DIOGO BARRETO PLANTIER

Discinesia ciliar primária e rinossinusite crônica: uma avaliação da tomografia computadorizada e da resposta ao tratamento com cirurgia endoscópica endonasal de pacientes adultos

Tese apresenta à Faculdade de Medicina da Universidade de São Paulo para obtenção do título de Doutor em Ciências

Programa de Otorrinolaringologia

Orientador: Prof. Dr. Richard Louis Voegels

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SUMÁRIO

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ABREVIATURAS E UNIDADES

CB	Concha média bolhosa
CM	Concha média
CMP	Concha média paradoxal
DCP	Discinesia ciliar primária
EPOS2020	do inglês: “European position paper on rhinosinusitis and nasal Polyps 2020”
ERS	do inglês: “European Respiratory Society”
ESS	do inglês: “Endoscopic sinus surgery”
FC	Fibrose cística
HVMA	do inglês: “High-speed video-microscopy analysis”
iPCD	do inglês: “*international* Primary Ciliary Dyskinesia *cohort*”
LK	Classificação de Lund-Kennedy
LM	Escore de Lund-Mackay
nNO	do inglês: “nasal Nitric oxide”
NOSE	do inglês: “Nasal Obstruction Symptom Evaluation”
RSA	Rinossinusite aguda
RSC	Rinossinusite crônica
SNOT-22	do inglês: “Sinonasal Outcome Test-22”
TC	Tomografia computadorizada
TEM	do inglês: “Transmission electron microscopy”
TMA	Tratamento médico apropriado
UPSIT	do inglês: “University of Pennsylvania Smell Identification Test”

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RESUMO

Plantier DB. *Discinesia ciliar primária e rinossinusite crônica*: uma avaliação da tomografia computadorizada e da resposta ao tratamento com cirurgia endoscópica endonasal de pacientes adultos [tese]. São Paulo: Faculdade de Medicina, Universidade de São Paulo; 2022.

A discinesia ciliar primária (DCP) é uma doença hereditária rara que afeta a função ciliar. Assim, estes pacientes podem apresentar estresse respiratório neonatal, alteração de lateralidade dos órgãos, infertilidade e infecções de vias aéreas de repetição ou crônica. Em relação às cavidades nasossinusais, pacientes com DCP podem apresentar rinorreia de início precoce, rinossinusite aguda de repetição, distúrbios do olfato, rinossinusite crônica (RSC) e alteração da pneumatização dos seios paranasais. O diagnóstico da RSC é feito pela associação do quadro clínico compatível, por 12 ou mais semanas, às alterações na endoscopia nasal e/ou da tomografia computadorizada (TC) dos seios paranasais. Por sua vez, o diagnóstico da DCP, é de difícil confirmação pois não existe exame considerado padrão-ouro e todos os exames são de difícil acesso. O tratamento da RSC é baseado no uso de corticoide tópico nasal, irrigação nasal com soro fisiológico e uso de corticosteroides sistêmicos e antibiótico, por curto período de tempo, para tratamento das agudizações. Para pacientes refratários ao tratamento clínico, a cirurgia endoscópica endonasal (ESS) é uma opção terapêutica segura e promove uma melhora na qualidade de vida dos pacientes. Até o presente momento, estudos avaliando tomograficamente a RSC em pacientes com DCP, focaram na descrição da pneumatização dos seios paranasais e no escore de Lund-Mackay (LM). Além disso, estes estudos incluíram crianças na amostra ou não descreveram detalhadamente os achados dos exames. Do mesmo modo, na literatura, não foram encontrados estudos avaliando o efeito da ESS na qualidade de vida associado ao efeito na endoscopia nasal ou no olfato, exclusivamente em pacientes adultos com DCP. O objetivo principal do primeiro artigo foi avaliar o impacto da ESS na qualidade de vida de pacientes com DCP e RSC. Os objetivos secundários foram avaliar o efeito da ESS nos achados endonasais e no olfato desses pacientes. Em relação ao efeito da ESS, antes da cirurgia, após 3 e 6 meses, os pacientes responderam aos questionários *Nasal Obstruction Symptom Evaluation* (NOSE) e *Sinonasal Outcome Test-22*(SNOT-22) e foram avaliados por endoscopia endonasal, sendo classificados, de acordo com a classificação de Lund-Kennedy (LK). Além disso, os pacientes tiveram a avaliação do olfato por meio do *University of Pennsylvania Smell Identification Test* (UPSIT) antes e após 3 meses da cirurgia. O objetivo do segundo artigo foi descrever os achados da TC de seios paranasais de pacientes adultos com DCP. Para isso, as TCs foram descritas por dois rinologistas e um radiologista, e um consenso dos resultados encontrados foi descrito no artigo. Nossos resultados mostram que todos os pacientes apresentaram melhora nos escores SNOT-22, NOSE e LK no período de acompanhamento. No entanto, os pacientes não apresentaram melhora do olfato após a cirurgia. No segundo estudo, 38,1% dos seios frontais e 14,3% dos

esfenoides eram aplásicos. Da mesma forma, foi identificada hipoplasia dos seios frontais em 47,6%, dos seios esfenoidais em 54,8%, dos seios maxilares em 40,5% e perda trabecular no etmoidal em 61,9% dos seios. A pontuação média de LM foi 13,5. Além disso, 9,5% dos pacientes tinham concha média bolhosa, 47,6% hipertrofia acentuada de concha nasal inferior, 38,1% hipertrofia acentuada de concha média e 47,6% desvio septal acentuado. Por fim, foram identificadas imagens sugestivas de bola fúngica, mucocele, osteoma, possível pólipo antrocoanal e erosões ósseas frontais. O presente estudo fornece uma descrição detalhada dos achados tomográficos em pacientes adultos com DCP. Foram descritas também variações anatômicas e possíveis lesões que devem ser identificadas para um planejamento cirúrgico mais seguro e que sugerem o diagnóstico de DCP se encontradas em pacientes com quadro clínico consistente. A ESS para RSC em adultos com DCP proporcionou melhora na qualidade de vida e nos achados endoscópicos. No entanto, não foi demonstrada melhora do olfato. Estudos com maior número de pacientes, incluindo grupo controle, devem ajudar a confirmar estes achados.

Descritores: Rinossinusite crônica; cirurgia endoscópica endonsal; Transtorno da motilidade ciliar; hiposmia; Síndrome de Kartagener; seios paranasais; aplasia; tomografia computadorizada.

ABSTRACT

Plantier DB. *Primary ciliary dyskinesia and chronic rhinosinusitis:* an assessment of computerized tomography and response to treatment with endoscopic endonasal surgery in adult patients [thesis]. São Paulo: "Faculdade de Medicina da Universidade de São Paulo"; 2022.

Primary ciliary dyskinesia (PCD) is a rare inherited disease that affects ciliary function. Therefore, these patients may present neonatal respiratory stress, abnormal laterality of internal organs, infertility and recurrent or chronic airway infections. Regarding the nasosinusal cavities, patients with PCD may present early-onset rhinorrhea, recurrent acute rhinosinusitis, smell disorders, chronic rhinosinusitis (CRS) and alterations in the pneumatization of the paranasal sinuses. The diagnosis of CRS is made by associating the clinical picture over 12 or more weeks with changes in nasal endoscopy and/or computerized tomography (CT) of the paranasal sinuses. The diagnosis of PCD, in turn, is difficult to confirm because there is no gold standard diagnostic test, and all tests are difficult to access. The treatment of CRS is based on the use of topical nasal corticosteroids, nasal irrigation with saline solution and the use of systemic corticosteroids and antibiotics, for a short period of time, to treat exacerbations. For patients who do not respond to conservative therapy, endoscopic sinus surgery (ESS) is a safe therapeutic option that can improve the quality of life of patients. To date, studies evaluating CT in patients with PCD have focused on the description of pneumatization of the paranasal sinuses and on the Lund-Mackay (LM) score. Furthermore, these studies included children in the sample or did not describe the test findings in detail. Likewise, we did not find any studies in the literature evaluating the effect of ESS on quality of life associated with the effect on nasal endoscopy or on olfaction, exclusively in adult patients with PCD. The aim objective of the first article is to assess the impact of ESS on the quality of life of patients with DCP and CRS. The secondary objectives were to evaluate the effect of ESS on nasal endoscopy and on olfaction of these patients. Regarding the effect of ESS, before surgery, after 3 and six months, patients answered the Nasal Obstruction Symptom Evaluation (NOSE) and Sinonasal Outcome Test-22 (SNOT-22) questionnaires and were evaluated by endonasal endoscopy and classified according to the Lund-Kennedy (LK) classification. In addition, patients were assessed for smell using the University of Pennsylvania Smell Identification Test (UPSIT) before and three months after surgery. The objective of the second article is to describe the findings of CTs of paranasal sinuses in adult patients with PCD. The CTs were described by two rhinologists and one radiologist, and a consensus on the results was reached and described in the article. Our results show that all patients showed improvement in SNOT-22, NOSE and LK scores in the follow-up period. However, patients' sense of smell did not improve after surgery. In the second study, 38.1% of the frontal sinuses and 14.3% of the sphenoids were aplastic. Likewise, we identified hypoplasia of the frontal sinuses in 47.6%, of the sphenoid sinuses in 54.8%, of the maxillary sinuses in 40.5% and trabecular loss in the ethmoid in 61.9% of the sinuses. The mean LM score was 13.5. Furthermore, 9.5% of the patients had

bullous middle concha, 47.6% had marked inferior turbinate hypertrophy, 38.1% had marked middle concha hypertrophy, and 47.6% had marked septal deviation. Finally, we identified images suggestive of a fungal ball, mucocele, osteoma, possible antrochoanal polyp and frontal bone erosions. The present study provides a detailed description of the CT findings in adult patients with PCD. We also describe anatomical variations and possible injuries that should be identified for safer surgical planning and that might suggest the diagnosis of PCD if found in patients with a consistent clinical picture. ESS for CRS in adults with PCD provided an improvement in quality of life and endoscopic findings. However, no improvement in smell was demonstrated. Studies with a larger number of patients, including a control group, should help to confirm these findings.

