生为主的患者进行了眼眶内壁减压联合脂肪减压,眼球突出度可减少 8.2±1.8 mm。目前行内侧壁减压术最常见的并发症为新发复视,其发生率可达 60%,而术中注意保留眶悬带(orbital sling)及眼眶内下壁支撑结构(orbital strut)可使新发复视率显著降低[19,33]。目前内侧壁减压常见的手术入路是经泪阜结膜入路及鼻内镜辅助下经鼻入路,这两种入路各有利弊。经鼻入路在内镜辅助下通过鼻腔通道来进行减压,可避免皮肤瘢痕且具有良好的可视性,在内镜下可清晰显示眼眶内壁和眶尖部位[34]。研究发现眶尖部位的总腱环(annulus of zinn)周围减压是减轻 DON 视神经压迫的关键,而通过内镜下操作可实现对眶尖部的充分减压[35]。Nishimura 等[36]研究对比了经泪阜结膜入路及经鼻入路的内侧壁减压术治疗

DON,发现经鼻入路术后视力的改善优于结膜入路($P<0.05$),且在内镜直视下操作更加安全。经泪阜结膜入路同样手术切口隐蔽,不遗留颜面部瘢痕,相较于经鼻入路其学习曲线更短、无需依赖内窥镜设备,且可以避免如鼻窦炎、鼻泪道损伤、鼻出血等鼻入路相关并发症[37-38]。但若患者存在 DON,经泪阜结膜入路因视野相对较窄可能会出现减压不充分,且术中不可避免的会对眶内组织产生压迫从而升高眶压。因此在眼眶内壁减压手术中,需根据患者的具体病情特征选择适宜的切口入路。若患者合并 DON 可首选鼻内镜辅助下经鼻入路,而对于单纯眼球突出的 TAO 患者,眼眶内壁减压经泪阜结膜入路即可达到减压效果。

1.4 多壁联合减压术　多壁联合减压可显著减少患者的眼球突出度,适合于单壁减压达不到减压效果的重度眼球突出 TAO 患者。近年来,同时联合内外侧壁减压的平衡减压术已成为眼整形外科医生最为青睐的技术,该术式通常可实现 4-7 mm 的眼球突出度减少[19,39-40]。研究表明平衡减压术保留了眶底,且同时去除内外侧眶壁,能够避免眶内容物的不对称移位,可有效降低术后复视的发生,复视发生率为 11%-16%[22]。除平衡减压术外,常见的术式还有内下壁减压术及三壁减压术。Pereira 等[41]的随机对照试验表明,平衡减压术在改善眼球突出度方面显著优于内下壁减压术(3.8±3.1 mm *vs* 2.4±1.9 mm)。以往研究认为内下壁减压术后较平衡减压术复视发生率(40%-65%)及眼球下斜(4.5%)的发生率高[33]。然而近期的研究发现内下壁减压术与平衡减压术在术后复视发生率(OR=1.20,95% CI:0.38-3.76,P=0.76)[42]及斜视发生率方面均无统计学显著差异(P>0.05)[43]。这一转变可能源于目前研究者们对手术认识的深化,特别是意识到术中保护眼眶内下壁支撑结构的重要性。三壁减压术在平衡减压术的基础上联合下壁减压,其减压效果更佳。Korkmaz 等[44]对比了平衡减压术与三壁减压术治疗 DON 患者的长期疗效,发现三壁减压术在改善患者的眼球突出度、最佳矫正视力、视野、色觉方面均优于平衡减压术,但存在更高的新发复视风险(28.5% *vs* 20%)及球后出血风险。为减少三壁减压术并发症的发生,Tian 等[45]对术式进行了优化,提出选择性三壁减压术。该术式的关键在于术中保护眼眶内下壁支撑结构及内直肌旁的眶骨膜,可显著降低患者术后新发复视发生率,并有效改善术前存在的斜视和复视症状。目前平衡减压术因其良好的风险收益平衡,仍是临床上最受青睐的治疗方案。不过随着其余多壁减压术式的技术持续优化,其手术风险已显著降低。特别是选择性三壁减压术,在有效减少并发症的前提下,有望为需要更大减压效果的 DON 患者提供更优的治疗选择。未来研究应着重验证该技术的长期疗效及广泛适用性,并进一步推动手术技术的精准化改进。

