

· 儿童耳鼻咽喉头颈外科 ·

鼻窦球囊扩张结合全降解药物支架治疗儿童慢性鼻窦炎的疗效分析

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[摘要] 目的:探讨鼻窦球囊扩张结合全降解药物支架治疗儿童慢性鼻窦炎(CRS)的疗效。方法:49例因CRS接受手术的患儿,均行腺样体切除术,77侧鼻窦行上颌窦口球囊扩张,依据是否留置鼻窦支架将患儿分为2组:①球囊组26例,其中16例行双侧上颌窦口球囊扩张,10例行单侧上颌窦口球囊扩张;②球囊支架组23例,其中12例行双侧上颌窦口球囊扩张及支架置入,11例行单侧上颌窦口扩张及支架置入。对于患儿的主观症状采用视觉模拟量表(VAS)以及SN-5量表进行评估,由监护人和患儿共同完成。同时行鼻窦CT检查,并进行CT评分(Lund-Mackey评分)。结果:球囊支架组患儿手术均成功,术中、术后未发生严重并发症(眶内、颅内并发症),无鼻腔粘连,无眼部不适;鼻窦支架未发生脱落和移位。球囊支架组VAS评分术前1d为6.9,术后6个月为2.0;SN-5评分术前1d为2.397,术后6个月为1.376;术侧CT评分术前为9.628,术后6个月为1.314。术后6个月,球囊支架组患儿的VAS评分、SN-5评分、CT评分均较术前显著下降,VAS评分和SN-5评分的术后缓解率分别为100%和95%;2组术前SN-5评分比较差异无统计学意义($P=0.647$),2组SN-5评分下降幅度比较差异有统计学意义($F=6.801, P=0.012$);2组术前SN-5评分<2.5的患儿SN-5评分比较差异无统计学意义($P=0.199$),2组评分下降幅度比较差异无统计学意义($F=2.336, P=0.14$);2组术前SN-5评分≥2.5的患者SN-5评分比较差异无统计学意义($P=0.628$),2组评分下降幅度比较差异有统计学意义($F=13.861, P=0.001$)。2组术前CT3~8分者,术前CT评分比较差异无统计学意义($P=0.411$),CT评分下降幅度差异无统计学意义($F=1.108, P=0.300$);2组术前CT9~12分者,术前CT评分比较差异无统计学意义($P=0.792$),CT评分下降幅度差异有统计学意义($F=13.059, P=0.001$)。结论:采用鼻窦球囊窦口扩张术结合全降解药物支架置入治疗药物治疗不佳的CRS患儿疗效确切,对于较为严重的CRS患儿,该术式明显优于单纯行鼻窦球囊扩张术。

[关键词] 鼻窦炎;内镜外科手术;鼻窦球囊扩张术;药物支架

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Use of balloon catheter dilation and bioabsorbable steroid-releasing sinus implants in pediatric chronic rhinosinusitis

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Abstract Objective: To evaluate the effect of use of balloon catheter dilation (BCD) with bioabsorbable steroid-releasing sinus implants in pediatric chronic rhinosinusitis (PCRS). **Method:** A retrospective study was performed of 49 children with failed medical therapy, who underwent surgery, and children all accepted adenoidectomy. 77 sides of sinus were performed with balloon catheter dilation sinuplasty. They were divided into two groups: the balloon group and the balloon with implant group. The balloon group included 26 cases, 16 cases of which accepted balloon catheter dilation sinuplasty of both maxillary sinuses, and 10 cases of which accepted one side. The balloon with implant group included 23 cases, 12 cases of which accepted balloon catheter dilation sinuplasty of both maxillary sinuses plus positioning of bioabsorbable steroid-releasing sinus implants, and 11 cases of which accepted one side. VAS and SN-5 scales were completed by children and their parents to evaluate subjective symptoms. Children all accepted CT of sinus and CT score (Lund-Mackey) was completed by a doctor. We use the SPSS 23.0 with the way of Repeated measures ANOVA to analyze the data between two groups, aiming to identify the effect of the operation manners. **Result:** The procedures were successful in all patients in the balloon with implant group. No complications happened. No sinus implants moving and no detachment. In the balloon