Descriptors: Chronic rhinosinusitis; endoscopic endoscopic surgery; Ciliary motility disorders; hyposmia; Kartagener's Syndrome; sinuses; aplasia; computerized tomography.

Apresentação

APRESENTAÇÃO

Esta tese é composta pela compilação dos dois artigos a seguir, que serão descritos e analisados: 1. Outcomes of endoscopic sinus surgery for chronic rhinosinusitis in adults with primary ciliary dyskinesia; 2. Computed tomography evaluation of the paranasal sinuses in adults with primary ciliary dyskinesia.

1 Introdução

1 INTRODUÇÃO

A Discinesia ciliar primária (DCP) é uma doença hereditária rara, transmitida sobretudo de forma autossômica recessiva. Afeta entre 1 para 10.000 a 40.000 nascidos vivos e está associada a alteração do transporte ciliar [1, 2]. O transporte ciliar ineficiente pode resultar em estresse respiratório neonatal, infecções de vias aéreas que se iniciam na infância, bronquiectasias, infertilidade e alteração da lateralidade dos órgão [3, 4]. Desta forma, estes pacientes apresentam, precocemente, um impacto físico e emocional na qualidade de vida [5, 6].

O transporte mucociliar é capaz de capturar e remover patógenos das vias aéreas, sendo uma primeira linha de defesa. Na DCP, esse transporte ineficiente leva a um acúmulo de secreção, proliferação bacteriana e inflamação da mucosa nasossinusal. Assim, estes pacientes apresentam rinorreia persistente de início precoce, que é o sintoma nasossinusal mais frequente, congestão nasal, rinossinusite aguda (RSA) de repetição ou rinossinusite crônica (RSC) [7]. Além disso, 35% dos pacientes apresentam sintomas nasossinusais, como primeiros sintomas de DCP e, em média, uma criança com DCP é medicada com antibiótico para rinossinusite 25 vezes até completar 10 anos de idade [8]. Somado a isso, a hipopneumatização dos seios frontais, maxilares e esfenoidais é mais prevalente nos pacientes com DCP que em indivíduos sem doença nasossinusal e em pacientes com RSC sem DCP [9, 10]. Por fim, pacientes com DCP também apresentam um maior acometimento do olfato que pacientes sem RSC ou com RSC sem DCP [11, 12].

1.1 DIAGNÓSTICO DA DISCINESIA CILIAR PRIMÁRIA

O diagnóstico da DCP é de difícil confirmação, visto que não há um teste padrão-ouro, sendo para isso necessária a combinação de exames de difícil acesso, sobretudo, em países, como o Brasil. De acordo com o *international PCD cohort* (iPCD), pacientes com quadro clínico sugestivo de DCP podem ser classificados

como “DCP definitivo” se apresentarem alterações na microscopia eletrônica de transmissão (TEM), compatíveis com DCP ou se apresentarem mutações bialélicas de genes associados à DCP. Além disso, os pacientes podem ser classificados, como “DCP provável” se apresentarem alterações na videomicroscopia de alta velocidade (HVMA) ou óxido nítrico nasal (nNO) baixo. Por fim, os pacientes podem ser classificados como “DCP clínica” se apresentarem quadro clínico característico e os resultados de exames são ambíguos, negativos ou não foram feitos [13].

Conforme a diretriz para diagnóstico da DCP publicada pela *European Respiratory Society* (ERS), o diagnóstico de DCP é confirmado se o paciente apresentar história clínica típica e alterações características da TEM ou mutação bilalélica de genes relacionados à DPC [14]. Por outro lado, a diretriz da *American Thoracic Society* considera o diagnóstico de DCP positivo se o paciente demonstrar os critérios apresentados pela ERS ou se apresentar repetidos testes de nNO com níveis baixos, associados à exclusão do diagnóstico de fibrose cística (FC) [15].

1.2 RINOSSINUSITE CRÔNICA NA DISCINESIA CILIAR PRIMÁRIA

A RSC em adultos é definida como a presença de obstrução nasal ou rinorreia, associada a, pelo menos, dor/pressão facial ou alteração do olfato. Estes sintomas devem ser contínuos por 12 ou mais semanas. Além disso, devem estar presentes sinais endoscópicos (pólipos nasais, secreção mucopurulenta ou edema de mucosa, sobretudo de meato médio) e/ou tomográficos (alteração do complexo ostiometal ou dos seios paranasais) sugestivos de RSC [16]. Deste modo, a tomografia computadorizada (TC) faz parte da investigação diagnóstica de pacientes com quadro clínico sugestivo de RSC. Ademais, a TC deve ser solicitada a todos os pacientes em programação de tratamento cirúrgico para RSC, pois possibilita avaliar a extensão da doença, bem como a presença de variações anatômicas que, se presentes, poderão aumentar o risco de complicações cirúrgicas.

Na cidade de São Paulo, a prevalência de RSC em pacientes maiores de 12 anos, foi estimada em 5,51%. Por outro lado, pacientes adultos com DCP apresentam uma prevalência de até 94,8% de RSC [17, 18].

A prevalência de RSC com pólipos nasais é difícil de ser determinada. Em estudos epidemiológicos, com diferenças metodológicas, a prevalência de pólipos nasais em adultos varia entre 1% e 4% [19]. Em revisão sistemática sobre variações demográficas da RSC nos Estados Unidos da América, 8.409 pacientes com RSC foram incluídos nos estudos. Dentre estes, 10,4% dos pacientes apresentavam RSC com polipose nasal reportada [20]. Em adultos com DCP, pólipos nasais podem estar presentes entre 34,4% e 56,4% dos pacientes [7, 17].

A DCP é um fator associado ao desenvolvimento da RSC em razão de seu impacto no transporte mucociliar [21]. Além disso, embora conflitante na literatura, alterações anatômicas, podem ser identificadas na TC, também são apontadas como possíveis contribuintes para o desenvolvimento ou agravamento da RSC. Assim, por exemplo, a drenagem dos seios frontais pode ser prejudicada pela presença de alterações como concha média bolhosa (CB), concha média paradoxal (CMP), célula etmoidal infraorbital (Haller), células frontoetmoidais, suprabulares ou supraorbitárias [16, 22].

De acordo com a classificação proposta pelo *European Position Paper on Rhinosinusitis and Nasal Polyps 2020* (EPOS2020) a RSC relacionada à DCP, com a FC, são exemplos de fenótipos da RSC secundária, difusa e com endótipo dominante mecânico [16]. No entanto, a alteração do transporte mucociliar da DCP não garante a exclusão de outros fenótipos de RSC associados no mesmo doente, como por exemplo, tumoral. Deste modo, a identificação de variações anatômicas e lesões nasossinusais devem integrar a avaliação de todos os pacientes com RSC.

1.3 TRATAMENTO DA RINOSSINUSITE CRÔNICA

Na literatura, há divergências em relação ao tratamento médico adequado para RSC, bem como quais os melhores critérios para considerar uma falha do tratamento. Orlandi et al., consideram o tratamento medicamentoso apropriado (TMA) para RSC o uso de corticoide tópico nasal, irrigação nasal com soro fisiológico e uso de corticosteroide oral e antibiótico, por curto período, nas agudizações. Além disso, consideram que o TMA é falho, quando os sintomas

permanecem incômodos associados a sinais tomográficos ou endoscópicos sugestivos de RSC [22]. O EPOS2020 considera a RSC como sem controle, se o paciente apresentar três ou mais dos critérios: obstrução nasal, rinorreia mucopurulenta ou dor facial na maioria dos dias da semana que levam ao desconforto, alteração do olfato, distúrbio do sono ou fadiga, mucosa com aparência doentia à endoscopia nasal ou sintomas persistentes, apesar do uso de tratamento medicamentoso de resgate [16].

No caso de pacientes que não obtiveram um controle adequado dos sintomas de RSC com o uso de medicações, a cirurgia endoscópica endonasal, do inglês *endoscopic sinus surgery* (ESS), é uma opção terapêutica capaz de aliviar os sintomas e melhorar a qualidade de vida do paciente, relacionada à RSC [23]. Além disso, a ESS melhora as condições nasossinusais para receber o tratamento tópico. O EPOS2020 sugere que, como o objetivo da ESS seria aliviar a gravidade dos sintomas do paciente, a decisão de realizar a cirurgia deve ser baseada na sintomatologia ou na presença de complicações. Somado a isso, considera que a intensidade dos sintomas no pré-operatório estão associados com os níveis de sucesso cirúrgico [16].

1.4 JUSTIFICATIVA DOS ESTUDOS

A raridade da DCP e a dificuldade de acesso a exames diagnósticos resulta em poucos estudos na literatura direcionados ao tratamento das queixas nasossinusais dessa população. Além disso, até o momento nenhum ensaio clínico avaliando o tratamento da RSC em pacientes com DCP foi identificado. Muitos dos tratamentos adotados são baseados na experiência de serviços de referência ou adaptados de tratamentos utilizados em outras doenças, como na FC [1, 24, 25].

Durante a investigação da RSC e avaliação pré-operatória de indivíduos adultos com DCP em nosso serviço, identificamos alterações tomográficas, como redução da pneumatização dos seios paranasais, variações anatômicas e lesões. Por outro lado, em nossa revisão da literatura, até o presente momento, identificamos que os estudos publicados, que apresentam resultados dos exames tomográficos nesses

pacientes, são focados na descrição do grau de pneumatização dos seios paranasais e no Escore de Lund-Mackay (LM), ou incluíram na amostra adultos e crianças [7, 9, 10, 17, 26–29].