2 手术方式的选择

目前绝大多数学者根据自己的偏好或临床手术经验选择熟练的手术方式,而选择不合适的手术方式不仅不能改善患者症状,还会增加患者二次手术的风险。而且过度的骨减压可能会加大复视、鼻窦炎、脑脊液漏和出血等术后并发症发生概率。关于眼眶减压手术方式的选择,Kikkawa 等[46]提出了基于眼球突出度的分级眼眶减压。但随着对眼眶减压手术的更深了解以及手术技术的进步,对于眼眶减压术的选择需考虑的不仅仅只是眼球突出度,应根据患者术前的综合个体特征及不同术式的优缺点选择需要去除的骨壁及切口入路,最大限度地提高每种术式的益处并减少其缺点。临床上 TAO 眼球突出的类型可分为脂肪组织增生型和眼肌增粗型,这两种类型可以并存或者单独存在[47]。Costan 等[48]提出根据患者的术前影像学评估患者眼球突出的类型有助于确定患者适合的减压手术方式。目前国内外尚缺乏根据此理念来设计手术方案的有效临床研究,未来可从此方向出发设计更适合患者的手术方案。

3 眼眶减压术的新技术及新理念

3.1 眼眶减压术的新技术应用　眼眶减压术的发展与演变已有百年历史,为更好地实现减压及减少并发症的发生,更多先进设备与技术开始应用于眼眶减压术。Yu 等[49]应用 3D 重建及打印技术设计了一种手术导板运用于眶外侧壁减压术中,做到了精准去除骨壁,并在手术过程中避免了硬脑膜暴露及损伤。Men 等[24]在眶外侧壁减压术中通过在外侧眶壁缺损处植入聚乙烯涂层钛网增加了患者的眼眶容积,并通过防止颞肌向内侧移位稳定了减压效果,患者平均眼球突出度减少 3.4 mm。计算机辅助图像导航系统通过医学影像与空间定位技术相结合可改善眼眶减压过程中的解剖定位和精确度,通过图像引导可更安全及积极的去除骨质[50]。使用该项技术在增大眼球突出减少的同时可降低医源性损伤的风险。Prevost 等[51]对比研究发现,使用计算机辅助图像导航系统进行减压手术后患者的眼球突出度减少量(3.8±0.2 mm)大于非导航组(3.2±0.2 mm),差异具有统计学意义(P=0.03)。Heisel 等[52]研究发现使用计算机辅助图像导航系统减压后需行矫正斜视手术的患者比例显著低于非导航组(39.1% *vs* 77.3%,P=0.012)。内镜导航辅助系统在眼眶减压术中也得到了应用,术中应用内镜导航技术,可有效提高手术的安全性和精准度。Zhang 等[53]对比研究发现内镜导航辅助系统能精准定位眼眶减压手术中的解剖结构,使用该系统进行减压手术后的患者眼球突出度减少量较非导航组平均增加 0.9 mm(P=0.004),且术后最佳矫正视力改善率显著提高(78.2% *vs* 52.6%,P=0.026)。眼眶周围分布着丰富的血管与神经,为减少眶内组织损伤需要精细且稳定的操作。而手术者有可能会出现不可避免的生理性手颤及疲劳等情况,机器人辅助眼科手术具有减少组织损伤、提高手术精度的潜力[54]。目前由机器人手术系统辅助的眼眶脂肪减压术和眼眶平衡减压手术已成功实施,在取得良好疗效的同时均未出现术后并发症[55-56]。Nguyen 等[57]使用了一种集立体定向导航定位、去骨、牵拉、冲洗、抽吸为一体的器械用于眼眶减压手术中,发现这种器械有助于确定去骨深度和保护眼眶软组织。尽管目前尚缺乏更高证据水平的研究来验证这些技术的长期安全性与优