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with implant group, VAS score declined from 6.9 before operation to 2.0 of six months after operation and SN-5 score declined from 2.397 to 1.376 and CT score of one side of operation declined from 9.628 to 1.314. VAS score, SN-5 score and CT score of the balloon with implant group all declined significantly after operation. The remission rate of the VAS and SN-5 score in the balloon with implant group were 100% and 95% respectively. The SN-5 score data of patients in two groups with SN-5 score <2.5 before operation was analyzed. There was no statistical significance between the data of two groups before operation ($P=0.199$), and there was no statistical significance between the data decline of SN-5 score of two groups after operation ($F=2.336, P=0.14$). The data of patients in two groups with SN-5 score ≥ 2.5 before operation was analyzed. There was no statistical significance between the data of two groups before operation ($P=0.628$), and, after operation, there was statistical significance between the data decline of SN-5 score of two groups ($F=13.861, P=0.001$). It meant the balloon with implant group declined more. The CT score data of patients in two groups with CT score (3-8) before operation was analyzed. There was no statistical significance between the data of two groups before operation ($P=0.411$), and there was no statistical significance between the data decline of CT score of two groups after operation ($F=1.108, P=0.300$). The data of patients in two groups with CT score (9-12) before operation was analyzed. There was no statistical significance between the data of two groups before operation ($P=0.792$), and, after operation, there was statistical significance between the data decline of CT score of two groups ($F=13.059, P=0.001$). It meant the balloon with implant group declined more. **Conclusion:** In our study, the use of balloon catheter dilation (BCD) with bioabsorbable steroid-releasing sinus implants made a clinical curative effect in the treatment of PCRS with failed medical therapy, and it was safety. In severe PCRS patients, balloon catheter dilation (BCD) with bioabsorbable steroid-releasing sinus implants was more effective than the use of balloon catheter sinuplasty (BCS) alone.

Key words sinusitis; endoscopic surgical procedures; balloon dilatation; drug stent

儿童慢性鼻窦炎(chronic rhinosinusitis, CRS)是鼻窦黏膜的慢性炎性疾病,病程超过12周,是困扰儿童健康的常见疾病,严重影响患儿的学习和生活。由于儿童CRS疾病特点与成人CRS有一定区别,因此需要选择适合儿童的治疗方式^[1]。目前,鼻用糖皮质激素是首选药物,全身抗生素治疗对于儿童的疗效尚存争议^[2]。部分患儿经药物治疗后无效仍需进行手术治疗。目前,有众多医师均把腺样体切除术作为经药物治疗不佳的CRS患儿的首选治疗方式^[3-4]。据相关的Meta分析报道,腺样体切除术后疾病缓解率在50%~70%^[5],若腺样体切除术治疗无效,功能性内镜鼻窦手术(functional endoscopic sinus surgery, FESS)是唯一的备选治疗方案。但常规的内镜鼻窦手术有各种严重的并发症,且儿童鼻窦尚在发育期,手术对于鼻窦发育是否有长期影响尚无定论^[2]。导管引导下鼻窦球囊扩张术的不断发展和日趋成熟,其对于儿童CRS的疗效明确^[6]。2012年EPOS建议CRS患儿经药物治疗无效时首选腺样体切除术伴上颌窦灌洗或鼻窦球囊扩张术。但儿童鼻腔生理及解剖学特点不同于成人鼻腔,容易出现术后窦口黏膜水肿、窦口狭窄及闭锁,导致疾病复发。虽然有成人研究表明全降解药物支架能防止窦口粘连,改善手术效果^[7],但有关其在CRS患儿中的应用却鲜有报道。因此,本研究主要探讨鼻窦球囊扩张结合全降解药物支架治疗儿童CRS的疗效。

1 资料与方法

1.1 临床资料

本研究回顾性分析了2016-01—2019-03复旦

大学附属儿科医院耳鼻咽喉头颈外科行手术治疗的49例CRS患儿。纳入标准:①年龄3~12岁;②符合CRS指南诊断标准(2012年,昆明);③鼻内镜检查可见鼻腔积涕,鼻窦CT检查见窦腔内软组织影(Lund-Mackey评分 ≥ 1 分);④经药物治疗3个月以上无效:遵照医嘱应用鼻用糖皮质激素3个月以上,联合(或不联合)全身抗生素应用2周以上、抗组胺药物、鼻腔盐水灌洗等。排除标准:①患有如下疾病:囊性纤维化、纤毛不动症、影响鼻腔功能的颌面部肿瘤或畸形、鼻窦肿瘤、真菌性鼻窦炎、全身性免疫性疾病、需要长期口服糖皮质激素的疾病;②既往接受鼻窦手术。