A conclusão da pneumatização dos seios paranasais ocorre no início da fase adulta. Do mesmo modo, a prevalência de variações anatômicas, como desvio septal, CB e célula de Haller, aumenta com a idade [30, 31]. Assim, consideramos importante a realização de um estudo descrevendo detalhadamente as alterações nasossinusais à TC na população exclusivamente adulta com DCP. Para isso, além de classificarmos o nível de pneumatização dos seios e o escore de LM, avaliamos variações anatômicas e lesões nasossinusais que também podem contribuir para os sintomas sinusais desses pacientes.

Em relação à avaliação da ESS, como tratamento para RSC em pacientes com DCP, na literatura não encontramos estudos avaliando o impacto deste tratamento na qualidade de vida desses pacientes, exclusivamente, adultos. Até o momento, foram publicados relatos de casos de pacientes menores de 18 anos, com DCP, operadas para RSC, mas que não usam questionários de qualidade de vida para avaliar esta resposta [32-34]. Além disso, apenas um estudo prospectivo utilizou questionário de qualidade de vida *Sinonasal Outcome Test-22* (SNOT-22) para avaliar a resposta da ESS para RSC em pacientes com DCP, mas incluiu na amostra adultos e crianças [28]. Ademais, nenhum desses estudos avaliou o impacto da ESS na qualidade de vida relacionada à obstrução nasal (NOSE) no olfato ou no aspecto endonasal, por meio do escore de Lund-Kennedy (LK).

Os sintomas nasossinusais, que se iniciam na infância, permanecem na fase adulta ou tendem a piorar com a idade. Bequignon et al., identificaram uma correlação significante entre idade e piora desses sintomas [7]. Somado a isso, Pifferi et al. identificaram que pacientes com DCP apresentaram 29% de anosmia e 45% de hiposmia, e pacientes com RSC sem DCP, mostraram 24% de hiposmia [11].

Assim, realizamos o que consideramos o primeiro estudo avaliando em conjunto o efeito da ESS na qualidade de vida, no olfato e no LK de adultos com DCP.

2 Artigos Aceitos para Publicação

2 ARTIGOS ACEITOS PARA PUBLICAÇÃO

2.1 ARTIGO 1

2.1.1 Objetivos do Artigo 1

Objetivo principal:

- Avaliar o impacto da cirurgia endoscópica endonasal (ESS) na qualidade de vida de pacientes adultos com DCP e RSC refratária ao tratamento clínico.

Objetivo secundário:

- Avaliar, antes e após 3 meses da cirurgia, o impacto na olfação desses pacientes por meio do UPSIT.
- Avaliar o impacto da ESS nos achados da endoscopia nasal, por meio da classificação proposta por Lund-Kennedy, antes, após 3 e 6 meses da cirurgia.

2.1.2 Artigo 1 aceito para publicação

O artigo “Outcomes of endoscopic endonasal surgery for chronic rhinosinusitis in adults with primary ciliary dyskinesia” foi aceito para publicação em 1 de março de 2022 na revista International Archives of Otorhinolaryngology.

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Outcomes of endoscopic endonasal surgery for chronic rhinosinusitis in adults with primary ciliary dyskinesia

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Abstract

Introduction: Primary Ciliary Dyskinesia is a rare inherited disease associated with impairment of mucociliary transport and, consequently, with a high incidence of chronic rhinosinusitis. For patients with chronic rhinosinusitis who remain symptomatic despite medical treatment, endoscopic sinus surgery is a safe and effective therapeutic option. However, to date, we have not found any studies evaluating the effect of surgery on the quality of life associated with the effect on olfaction and nasal endoscopy findings of patients with primary ciliary dyskinesia and chronic rhinosinusitis. **Objective:** To describe the effect of endoscopic sinus surgery on the quality of life, on olfaction and on nasal endoscopy findings of adults with Primary Ciliary Dyskinesia and chronic rhinosinusitis. **Methods:** Four patients who underwent endoscopic sinus surgery were included. The SNOT-22 score, NOSE questionnaire and the Lund-Kennedy score were collected preoperatively and at 3 and 6 months postoperatively. The olfaction was assessed with the UPSIT, which was administered preoperatively and 3 months postoperatively. **Results:** A total of 4 patients (mean age 39.3 years; 3 men, 1 woman) completed the study. All patients showed clinically significant improvement in the SNOT-22, NOSE, and Lund-Kennedy scores at 3 months postoperatively, and this improvement was sustained throughout the follow-up period. However, olfaction did not improve after surgery. **Conclusion:** The endoscopic sinus surgery treatment of chronic rhinosinusitis in adults with Primary Ciliary Dyskinesia was associated with improvement in quality of life and endoscopic findings in. However, no improvement in olfaction was demonstrated. Studies with a larger number of patients and control groups should help confirm these findings.

Key words: Chronic rhinosinusitis, endoscopic sinus surgery, hyposmia, Kartagener syndrome, paranasal sinuses, primary ciliary dyskinesia.

Introduction

Primary ciliary dyskinesia (PCD) is a rare hereditary disorder associated with abnormal ciliary function. Impairment of mucociliary transport results in neonatal respiratory distress, recurrent airway infections, and infertility, as well as abnormal laterality of internal organs (situs inversus or ambiguus). [1, 2]. Thus, these patients experience early impact on physical and emotional quality of life [3, 4].

According to the international PCD (iPCD) cohort, patients with a clinical picture suggestive of PCD can be classified as having “definite PCD” if they are found to have transmission electron microscopy findings or a biallelic genetic mutation known to be associated with PCD. Patients can be classified as having “probable PCD” if they present abnormal findings on high-frequency video microscopy or low nasal nitric oxide levels. Finally, they can be classified as having a “clinical diagnosis of PCD” if the results of the aforementioned tests are negative or ambiguous, or if they have not been tested [5].

In PCD, a malfunction of sinonasal mucociliary clearance leads to stasis of secretions and inflammation of the mucosal lining. Thus, up to 94.8% of adults and 45% of children with PCD have chronic rhinosinusitis (CRS), and up to 56.4% of adults have nasal polyps [6, 7]. CRS can have a greater impact on quality of life than many other chronic diseases, including angina, congestive heart failure, and chronic obstructive pulmonary disease [8].

Endoscopic sinus surgery (ESS) is a safe treatment modality capable of relieving symptoms and improving the quality of life of patients with CRS who do not respond to conservative therapy [9].

To the best of our knowledge, no studies have yet evaluated the impact of ESS on quality of life associated with the effect on olfaction and nasal endoscopy findings in adult patients with PCD and CRS refractory to conservative treatment. Furthermore, studies on treatment of CRS usually exclude patients with PCD, which makes a targeted assessment of these patients even more relevant.

Within this context, the primary objective of the present study It is to evaluate the impact of ESS on the quality of life of adults with PCD and CRS. As a

secondary objective, we assessed the impact of ESS on olfaction and on nasal endoscopy findings in these patients.

Methods

Patient Recruitment

We carried out a prospective exploratory study of patients recruited from the Outpatient Rhinology Clinic of the Department of Otorhinolaryngology of a tertiary hospital. Patients over 18 years of age with PCD and indications for ESS for CRS, alone or combined with septoplasty and turbinate surgery, were included in the study.

Access to specific tests for diagnostic confirmation of PCD is very limited in Brazil, and there is no referral center for diagnosis anywhere in the country. Thus, patients with a confirmed, probable, or clinical diagnosis of PCD were eligible for inclusion [5]. Confirmation of PCD diagnosis was based on leading published guidelines [10, 11]. The diagnosis of CRS was based on the European Position Paper on Rhinosinusitis and Nasal Polyps [12]. Finally, we defined appropriate medical therapy (AMT) of CRS to be the use of topical nasal corticosteroids and nasal irrigation with saline solution; a short trial of oral corticosteroids and antibiotics may be attempted. AMT was considered to have failed when uncomfortable symptoms remained in combination with CT or endoscopic evidence of CRS [13]. For patients in whom AMT failed after at least 8 weeks of treatment, ESS was indicated.

Patients unfit to undergo surgery, those who did not wish to undergo the surgery, and those who had undergone previous sinus surgery were excluded from the study.

All patients underwent ESS under general anesthesia. In accordance with institutional protocols, the surgical technique adopted was based on the wide opening of paranasal sinuses to facilitate drainage of the sinuses by gravity and access of saline solution and medications to the sinuses. However, we did not perform more radical surgeries such as mega-antrostomy and Draf III in the first surgery. All

patients were discharged the day after surgery on a 7-day course of antibiotic and prednisolone, in addition to continuous large-volume, low-pressure nasal irrigation with 0.9% saline solution. The choice of antibiotic used took in account the result of the most recent culture of the patient (sputum or nasal) and the prednisolone was to reduce mucosal edema and discomfort, considering that the topical corticosteroid had not yet been reintroduced. Patients were evaluated weekly at the clinic until the mucosa of the nasal cavities was completely healed, with no crusting. At this point, topical nasal budesonide 50 mcg was resumed in all patients.

Outcome Measures

Primary outcomes: Quality of life was assessed with the Sinonasal Outcome Test-22 (SNOT-22) [14] and Nasal Obstruction Symptom Evaluation (NOSE) questionnaire [15], both of which have been validated for use in Brazilian Portuguese. The questionnaires were administered preoperatively and 3 and 6 months after ESS.

Secondary outcome:

Olfaction was assessed with the Brazilian version of the University of Pennsylvania Smell Identification Test (UPSIT) [16] at baseline and 3 months after surgery.

The Lund-Kennedy score was used to assess nasal endoscopy findings preoperatively and 3 and 6 months after ESS. Finally, preoperative CT scans were evaluated and classified with the Lund-Mackay score.

Results

The present study included 4 patients with mean age 39.3 years (3 men, 1 woman) who underwent ESS consecutively between 2018 and 2021. Three had a definite diagnosis of PCD, while one had clinical PCD. The clinical diagnosis of PCD had been established on the basis of persistent cough since childhood, recurrent

pneumonia and otitis, early-onset CRS, immotile sperm, a history of pulmonary lobectomy and bronchiectasis, consanguineous parents, and negative testing for immunodeficiencies and cystic fibrosis. Two patients had undergone lung transplantation, and one had undergone pulmonary lobectomy (Table 1).