越性,但这些技术在提升手术精准度、安全性及效果可预测性方面展现出巨大潜力,有望在未来为患者提供更加完美的手术方案。

3.2 精准化减压治疗 随着眼眶减压手术技术的不断进步以及生活水平的提高,以美容为目的行眼眶减压手术的患者越来越多[58]。而眼眶减压矫正不足及过度会引起双眼不对称,更加影响患者美观。根据患者的具体情况及需要制定手术技术,并且在术前就能预测术后结局已成为目前眼眶减压手术的发展趋势[59]。但在临床实践中发现眼眶减压手术的疗效难以预测,即使使用相同的手术策略,不同的患者其术后眼球突出的减少也存在巨大差异。研究者们提出了影响 TAO 患者减压手术结果的因素,包括切除的眶壁的类型、去除的眶脂肪量、减压的部位和面积、眼眶及其临近解剖结构的差异以及个体的眼眶软组织状态等[41,48,60]。

Kim 等[61]发现眼眶脂肪减压术和深外侧壁减压术相较于其他术式具有更好的可预测性。且相较于其他术式,深外侧壁减压手术每增加 1 cm^3 的眼眶容积,可带来更大程度的眼球突出度减少。Wu 等[12]发现在眶脂肪减压中可通过肌锥内脂肪去除量预测眼球突出度减少,提出的具体预测方程为眼球突出度减少值=0.72×去除肌锥内脂肪量(mL)-0.001×年龄-0.22×性别(男 1,女 0)-0.19×术前复视(有 1,无 0)+1.02。Krause 等[60]定量测量了减压手术中眶壁的切除面积,发现眶壁的切除面积与眼球突出度的减少有明显相关性,每切除 1 cm^2 的眶壁可实现 1 mm 的眼球突出度减少。影响眶壁减压疗效的还有眼眶及其临近解剖结构的差异,目前研究者根据眼眶及其临近解剖结构的差异,提出了一系列基于 CT 测量的眼眶形态学参数,这些参数既包括二维测量的眼眶长度、圆锥角、蝶骨三角体(sphenoid trigone)宽度等,也包括三维测量的眼眶容积、眼球体积、蝶骨三角体体积、筛窦体积等[40,62-63]。部分参数已证实为眼眶减压手术的积极预测因素。例如骨性眼眶容积的改变与眼球突出度之间存在线性相关,眼眶容积每增加 1 cm^3 可实现 0.7-0.8 mm 的眼球突出度减少[64]。在深外侧壁减压中,眼外肌的肌肉厚度($r=-0.3$, $P=0.043$)以及蝶骨三角体体积($r=0.2$, $P=0.068$)与眼球突出减少程度之间存在明显相关性[65]。在内侧壁减压中,筛窦体积与术后眼球突出减少也存在明显的相关性($r=0.49$, $P<0.001$)[66]。目前关于影响内外侧壁平衡减压术后疗效的研究较少,影响因素尚不明确。Oeverhaus 等[67]发现在平衡减压手术中基于二维 CT 测量的解剖参数如眶内外壁长度、内外眶壁缺损长度、筛窦深度和水平肌肉直径等无法预测眼球突出的减少情况,提示三维形态学参数可能是平衡减压手术后疗效的积极预测因素。除个体眼眶形态学的差异外,眼眶软组织的生物力学特性(如组织的强度、韧度、黏弹性)也会影响术后疗效,通过对眶内软组织的生物力学模拟建立可靠的有限元模型有助于进一步实现精准化减压治疗[68]。

4 总结与展望

目前国内外对 TAO 不同眼眶减压手术进行了大量研究,但如何根据患者具体的临床分型、突眼程度、视功能、美容需求和解剖特点选择最优的减压方式目前尚无较好的参考标准。此外患者的综合个体差异对手术效果的影响尚未完全阐明,现有的预测模型多基于单一术式或参数,对于多壁联合减压及根据患者综合个体差异来预测疗效的能力有限。而随着多种新技术在眼眶减压手术中的应用以及人工智能技术的快速发展,未来有望通过各种创新手段实现更为精准的医疗。因此,未来的研究应着重关注以下几个方面:(1)建立科学规范的手术设计方案;(2)深入探索患者个体差异对治疗效果的影响机制,建立基于个体解剖和生物力学的精准预测模型;(3)不断发展并完善新兴技术,充分发挥现代科技的优势,以最大限度地提升手术效果并降低术后并发症的发生率。

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