1.2 方法

49例因CRS接受手术的患儿,均行腺样体切除术,77侧鼻窦行上颌窦口球囊扩张,依据是否留置鼻窦支架将患儿分为2组:①球囊组26例中男14例,女12例,年龄3岁~11岁8个月,平均6岁8个月;其中16例行双侧上颌窦口球囊扩张,10例行单侧上颌窦口球囊扩张;②球囊支架组23例中男14例,女9例,年龄3岁1个月~12岁,平均6岁3个月;12例行双侧上颌窦口球囊扩张及支架置入,11例行单侧上颌窦口扩张及支架置入。

术前对所有患儿进行全身麻醉前的常规检查。49例患儿的手术均由同一名主任医师完成。全身麻醉下腺样体切除术在内镜下经口操作,手术采用低温等离子消融术。上颌窦口球囊扩张术参照Ramadan等^[6]的操作方法,通过90°上颌窦口引导管将光导纤维导入窦腔内,见上颌窦腔透光试验呈

阳性后将2/3的鼻窦球囊(注水扩张时直径7 mm)插入窦口,内镜观察下以10 ATM扩张窦口3次,每次10 s,退出球囊,扩张后可见上颌窦口明显扩大(图1a)。球囊支架组置入鼻窦支架的操作参照Murr等^[7]的操作方法及器械说明的要求,在鼻内镜直视下采用单手操作支架输送器将全降解药物支架置于上颌窦口,保证支架部分突出窦口,间隔于窦口和中鼻甲之间(图1b),保证从支架收纳到置于靶部位不超过3 min,且在2次内完成。支架载有652 μg糠酸莫米松,在支架吸收期间缓慢释放。术后鼻腔予以可吸收敷料填塞。术后当天起全身应用抗生素2周(头孢地尼或克拉霉素),局部鼻用激素治疗1个月同时予以鼻腔灌洗。

1.3 疗效评估

对于患儿的主观症状采用视觉模拟量表(visually analogue scale, VAS)以及SN-5量表^[8]进行评估,由监护人和患儿共同完成;同时行鼻窦CT检查,并进行CT评分(Lund-Mackey评分)。VAS评分分别于术前1 d、术后6个月进行(下降<3分为无变化,下降≥3分为缓解,降至0分为完全缓解);SN-5评分(下降值≤0.5为无变化,>0.5~1为轻度缓解,>1~1.5为缓解,>1.5为显著缓解)于术前1 d和术后6个月进行;CT评分(Lund-Mackey评分)分别于术前1周内和术后6个月进行;鼻内镜检查于术前1周内及术后15 d、1个月、2个月、6个月进行。

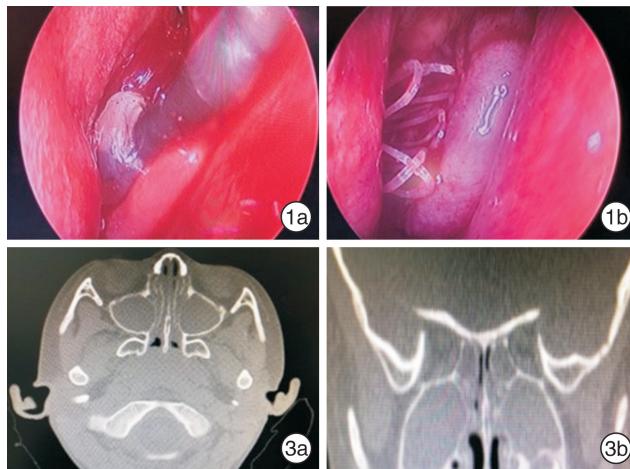


图1 术中所见 1a: 鼻窦球囊扩张上颌窦口; 1b: 支架置于上颌窦口;

1.4 统计学分析

采用SPSS 23.0软件对所有数据进行统计学分析。术前组间数据若符合正态分布则行t检验,若非正态分布则行秩和检验以明确术前组间数据是否存在差异;采用重复测量资料的两因素方差分析进行组间术前术后连续数据的统计学检验。以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 球囊支架组手术前后VAS、SN-5及术侧CT评分