Table 1 - Clinical, demographic, and surgical characteristics of patients with PCD

	Patient 1	**Patient 2**	**Patient 3**	**Patient 4**
Age	34	53	38	32
Gender	M	M	F	M
PCD diagnosis	Clinical PCD	Definite PCD	Definite PCD	Definite PCD
Situs inversus	No	Yes	Yes	Yes
Pulmonary surgery	LL	LT	No	LT
Nasal polyps	No	Yes	Yes	Yes
Septal deviation	No	Yes	Yes	Yes
Lund- Mackay	13	17	16	18

Abbreviations: F, female; M, male; LL, lung lobectomy; LT, lung transplant

No patient had any intraoperative or postoperative complications.

The primary outcomes and Lund-Kennedy scores are shown in Table 2. Endonasal endoscopic evaluation showed a mean preoperative Lund-Kennedy score of 8.75. By 3 months postoperatively, the mean score had improved to 3.75, and continued to improve thereafter, reaching 1.25 at 6 months after surgery. Thus, all patients showed improvement in the endoscopic appearance of the nasal cavities.

Table 2 - Lund-Kennedy score, SNOT-22, and NOSE scores in each patient in the preoperative period and 3 and 6 months after surgery

Variable	Endoscopy and quality of life scores			
	Patient 1	**Patient 2**	**Patient 3**	**Patient 4**
Lund-Kennedy score				
Preoperative	5	10	14	6
3 mo	5	4	4	2
6 mo	0	2	1	2
SNOT-22				
Preoperative	93	26	59	49
3 mo	40	10	23	15
6 mo	27	8	21	25
NOSE				
Preoperative	15	11	17	15
3 mo	2	0	0	2
6 mo	1	0	0	1

Abbreviations: NOSE, Nasal Obstruction Symptom Evaluation questionnaire, SNOT-22, Sinonasal Outcome Test-22.

SNOT-22: The mean preoperative SNOT-22 score was 56.8. Three months after surgery, the mean score had declined to 22, and continued to fall thereafter, reaching 20.3 at 6 months. Thus, all patients experienced improvement in quality of life after surgery, persisting throughout the follow-up period.

NOSE: Nasal obstruction-related quality of life was quite impaired in the preoperative period, with a mean NOSE score of 14.5. Three months after surgery, the mean score had dropped to 1 and, after 6 months, to 0.5. Thus, all patients achieved relief from the negative impact of nasal obstruction.

UPSIT: Subjective assessment of preoperative olfaction ranged between 7 and 30 (mean, 14). Three months postoperatively, scores ranged from 10 to 25 (mean, 15.8) (Table 3).

Table 3 - Olfaction outcomes of each patient preoperatively and 3 months after operation

UPSIT	Patient 1	Patient 2	Patient 3	Patient 4
Preoperative	30	12	7	7
3 mo	25	14	14	10

Abbreviations: UPSIT, University of Pennsylvania Smell Identification.

According to the UPSIT criteria, one patient had mild microsmia (UPSIT score 30–33) [16] and three patients had anosmia (UPSIT score 6–18) preoperatively. At 3 months postoperatively, one patient had progressed to severe microsmia (UPSIT score 19–25) and the other three patients remained anosmatic.

Discussion

In the present study, we found that patients with PCD and CRS who underwent ESS experienced improvement in SNOT-22 and NOSE scores at the third postoperative month, and remained improved until the sixth month. In addition, these patients showed improvement in endonasal endoscopy findings, as measured by the Lund-Kennedy score, throughout the follow-up period. While waiting for all patients to complete 6 months of follow-up after surgery, we continued to assess SNOT-22, NOSE, and Lund-Kennedy score in the first 3 patients to undergo surgery (Table 4). We were able to observe that, even after an average of 26.3 months after surgery, these patients continued to show improvement in all three scores, confirming the trend observed at 6-month follow-up.

Table 4 - Results of evaluation of Lund-Kennedy score, SNOT-22, and NOSE until the last patient had completed 6 months of follow-up

Patient (months after surgery)	Endoscopy and quality of life scores		
	Lund-Kennedy	SNOT-22	NOSE
1 (20 mo)	2	9	0
2 (26 mo)	1	14	0
3 (33 mo)	1	9	0

Abbreviations: NOSE, Nasal Obstruction Symptom Evaluation questionnaire, SNOT-22, Sinonasal Outcome Test-22.

The improvement in quality of life observed in the present study coincides with that previously described by Parson et al., who reported the cases of 3 children with PCD who underwent ESS for CRS. The authors identified improvement in upper and lower airway symptoms in all 3 children, but did not use questionnaires for evaluation [17]. Likewise, Tang et al. reported the case of a patient with Kartagener's syndrome who underwent ESS for the treatment of CRS and experienced improvement in upper and lower airway symptoms, but they also did not administer quality of life questionnaires [18]. Finally, Alanin et al. identified improvement in quality of life measured by SNOT-22 in 24 patients (adults and children) with PCD who underwent ESS either to identify a possible focus of infection or to treat CRS with symptoms refractory to medical treatment [19]. According to the authors, patients showed significant improvement from baseline at the 3rd month postoperatively, and this improvement was maintained throughout the 12-month period of assessment.

In the version of the SNOT-22 validated for Brazilian Portuguese, a change $\geq$ to 14 points is necessary to be perceived as improvement or worsening by the patient. The authors consider 10 as the upper limit of normal for the score [14]. Thus, all patients in the present study showed a noticeable improvement between the preoperative period and the 3rd month after surgery. Between the third and sixth months after surgery, scores changed by values of less than 14 points. The patient who experienced a 10-point increase in score between the 3rd and 6th months was re-evaluated 33 months after surgery and again had experienced a reduction in score, to 9 (within normal range). Finally, although all patients showed significant improvement in CRS-related quality of life, only one patient had reached normal

range (i.e., a score ≤ 10) at 3-month follow-up. We also reassessed this patient 22 months after surgery, and his score remained within normal range (9 points). The mean preoperative SNOT-22 score reported by Alanin et al. was 39, reducing to 23 by the third postoperative month [19]. In our study, the mean SNOT-22 decreased from 56.8 preoperatively to 22 on the third month after surgery. Despite our small sample size, we believe that patients with a higher preoperative score may experience a more marked improvement in the postoperative period. Furthermore, 3 (75%) of our patients had polyps and, according to Kosugi et al., patients with CRSwNP show greater variation between preoperative and postoperative scores [14].

Assessing olfaction through the Sniffin' Sticks extended test, Pifferi et al. found that hyposmia and anosmia were more common in patients with PCD than in patients with CRS without PCD and in a control group. Likewise, the authors found that patients with PCD and worse Lund-Mackay scores or lower nasal nitric oxide levels have a worse sense of smell [20]. In the present study, the patient with the best Lund-Mackay score also performed best on the preoperative and postoperative assessments of olfaction. According to the results of UPSIT performed preoperatively and at 3 months after surgery, no patient experienced enough improvement in scores to achieve normosmia or even improve in classification.

Limitations of the present study include the small sample size; the fact that some patients had undergone surgery before publication of a PCD-specific quality of life questionnaire (QOL-PCD) [21], which precluded use of this instrument; and the absence of a control group.

Conclusions

The present study showed that ESS can lead to improvement in quality of life as measured by the SNOT-22 and NOSE instruments. However, it was not able to improve olfaction during the follow-up period. We believe that further research with a larger sample and a control group is warranted to confirm these findings.

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2.1.3 Análise Crítica do Artigo 1

Pacientes com DCP apresentam queixas nasossinusais de início precoce. Ainda na infância, múltiplos tratamentos para RSA são necessários e 45% dos pacientes podem ter diagnóstico de RSC até os 18 anos. Em investigação de crianças com DCP, Sommer et al. identificaram que 69% das crianças com RSA de repetição necessitam de ESS, ao menos uma vez [8]. Em avaliação de 54 pacientes com DCP de até 18 anos, Bhatt et al. identificaram que 29,6% tinham sido submetidos a ESS [35]. Na fase adulta, a quase totalidade dos pacientes vai evoluir para RSC e muitos receberão indicação de ESS.

Não existe um consenso em relação à indicação cirúrgica para RSC em DCP. Na literatura, encontramos indicações para ESS em DCP, como para alívio dos sintomas refratários ao tratamento clínico, para pacientes com piora da função pulmonar ou para buscar um possível reservatório para reinfecção por *`Pseudomonas aeruginosa* pulmonar[36].

Até o momento, relatos de casos de ESS para RSC em pacientes com DCP avaliam pacientes com 17 anos ou menos [32-34]. Nesses estudos, todos os pacientes apresentaram alívio dos sintomas sinusais no período avaliado, mas não foram aplicados questionários de qualidade de vida. Alanin et al.[36] avaliaram a resposta da ESS para RSC, pelo SNOT-22, em pacientes com DCP entre 10 e 65 anos. Os pacientes apresentaram uma melhora significativa da qualidade de vida já no 3º mês pós-operatório e essa melhora manteve-se até 1 ano, após a cirurgia. No entanto, não descreveram a evolução dos achados endoscópicos, por exemplo LK, antes e após a cirurgia ou avaliaram o olfato desses pacientes por meio de teste específico.

No presente estudo, todos os pacientes mostraram melhora da qualidade de vida e do LK no 3º mês pós-operatório, esta melhora manteve-se no 6º mês. Os pacientes que completaram o seguimento de mais de 20 meses após a cirurgia, mantiveram a melhora da qualidade de vida e do LK. No entanto, nenhum paciente apresentou uma melhora perceptível do olfato, após a cirurgia. Por fim, nenhum paciente mostrou complicações relacionadas à ESS, demonstrando a segurança do procedimento para esses pacientes.