球囊支架组患儿手术均成功,术中、术后未发生严重并发症(眶内、颅内并发症),无鼻腔粘连,无眼部不适。鼻窦支架未发生脱落和移位。球囊支架组VAS评分术前1 d为6.9,术后6个月为2.0;SN-5评分术前1 d为2.397,术后6个月为1.376;术侧CT评分术前为9.628,术后6个月为1.314。术后6个月,球囊支架组患儿的VAS评分、SN-5评分、CT评分均较术前显著下降,VAS评分和SN-5评分的术后缓解率分别为100%和95%。球囊支架组术后15 d随访鼻内镜检查,35侧支架中5侧支架已吸收(图2a);术后1个月35侧支架30侧支架已吸收;术后2个月35侧支架均吸收(图2b)。依据VAS评分标准,本组2例达到完全缓解,21例达到部分缓解。依据SN-5评分的判断标准^[8],轻度缓解12例、缓解5例、明显缓解5例、1例无变化。1例患儿术前与术后6个月CT比较见图3。

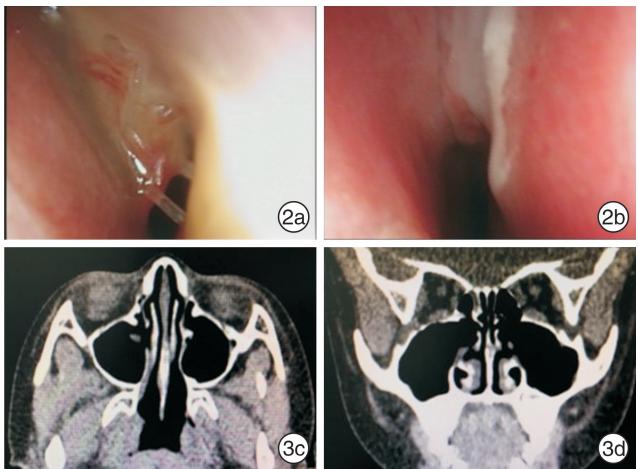


图2 留置支架情况 2a: 术后15 d留置支架; 2b: 术后2个月支架吸收,鼻腔黏膜上皮化;

2.2 球囊组和球囊支架组的SN-5评分

球囊组SN-5评分术前为 2.321 ± 0.635 ,术后为 1.586 ± 0.540 ;球囊支架组SN-5评分术前为 2.397 ± 0.512 ,术后为 1.376 ± 0.206 ,2组术前SN-5评分比较差异无统计学意义($P = 0.647$),2组SN-5评分下降幅度比较差异有统计学意义

($F = 6.801, P = 0.012$)。

2.3 术前SN-5评分<2.5的患儿SN-5评分比较

球囊组术前SN-5评分<2.5的患儿14例,术前评分为 1.825 ± 0.325 ,术后为 1.282 ± 0.172 ;球囊支架组术前SN-5评分<2.5的患儿12例,术前评分为 1.991 ± 0.314 ,术后为 1.312 ± 0.196 ,2组

术前 SN-5 评分比较差异无统计学意义 ($P = 0.199$)，2 组评分均数下降幅度比较差异无统计学意义 ($F = 2.336, P = 0.14$)。

2.4 术前 SN-5 评分 ≥ 2.5 的患儿 SN-5 评分比较

球囊组术前 SN-5 评分 ≥ 2.5 的患儿 12 例，术前评分为 2.900 ± 0.335 ，术后为 1.941 ± 0.611 ；球囊支架组术前 SN-5 评分 ≥ 2.5 的患儿 11 例，术前评分为 2.808 ± 0.252 ，术后为 1.437 ± 0.195 ，2 组术前 SN-5 评分比较差异无统计学意义 ($P = 0.628$)，2 组评分均数下降幅度比较差异有统计学意义 ($F = 13.861, P = 0.001$)。

2.5 2 组术侧术前 CT 评分比较

术侧鼻窦 CT 评分 (Lund-Mackey 评分) 分为术前 3~8 分和 9~12 分两类。球囊组中有 3 侧鼻窦 CT 评分 <3 分，且行上颌窦口球囊扩张术，故未计入统计学数据。

球囊组术前 CT 3~8 分者共 27 例，术前 CT 评分为 5.888 ± 1.717 ，术后为 0.777 ± 0.891 ；球囊支架组术前 CT 3~8 分者共 8 例，术前 CT 评分为 6.500 ± 1.069 ，术后 0.875 ± 0.991 ，2 组术前 CT 评分比较差异无统计学意义 ($P = 0.411$)，2 组 CT 评分下降幅度差异无统计学意义 ($F = 1.108, P = 0.300$)。