Estudos anteriores que descreveram o efeito da ESS em pacientes com DCP não mencionaram os resultados e a segurança do procedimento especificamente em pacientes com DCP, após transplante pulmonar. Para pacientes com FC, há evidência de que a ESS pode ser benéfica, após a realização do transplante [37]. No presente estudo, dois dos pacientes eram transplantados, não apresentaram complicações relacionadas à cirurgia e também mostraram melhora da qualidade de vida e do escore de LK, que se manteve durante todo o seguimento.

Cílios não motores estão presentes no epitélio olfatório e mutações que gerem alterações da estrutura ou função desses cílios podem afetar o olfato [38]. Pifferi et al. identificaram que pacientes com DCP apresentaram anosmia e hiposmia

significativamente piores do que pacientes com RSC sem DCP. Os autores hipotetizam que além de alterações obstrutivas, pacientes com DCP podem apresentar alterações de cílios primários (sensitivos) [11]. A ausência de melhora do olfato nos participantes deste estudo, após a ESS, poderia então estar associada à ciliopatia de base dos pacientes, além das causas obstrutivas.

O presente estudo é inédito e é relevante, pois avaliou pacientes com DCP, que é rara e de difícil confirmação diagnóstica, sobretudo no Brasil. No entanto, como importantes limitações de nosso estudo estão o número pequeno de participantes, a seleção dos pacientes, a ausência de um grupo controle e o tempo curto de seguimento. Do mesmo modo, o uso de questionário para avaliação da qualidade de vida relacionada à DCP, validado para a língua portuguesa, após o início da coleta dos dados do presente estudo, também contribuirá para entender melhor o impacto do tratamento nesses pacientes.

Apesar de também considerarmos a inclusão de um paciente com diagnóstico clínico de DCP como uma limitação do presente estudo, acreditamos que a apresentação do efeito da ESS nesse paciente é relevante. O acesso a exames de confirmação diagnóstica de DCP no Brasil é difícil e poucos pacientes terão o diagnóstico confirmado. No entanto, mesmo sem a confirmação diagnóstica de DCP, é importante o conhecimento do efeito do tratamento na RSC de paciente com história e quadro clínico sugestivos da doença.

2.2 ARTIGO 2

2.2.1 Objetivos do Artigo 2

Objetivo principal:

- Descrever os achados tomográficos nasossinusais de pacientes adultos com DCP e RSC.

2.2.2 Artigo 2 aceito para publicação

O artigo “Computed tomography evaluation of the paranasal sinuses in adults with primary ciliary dyskinesia.” foi aceito para publicação em 01 de março de 2022 na revista International Archives or Otorhinolaryngology.

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Computed tomography evaluation of the paranasal sinuses in adults with primary ciliary dyskinesia.

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Author´s contribution: All authors contributed to the study conception and design. Material preparation and data collection was performed by Diogo Plantier. CT scans analysis were performed by Diogo Plantier, Renata Pilan and Eloisa Gebrim. The first draft of the manuscript was written by Diogo Plantier and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Abstract

Introduction: Primary ciliary dyskinesia is a rare inherited disease that results in a malfunction of mucociliary clearance and sinonasal complaints. Aplasia/hypoplasia of the frontal and sphenoid sinuses has been described as more frequent in this population. However, to date, no studies have provided a detailed description of computed tomography findings in adult patients with a diagnosis of this condition. **Objective:** To describe the computed tomography (CT) findings of adult patients with primary ciliary dyskinesia. **Methods:** Retrospective observational study of adult patients with primary ciliary dyskinesia who underwent CT. **Results:** Twenty-one adults were included in the study. Aplasia of the frontal sinuses occurred in 38.1% and of the sphenoid sinuses in 14.3% of the sinuses. Likewise, there was hypoplasia of the frontal sinuses in 47.6%, of the sphenoid sinuses in 54.8%, of the maxillary sinuses in 40.5%, and trabecular loss in the ethmoid in 61.9% of the sinuses. The mean Lund-Mackay score was 13.5. In addition, 9.5% of the patients had concha bullosa, 47.6% had marked bilateral inferior turbinate hypertrophy, 38.1% had marked middle turbinate hypertrophy, and 47.6% had marked septal deviation. Finally, we identified images suggestive of fungus ball, mucocele, osteoma, a possible antrochoanal polyp, and frontal bone erosions. **Conclusion:** The present study provides a detailed description of CT findings in patients with primary ciliary dyskinesia. We also describe abnormalities that must be identified for safer surgical planning and that suggest a diagnosis of primary ciliary dyskinesia if found in patients with a consistent clinical picture.

Key words: Aplasia, computed tomography scanner, Kartagener syndrome, paranasal sinuses, primary ciliary dyskinesia.

Introduction

Primary ciliary dyskinesia (PCD) is a rare inherited disorder that results in a malfunction of mucociliary clearance and affects 1 in 10,000 to 1 in 40,000 individuals [1, 2]. These patients may present with recurrent airway infections, organ laterality defects, and infertility [3].

These patients often experience early-onset rhinorrhea, recurrent acute rhinosinusitis, or chronic rhinosinusitis (CRS) [4]. The prevalence of CRS in the population over 12 years of age has been estimated at 5.51% in the city of São Paulo, Brazil [5], while in adults with PCD, studies have shown a prevalence of up to 94.8% [6].

PCD is as a factor associated with the development of CRS due to ineffective mucociliary clearance [7]. Furthermore, despite conflicting reports in the literature, anatomical changes which can be identified on computed tomography (CT) of the paranasal sinuses have also been identified as possible contributors to the development of CRS. Thus, for example, frontal sinus or ostiomeatal complex drainage could be impaired by the presence of a concha bullosa (CB), paradoxical middle turbinate (PMT), infraorbital ethmoid (Haller's) cells, frontoethmoidal cells, suprabullar cells, and supraorbital cells [8].

Under normal conditions, the maxillary and ethmoid sinuses are already present, albeit with a reduced volume, at birth [9]. The sphenoid, however, is best identified after 3 or 5 years of age [10, 11]. The frontal sinuses, which are the last to form, are absent at birth, and their pneumatization is visible from the 6th year of life onwards [11]. With growth, the paranasal sinuses become progressively pneumatized and take on their definitive appearance by late adolescence [10, 12].

In addition to pneumatization, the incidence of anatomical variants also differs with age. Variants such as Kuhn and sphenoethmoidal (Onodi) cells present in early childhood, while the incidence of septal deviation, CB, and Haller's cells increases with age [10].

To date, studies in PCD have focused mainly on the description of Lund–Mackay (LM) score and pneumatization of the paranasal sinuses. Those studies have

identified a higher prevalence of sinus aplasia and hypoplasia in this population. Due to the progressive pneumatization of the paranasal sinuses, which is completed only in early adulthood, and to the fact that anatomical variability increases with age, we believe a detailed description of paranasal sinus CT findings exclusively in the adult population with PCD would be relevant. On the other hand, in addition to the changes in mucociliary clearance observed of these patients, it is also important to identify sinonasal lesions, and anatomical variants, all of which can contribute to altered drainage of the paranasal sinuses and subsequent development of sinonasal symptoms. The present study is relevant for safe surgical planning, should help maintain heightened diagnostic suspicion of PCD, and proposes a standard to describe CT findings in these patients. To date, we have not identified another study with such detailed tomographic description of adults with PCD.

Materials and Methods

We conducted a retrospective study of paranasal sinus CT scans of adult (age >18 years) patients with PCD requested for investigation of CRS at a tertiary hospital, using a non-probabilistic convenience sampling strategy.

According to the European Respiratory Society (ERS) Task Force Guidelines for diagnosing PCD, patients have a confirmed diagnosis of PCD if they present a typical history of PCD and hallmark ciliary ultrastructure defects for PCD assessed by transmission electron microscopy (TEM), or non-ambiguous biallelic mutations in PCD causing genes [13]. The American Thoracic Society guideline considers the diagnosis of PCD to be positive if the patient presents the alterations adopted by the ERS guideline or repeated low nasal nitric oxide (nNO) levels associated with exclusion of the diagnosis of cystic fibrosis [14]. Thus, PCD diagnosis in this sample was based on presence of typical clinical history and of different combinations of the following tests: low nNO measurement or high-speed video analysis showing altered cilia beat frequency and cilia beat pattern, plus homozygosity for a proven PCD variant gene or TEM showing altered cilia

ultrastructure consistent with PCD. Finally, some patients also underwent immunofluorescence, demonstrating absence of staining of ciliary proteins.

The present study was approved by the local Research Ethics Committee (approval number: 4.408.630).

The scans were analyzed by two specialist rhinologists and by a radiologist specializing in head and neck CT.

CT scans were described according to the characteristics seen in each of the paranasal sinuses. To describe the pneumatization of each sinus, we adopted the classification suggested by Eggesbo et al. [15] for a study conducted in patients with cystic fibrosis (CF). We adopted this classification because it is based on anatomical parameters, which allows its application for safer surgical planning and permits comparison with relevant previous studies.

We classified the sphenoid sinus as aplastic when there was no pneumatization posterior to the sphenoidal rostrum [10], hypoplastic when it was very small and located only in the anterior part of the sphenoid, or normoplastic if its pneumatization extended posteriorly beyond a vertical line in the sagittal plane which touches the anterior wall of the pituitary fossa [15] (Figure 1).