球囊组术前 CT 9~12 分者共 12 例，术前 CT 评分为 10.416 ± 0.996 ，术后为 3.000 ± 1.044 ；球囊支架组术前 CT 9~12 分者共 27 例，术前 CT 评分为 10.555 ± 1.154 ，术后为 1.444 ± 0.933 ，2 组术前 CT 评分比较差异无统计学意义 ($P = 0.792$)，2 组 CT 评分下降幅度差异有统计学意义 ($F = 13.059, P = 0.001$)。

3 讨论

儿童 CRS 是儿童耳鼻咽喉头颈外科的常见疾病，严重影响儿童的日常生活。儿童发生上呼吸道感染的概率较成人高，其中 5%~13% 可能并发急性鼻窦炎，部分患儿炎症迁延、鼻窦黏膜长期处于炎症状态^[9]。

鼻用糖皮质激素、口服抗生素等药物仍是首选治疗方案^[1]。当药物治疗无效时则需要进行手术。据文献报道腺样体切除术伴鼻窦球囊扩张术的有效率约为 80%^[10]。若术后症状反复则行 FESS，但 FESS 存在眶内、颅内等严重并发症可能，是否影响儿童的鼻窦发育尚无定论^[11]。

自 2005 年美国 FDA 批准球囊导管扩张术应用于 CRS 的治疗，国内外均已广泛应用^[6,9,12]；自 2012 年全降解药物支架经美国 FDA 批准后应用于临床，取得良好疗效^[13-14]。虽然 2017 年全降解药物支架经中国 CFDA 批准于国内开始应用，但笔者未见应用于儿童的研究报道。

鼻窦球囊扩张结合全降解药物支架置入手术适用于药物治疗无效，需要进行鼻窦窦口开放的

CRS 患儿(筛窦炎除外)。其禁忌证主要有：无法耐受全身麻醉(严重的心肺功能异常等)、凝血功能障碍(血小板减少、血友病等)、因咽喉部梗阻导致的重度阻塞性睡眠呼吸暂停、头面部肿瘤或畸形(导致术腔无法暴露或手术无法操作)、无法耐受激素治疗的患儿。鼻窦球囊扩张手术其并发症和 FESS 并发症相似，主要包括：局部并发症(鼻腔出血、粘连)；眶内并发症(眶壁骨折、眶内出血等)；颅内并发症(脑脊液鼻漏、中枢感染等)；影响鼻窦发育^[15]，但颅内、眶内并发症的发生率较 FESS 手术低。国外学者提出的全降解药物支架置入的并发症包括：支架移位、脱落，异物反应，眼压升高^[13,16-17]。但本组患儿均未出现以上并发症。经鼻内镜检查，鼻窦支架术后吸收率 15 d 为 14%，30 d 为 85%，2 个月为 100%，与 Forwith 等^[13]的研究结果相似。在国内外学者的报道中，鼻窦球囊扩张手术有用于 4 岁以上儿童、也有用于 6 岁以上儿童^[6,10,12]。本研究中最小年龄为 3 岁，但鉴于鼻窦球囊导管和药物支架的传送装置国内尚无相应的儿童型号，因此建议此术式适应年龄为 4 岁及以上。

本研究主要在 VAS 评分、SN-5 评分、CT 评分 (Lund-Mackey 评分) 3 个方面对鼻窦球囊扩张术结合全降解药物支架置入治疗 CRS 患儿的疗效进行评价。手术后三类评分均数都明显下降，提示手术疗效好。其中 1 例患儿的 SN-5 评分差未达到缓解，其为 9 岁男性患儿，术前 SN-5 评分为 1.6，术后 6 个月 SN-5 评分为 1.1，患儿双侧鼻窦 CT 评分均为 7 分，术前鼻内镜检查左侧上颌窦口见息肉样变组织，中鼻道积涕，右侧见中鼻甲及钩突水肿，因此仅于左侧鼻窦行上颌窦口扩张及支架置入，术后 6 个月 CT 评分为左侧 2 分，右侧 4 分，患儿术后左侧流涕鼻塞好转，右侧鼻腔仍有鼻窦感染症状，考虑 SN-5 评分未达缓解与右侧鼻腔疾病相关。