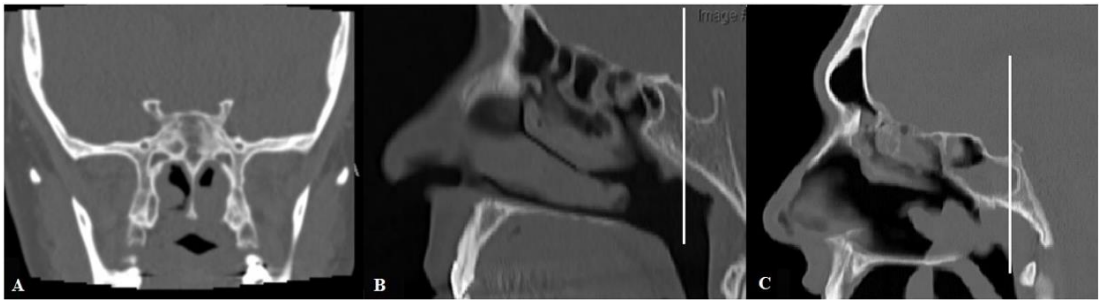

Figure 1 - (**A**) Aplasia of sphenoid sinuses. (**B**) Hypoplasia of sphenoid sinus. (**C**) Normoplastic sphenoid sinus

The frontal sinus was classified as aplastic if it exhibited no pneumatization superior to the frontal beak or to a horizontal line passing through the superior border of the orbit. We classified it as hypoplastic if the superior border of the sinus was smooth, there was no septation within the sinus, and its pneumatization did not extend beyond a vertical line that crossed the midline of the orbit. In cases where the

sinus was pneumatized beyond this vertical line, we classified it as normoplastic [10, 15] (Figure 2).

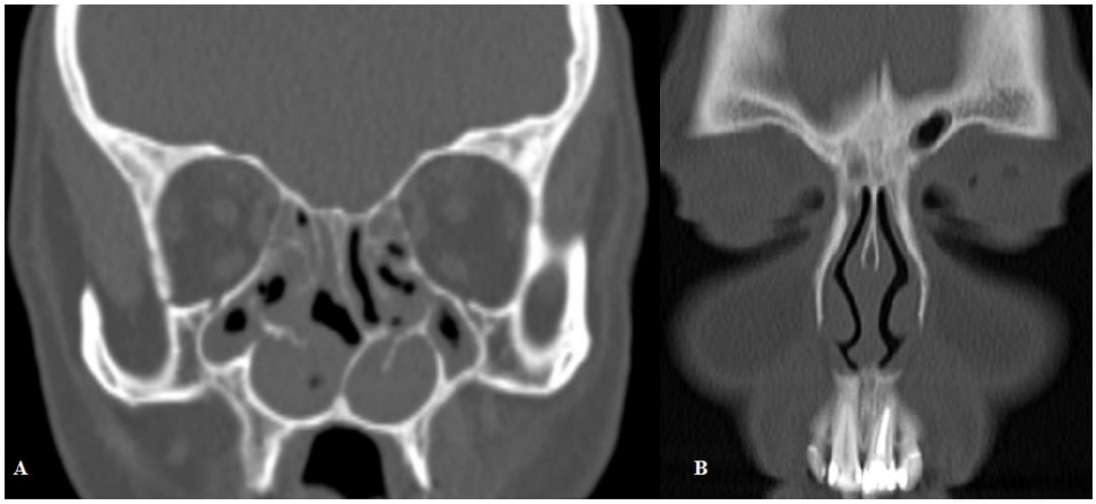

Figure 2 - (**A**) Hypoplastic maxillary sinuses. (**B**) Right frontal sinus aplasia and left frontal sinus hypoplasia

Maxillary sinuses were classified as aplastic if there was no pneumatization. Hypoplasia was defined if the sinus met 4 of the following 5 criteria: oval shape, absence of pneumatization below the level of the nasal floor, enlarged and oval-shaped orbit, medial sinus wall lateral to a vertical line drawn tangent to the medial border of the orbit (the insertion of the inferior turbinate at the lateral wall of the nose was used as a landmark when sinus surgery had been performed prior to examination), and lateral extension of the sinus medial to a vertical line drawn through the midline of the orbit at the level of the infundibulum, in the coronal plane. Finally, we classified it as normoplastic if it did not meet the criteria for hypoplasia [15].

We also described changes suggestive of osteoma, mucocele, bone erosion, fungus ball, polyp, and anatomical variations such as CB, PMT, agger nasi, Haller's cells, frontoethmoidal cells and Onodi cells.

We performed Lund-Mackay(LM) classification of all CT scans[16]. As recommended by Lund et al. [17], if the patient had undergone sinonasal surgery prior to the CT scan, we still classified the sinuses according to their degree of opacification. Partially opacified sinuses were assigned a score of 1; fully opacified

sinuses, 2; and sinuses free of opacification, 0. The osteomeatal complex was classified as 0 when free of opacification or open due to previous maxillary antrostomy, and as 2 if blocked or stenotic due to previous antrostomy. For patients who had aplasia of one or more paranasal sinuses, we assigned a score of 0 for each aplastic sinus [17] and used the rule of three to derive what score would be assigned if the patient had all sinuses. To do so, we multiplied 24 (the maximum score for a patient with all sinuses) by the score actually assigned to the patient, and divided the product by the maximum possible score for that particular patient [18].

Septal deviations were described in terms of presence, location, and contact with the turbinates. Finally, we considered the inferior turbinate hypertrophic if it touched the floor of the nasal cavity at any point and the middle turbinate (MT) hypertrophic if it touched the inferior turbinate.

To identify the severity of lower-airway disease, we considered patients who had a forced expiratory volume in the first second (FEV_1) of less than 50% of predicted on diagnostic spirometry as having severe lung disease [19].

Results

Twenty-one adult patients with confirmed PCD (13 men and 8 women), aged 18 to 62 years (mean, 38.1 years), were included in the study. Of these, 4 (19%) had undergone endoscopic endonasal surgery (EES) prior to the CT scan we evaluated (Table 1). Overall, 10 (47.6%) of the patients had situs inversus (SI), 5 (23.8%) were lung transplant recipients, and 1 (4.8%) had undergone lung lobectomy. Severe pulmonary disease was present in 11 (52.4%) patients at the time of diagnosis.

Table 1 - Clinical and demographic data from PCD patients

Patient	Age(y)	Sex	Positive tests	FEV_1 <50%	ESS before CT
1	62	M	Low nNO;HSVA (altered cilia movement); TEM(ODA); PCD gene: DNAI2.	No	Yes
2	37	M	Low nNO; HSVA (altered cilia movement); TEM(MTD+IDA); PCD gene: CCDC40.	No	No
3	34	M	Low nNO; HSVA (altered cilia movement); TEM(MTD+IDA); PCD gene: CCDC40.	No	Yes
4	55	F	Low nNO; HSVA (Altered Cilia Movement); TEM(OIDA).	Yes	No
5	37	F	Low nNO; HSVA (altered cilia movement); TEM(MTD+IDA); PCD gene: CCDC39; IF(CCDC39).	Yes	No
6	18	M	Low nNO; HSVA (altered cilia movement); TEM(MTD+IDA); PCD gene: CCDC40; IF(CCDC39).	Yes	No
7	54	M	Low nNO; HSVA (altered cilia movement); TEM(MTD+IDA); IF(CCDC39).	Yes	Yes
8	30	F	Low nNO; PCD gene: DNAAF3.	No	TIB
9	51	F	Low nNO; PCD gene:RSPH1.	No	No
10	40	M	Low nNO; HSVA (altered cilia movement); TEM(OIDA).	No	No
11	26	M	Low nNO; PCD gene: DNAH11.	Yes	No
12	23	F	Low nNO; HSVA(altered cilia movement); TEM(ODA); PCD gene:DNAH5; IF(DNAH5).	No	No
13	41	M	Low nNO; TEM(OIDA); PCD gene: DNAAF3.	Yes	No
14	18	F	Low nNO; HSVA (altered cilia movement); PCD gene: RSPH1.	No	No
15	54	M	Low nNO; HSVA (altered cilia movement); TEM(ODA); PCD gene: DNAH5.	Yes	No
16	47	M	TEM(ODA); PCD gene: DNAH5.	Yes	No
17	29	F	Low nNO; TEM(MTD+IDA); PCD gene: CCDC40; IF(CCDC39).	Yes	No
18	18	M	Low nNO; TEM(ODA); IF(DNAH5).	No	No
19	37	M	Low nNO; HSVA(altered cilia movement); TEM(MTD+IDA).	Yes	No
20	40	M	HSVA (altered cilia movement); PCD gene: DYX1C1-CCGP1	No	No
21	50	F	Low nNO; HSVA (altered cilia movement); TEM(ACP).	Yes	Yes

Abbreviations: F, female; M, male; nNO, nasal nitric oxide; TEM, transmission electron microscopy; ODA, outer dynein arm; OIDA, outer inner dynein arm; MTD+IDA, microtubular disarrangement and inner dynein arm; ACP, absence of central pair; ACP+T: absence of central pair and transposition; HSVA, high-speed video analysis; Altered Cilia Movement, altered cilia beat frequency and cilia beat pattern; IF, Cilia Immunofluorescence; PCD gene, Proved PCD variant gene (homozygotes); FEV_1, forced expiratory volume in the first second of the forced vital capacity; ESS, endoscopic sinus surgery; IT, inferior turbinectomy; CT, computerized tomography.

The incidence of aplasia and hypoplasia of each paranasal sinus can be seen in Table 2.

Table 2 - Paranasal sinus pneumatization

	Frontal n(%)	**Sphenoid n(%)**	**Maxillary n(%)**
Aplasia	16(38.1)	6(14.3)	0
Hypoplasia	20(47.6)	23(54.8)	17(40.5)
Normoplasia	6(14.3)	13(30.9)	25(59.5)

Frontal sinus: Analysis by patient revealed that 11 (52.4%) had frontal aplasia, 5 (23.8%) bilateral and 6 (28.6%) unilateral, all with a hypoplastic contralateral sinus. We identified bilateral hypoplasia in 7 patients (33.3%) and bilateral normoplasia in 3 (14.3%).

Sphenoid sinus: On analysis by patient, 5 (23.8%) presented with bilaterally normoplastic sphenoids and 3 (14.3%) with unilateral normoplasia. Aplasia was bilateral in 2 (9.5%) and unilateral in 2 (9.5%). We found bilateral hypoplasia in 9 patients (42.8%) and unilateral hypoplasia in 5 (23.8%).

Maxillary sinus: On analysis by patient, 11 (52.4%) presented with bilaterally normoplastic maxillary sinuses and 3 (14.3%) with unilateral normoplasia. Finally, 7 (33.3%) had bilateral hypoplasia.

Ethmoid sinus: We observed loss of ethmoid trabeculae in 13 patients (61.9%).

Lund-Mackay score: The LM score ranged between 8.7 and 18 (mean, 13.5 and median (IQR), 14.2(3.3)). Of the 147 pneumatized sinuses, only 6 (4.1%) had a score of 0; of these, 3 were frontal sinuses and 3 were sphenoid sinuses (Table 3).

Table 3 - Lund-Mackay score for each pneumatized sinus, anatomical variations and lesions.

	Maxillary n(%)	**Ethmoid n(%)**	**Frontal n(%)**	**Sphenoid n(%)**
LM 0	0(0)	0(0)	3(12)	3(8,8)
LM 1	37(88,1)	37(88,1)	17(68)	30(88,2)
LM 2	5(11,9)	5(11,9)	5(20)	1(2,9)

Anatomical Variations n(%)
Turbinate variants:
Hypertrophic inferior turbinate: 10(47.6%)
Hypertrophic middle turbinate: 8(38.1%)
Concha bullosa: 2(9.5%)
Paradoxical middle turbinate: 2(9.5%)
Agger nasi: 17(81%)
Onodi cell: 5(23.8%)
Frontoethmoidal cell: 1(4.8%)
Marked septal deviation: 10(47.6%)
Lesions
Probable fungus ball: 1(4.8%)
Osteoma: 1(4.8%)
Mucocele: 1(4.8%)
Probable antrochoanal polyp: 1(4.8%)
Probable bone erosion: 1(4.8%)

Abbreviations: LM, Lund-Mackay score.

Gender differences: Bilateral sphenoid sinus aplasia was identified in 2 men and no women. Likewise, bilateral frontal aplasia was identified in 5 men and in none of the women. However, women and men accounted for 3 cases of unilateral frontal aplasia each. Regarding the maxillary sinus, neither sex had sinus aplasia, but 4 men and 3 women had bilateral hypoplasia. The men's LM score ranged between 9.3 and 17 (mean: 13.7). In women, the score ranged between 8.7 and 18 (mean: 13.1).

Turbinate variants: Among the anatomical variations identified in the nasal turbinates, 2 patients (9.5%) had a CB. The inferior turbinate exhibited marked hypertrophy bilaterally in 10 patients (47.6%). On the other hand, 8 (38.1%) patients had marked bilateral hypertrophy of the MT. We found paradoxical curvature of the MT in 2 patients (9.5%).

Anatomical variations: We identified agger nasi in 17 patients (81%), Onodi cell in 5 (23.8%), frontoethmoidal cell in 1 (4.8%) and 10 patients (47.6%) had marked septal deviation.

Lesions: One patient had a probable frontal fungus ball, one patient had an image suggestive of anterior ethmoid osteoma, and one patient a small mucocele in the left anterior ethmoid. (Figure 3).

In one patient who had undergone maxillary antrostomy before CT, we observed a lesion suggestive of an antrochoanal polyp, and the patient was referred for further investigation (Figure 3). The same patient had a homogeneous soft-tissue density with rounded borders within the right maxillary sinus, suggesting a cyst or polyp.

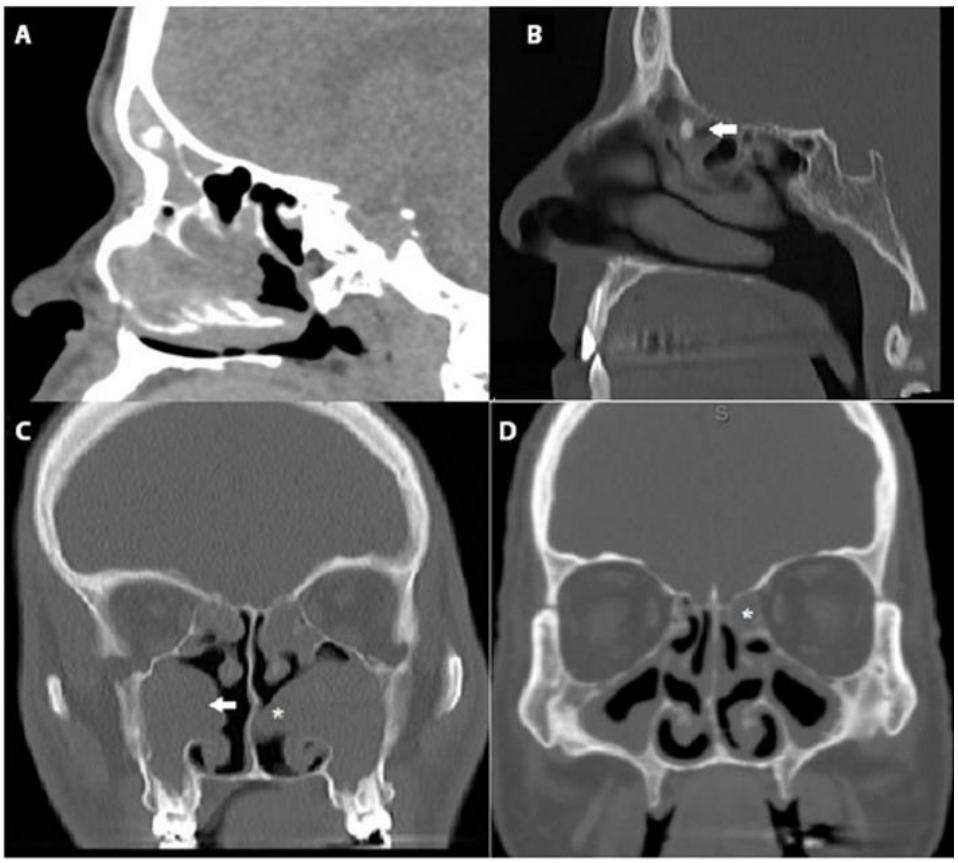

Figure 3 - Images suggestive of: (**A**) Left frontal sinus fungal ball. (**B**) Left ethmoid sinus osteoma (arrow). (**C**) Left maxillary sinus antrochoanal polyp (*) and a right maxillary sinus cyst (arrow). (**D**) Left ethmoid sinus mucocele (*)

Bone erosion: We identified an image suggestive of bone erosions in the frontal sinuses of one patient (4.8%). These defects were found in the posterior table and floor of the right frontal sinus, and an additional probable erosion was seen in the posterior table of the left frontal sinus (Figure 4). This patient underwent EES for treatment of CRS and did not present any evidence of CSF leak.

Discussion

In the present study, we found a high prevalence of aplastic (38.1%) and hypoplastic (47.6%) frontal sinuses. Overall, 52.4% of patients had frontal sinus aplasia (bilateral in 23.8%). Bilateral hypoplasia was identified in 33.3% of patients. The prevalence of sinus aplasia was higher than that reported by Marino et al., who found that 18.4% of the frontal sinuses of patients without sinonasal disease were entirely absent or did not extend beyond the superior border of the orbit (which, in the present study, was classified as aplasia) [20]. Park et al. identified frontal aplasia in 5.3% of volunteers without sinonasal disease, but the authors' definition of aplasia is unclear [21]. Pifferi et al. and Bequignon et al. used the criteria proposed by Orlandi et al. [18]. Thus, they defined aplasia as absence of pneumatization of the frontal sinus and hypoplasia if the sinus met the same criteria adopted in the present study. In a sample of children and adults with PCD, Pifferi et al. observed aplasia in 32% of frontal sinuses and hypoplasia in 21%, which was statistically superior to that found in patients with SCD (11% and 17% respectively). The authors believe that the fact that patients with SCD also have a higher incidence of sinus hypoplasia and aplasia than the normal population could support the hypothesis of an influence of the inflammatory process on sinus underdevelopment [22]. Bequignon et al. evaluated frontal sinus pneumatization in adults with PCD and identified a lower prevalence, with complete aplasia in 17.1% and hypoplasia in 14.6% of patients [23]. El-Sayed et al. identified a 56.3% combined rate of frontal sinus hypoplasia and aplasia in patients aged 2 years and older with PCD. However, the authors did not report clear criteria for aplasia and hypoplasia [24]. Alanin et al., during preoperative evaluation of

adults and children with PCD, identified frontal or sphenoid hypoplasia in 58% of patients, but again did not report clear criteria [25].

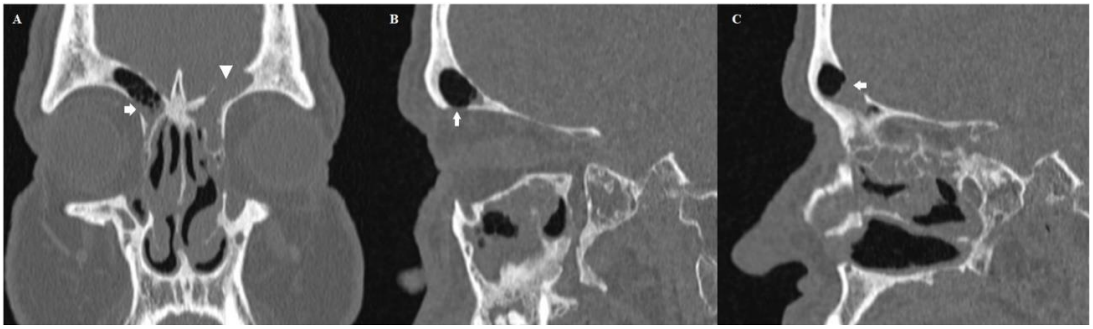

Figure 4 - Images suggestive of: (**A**) Left frontal sinus with posterior table erosion (arrowhead) and right frontal sinus with floor erosion (arrow). (**B**) Right frontal sinus with floor erosion (arrow). (**C**) Left frontal sinus with posterior table erosion (arrow)

Of the total number of sphenoid sinuses evaluated, we observed aplasia in 14.3% and hypoplasia in 54.8%. Considering the analysis performed per patient, 19% had at least one aplastic sinus. We identified bilateral hypoplasia in 42.8% of patients and unilateral hypoplasia in 23.8%. These percentages are in stark contrast to those described in adults with PCD by Bequignon et al., who found hypoplasia in only 24.4% of patients and no cases of sphenoid aplasia [23]. In a study of adults and children with PCD, Pifferi et al. found aplastic sphenoid sinuses in 15% and hypoplastic sinuses in 32%. Among patients with SCD, 7% had aplastic sphenoids and 3% had hypoplasia [22]. Both studies used criteria similar to those adopted in the present investigation to classify sphenoid pneumatization.