儿童 CRS 首选鼻喷激素治疗，药物治疗无效则考虑行腺样体切除结合鼻窦球囊扩张手术。严重的儿童 CRS 和内镜下鼻窦手术后鼻窦炎复发的原因主要有鼻黏膜息肉样变、AR、鼻腔及鼻窦窦口粘连、瘢痕形成等^[18-19]。而全降解药物支架有抗炎、防止粘连和瘢痕形成作用。既往研究表明，仅有少部分的鼻喷激素可以弥散至中鼻道^[20]。而全降解药物支架留存期间会缓慢释放激素并直接作用于鼻窦口周边的黏膜，降低鼻-鼻窦黏膜的高反应性及血管通透性，起到抗炎作用^[21]，对鼻窦口周围黏膜息肉样变、黏膜的过敏性炎症有治疗作用。诸多随机对照研究表明：内镜鼻窦手术后，鼻腔置入含激素药物的支架和置入不含药物的支架相比较，前者能有效防止黏膜息肉样变及息肉复发^[22-24]。鼻窦支架为高分子材料，有一定弹性，可塑形窦口，在手术创面上皮化期间可防止粘连和瘢痕形成^[25]。Xu 等^[21]的研究表明降解支架的防粘

连效果较不降解支架更好; Marple 等^[14]和 Forwith 等^[23]的研究表明全降解支架组较对照组有更好的防粘连及防止组织瘢痕形成的效果; Huang 等^[26]报道难治性额窦炎及额窦囊肿病例术后置入全降解药物支架 1 年后,仍能有效保持额窦开放。Luong 等^[27]对 FESS 术后置入可吸收药物支架和未置入支架患者随访 90 d,发现置入组的 VAS 评分、CT 评分和粘连发生率均较未置入组有所下降,置入组窦口开放直径较未置入组大,2 组比较差异有统计学意义。Forwith 等^[23]研究表明,复发性鼻窦炎伴鼻息肉的患儿接受 FESS 并置入降解药物支架 6 个月后,患儿的主观评分及鼻内镜评分(鼻息肉等级和窦口阻塞度评分)均明显下降,且和未置入支架的患儿比较差异有统计学意义。Minni 等^[28]也进行了相似的研究,发现术后随访 1 年的患儿 SN-20 和 CT 评分较术前明显下降。Matheny 等^[17]报道的相关病例术后随访 2 年,手术效果良好。本研究显示:在术前 SN-5 以及鼻窦 CT 评分较高的患儿中,留置全降解药物支架的患儿其术后疗效优于未留置支架的患儿,研究结果与 Marple 等^[14]和 Forwith 等^[23]报道的结果相似。因此鼻窦球囊扩张结合全降解药物支架置入对于严重的 CRS 患儿疗效优于单纯行鼻窦球囊扩张术。

虽然本研究中无相关并发症及药物不良反应发生,但仍有相关并发症的报道。Lavigne 等(2014)报道 1 例患儿支架置入后有流泪、眼干、鼻部不适症状,后自行缓解; Adriaensen 等^[16]报道有术后出血病例,经对症治疗后缓解。

本研究为回顾性且非随机对照研究,故数据可能存在选择性偏倚。鼻窦球囊扩张结合全降解药物支架置入手术未和传统的内镜下鼻窦手术效果相比较,因此其对于严重鼻窦炎的治疗效果是否优于传统内镜下鼻窦手术尚无法确定。鼻窦球囊窦口扩张术联合全降解药物支架置入对于药物治疗不佳的 CRS 患儿疗效明确,对于较严重的 CRS 患儿,此术式的效果明显优于单纯行鼻窦球囊扩张术。

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发挥重要生理功能的上皮屏障系统,如血脑屏障、肠上皮屏障、肺上皮屏障及耳蜗血迷路屏障等。屏障功能破坏常是疾病发展的关键,以血迷路屏障为例,目前已发现噪声性聋、老年性聋及迷路炎等多种内耳疾病均有显著的血迷路屏障功能障碍。基于多重免疫荧光3D渲染技术可对上皮屏障结构中的毛细血管、血管旁细胞数量、体积及细胞分布进行定量分析并清晰显示细胞间连接模式,该技术在屏障功能研究中具有独特优势,值得推广。

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