We found that 40.5% of maxillary sinuses were hypoplastic. Analysis by patients showed bilateral maxillary hypoplasia in 33.3% and unilateral hypoplasia in 14.3%. Pifferi et al. identified hypoplasia in 12% of maxillary sinuses of adults and children with PCD [22]. Pappa et al. identified that 88% of maxillary sinuses of adults with PCD had a smaller volume than the average volume of patients in the control group [26]. Bequignon et al. identified maxillary sinus aplasia in 2.4% of adult patients with PCD and hypoplasia in 4.9% [23]. On the other hand, Lorkiewicz-Muszyńska et al. evaluated CT scans of 170 children without sinonasal diseases, and all patients had maxillary sinuses [12]. Bequignon et al. and Pifferi et al. adopted

criteria similar to those used in the present study and that, if adopted, would not change our findings.

Several factors can be considered to at least partly explain the high prevalence of altered pneumatization of the paranasal sinuses in our sample: our patients were followed up at a tertiary hospital, 28.6% underwent lung surgery, more than half had severe lung disease, and we did not perform CT in patients without sinonasal complaints.

Kayabasi et al. found that patients with frontal, sphenoid, or maxillary sinus hypoplasia have a deeper olfactory fossa and a longer lateral lamella of the cribriform plate. These patients are thus at greater risk of skull base injury during EES [27]. Due to the higher incidence of paranasal sinus hypoplasia and aplasia in adults with PCD, these patients may be at increased risk of iatrogenic skull base injury.

In the present study, the LM score ranged between 8.7 and 18 (mean, 13.5 and median (IQR), 14.2 (3.3)). Pappa et al. identified LM scores between 6 and 16 (mean, 10.6) in adults with PCD, while the mean score in the control group was only 0.7 [26]. Frija-Masson et al. found LM with a median of 15 in 50 adults with PCD [6] and Bhatt et al. found median ± SD of 15.8±2.6 in children with PCD [28]. Pifferi et al. identified a median (IQR) score of 9.0 (6.5) in adult and pediatric patients with PCD and 3.5 (7) in patients with SCD, with a statistically significant difference between these groups [22]. Bequignon et al. found that 12% of CT scans were normal, and the mean LM score was 6.2±3.6 in adults with PCD [4].

In a study of 323 CT scans of patients without sinonasal diseases, Marino et al. identified CB in 28.9% of middle turbinates [20]. Sedaghat et al. identified CB in 41.7% of patients with allergic rhinitis who progressed to CRS [29]. In the present study, 9.5% of the patients had CB and 9.5% had paradoxical curvature of the MT, which can lead to obstruction of the middle meatus. Just as the paranasal sinuses of these patients are less pneumatized than those of individuals without disease, so too may their middle turbinates. Agger nasi cells were identified in 81% of patients, Onodi cells in 23.8%, and frontoethmoidal cells in 4.8%. According to Lund et al., depending on the method of analysis, the incidence of agger nasi cell ranges from 70

to 90% in the literature [30]. These anatomical variations, associated with altered mucociliary clearance, can hinder drainage of the paranasal sinuses. The finding of bilateral inferior turbinate hypertrophy in 47.6% of patients and middle turbinate hypertrophy in 38.1% can also contribute to sinonasal obstructive symptoms. Assessing nasal endoscopy in 64 adults with PCD, Bequignon et al. [4], identified inferior turbinate hypertrophy in only 34.4%.

In the present study, we found that only men had bilateral sphenoid and frontal aplasia, even with a similar mean LM score between genders. Previous studies did not differentiate between genders, but we believe that a study with a larger number of patients can help elucidate whether a real gender difference exists.

Among other lesions, we identified images suggestive of fungus ball within the frontal sinus, antrochoanal polyp, ethmoidal mucocele and ethmoidal osteoma. The frontal sinus is the rarest location for a fungus ball among the paranasal sinuses. In a review of the literature published between 1973 and 2008, Popko et al. identified only 20 cases of frontal sinus fungus ball [31]. Bequignon et al. did not identify lesions such as mucocele on CT scans of 41 adults with PCD [23]. Berlucchi et al. described what they considered to be the first report of ethmoidal mucocele in PCD and the authors suggested that, in children, the presence of mucoceles should raise diagnostic suspicion of PCD [32]. In a survey of patients who underwent surgery for mucocele over a 10-year period, only 6.5% had exclusively ethmoidal mucocele [33]. Finally, we identified bone dehiscence in the frontal sinuses in 4.8% of patients.

Limitations of this investigation include the lack of a control group for comparison and the small sample size. However, given that PCD is a rare disease and a particularly difficult diagnosis to confirm, it is relevant as one of the largest series in the literature limited to adults with known PCD.

Conclusion

The present study proposes a standardized description of CT findings in patients with PCD. We identified a high incidence of paranasal sinus hypoplasia and aplasia in adults. Notably, we did not identify a single CT scan in which all paranasal

sinuses were completely free. These findings, combined with characteristic clinical picture or even specific questionnaires such as PICADAR [34], may help heighten diagnostic suspicion of PCD, especially in countries with limited access to diagnostic methods. The presence of anatomical variants, hypertrophy of the middle and lower turbinates, septal deviation and lesions can also contribute to sinonasal symptoms and impair drainage of the paranasal sinuses. The present study highlights the need to consider these findings in the preoperative planning of patients who require surgery.

Declaration Of Conflicting Interests

The authors declare that there are no competing financial or nonfinancial interests and there are no personal relationships with other people or organizations that could inappropriately influence (bias) their work.

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2.2.3 Análise Crítica do Artigo 2

No artigo 2, analisamos a TC de seios paranasais de 21 adultos com diagnóstico confirmado de DCP. Nosso estudo identificou que mais da metade dos pacientes (52,4%) apresentou aplasia do frontal, sendo 23,8% bilateral. Estes valores são superiores aos descritos por Marino et al., e Park et al., que identificaram 18,4% e 5,3%, respectivamente, de aplasia do frontal em indivíduos sem doença nasossinusal. Do mesmo modo, foi superior ao encontrado por Pifferi et al., que em uma análise de adultos e crianças, identificaram que 32% dos frontais de pacientes com DCP eram aplásicos [(10)]. Por fim, Bequignon et al., analisaram adultos com DCP e identificaram aplasia de frontal em 17,1% [(26)].

Em relação ao esfenoide, identificamos aplasia em 14,3% e hipoplasia em mais da metade dos seios avaliados (54,8%). Este valor também foi superior ao identificado por Bequignon et al., que não identificaram aplasia de esfenoide em adultos com DCP(26). Do mesmo modo, foi superior ao descrito por Pifferi et al., que identificaram 15% dos seios de adultos e crianças com DCP eram aplásicos [(10)].

Em relação ao seio maxilar, identificamos um número de seios hipoplásicos superior ao descrito por Bequignon et al., (4,9% dos adultos com DCP) e Pifferi et. al., (12% dos seios de adultos e crianças com DCP). No entanto, Bequignon et al.,

identificaram que 2,4% dos adultos com DCP apresentavam aplasia de maxilar, o que não foi visto em nosso estudo [10, 26].

Pifferi et al., identificaram que pacientes com RSC sem DCP possuem maior incidência de hipoplasia de seios paranasais do que os indivíduos sem RSC, mas essa incidência foi menor do que a identificada em pacientes com DCP e RSC. Assim, os autores acreditam que o processo inflamatório nasossinusal e sua intensidade podem estar relacionados com o hipodesenvolvimento dos seios [10].

Acreditamos que a alta incidência de aplasia e hipoplasia de seios paranasais identificadas em nosso estudo e superiores ao descrito na literatura para pacientes com DCP e RSC, possa estar relacionada a uma associação de fatores. Em nosso serviço, só realizamos TC em pacientes com quadro clínico sugestivo de RSC ou complicações. Nossos pacientes são acompanhados em um serviço terciário e a gravidade da doença dos pacientes de nossa amostra pode ser representada pela doença pulmonar severa, presente em 52,4% dos pacientes, também pode estar relacionada.

Esta variação da pneumatização dos seios paranasais associada a uma história clínica compatível pode contribuir para aumentar a suspeição de DCP, sobretudo, em países, como o Brasil onde a confirmação diagnóstica é difícil. Além disso, estas informações são relevantes em um possível planejamento cirúrgico, pois pacientes com hipoplasia de seios paranasais possuem fossa olfatória mais profunda e lamela lateral mais longa, o que aumenta o risco de lesão da base de crânio no intraoperatório, por exemplo [39].

No presente estudo, identificamos alterações que também podem contribuir para agravar os sintomas nasossinusais. Identificamos CMB e CM paradoxal em 9,5% dos pacientes, hipertrofia de concha inferior em 47,6% e de concha média em 38,1% dos pacientes. Desvio septal tocando as conchas nasais foi identificado em 47,6% dos pacientes. Por fim, identificamos uma provável mucocele etmoidal, um provável osteoma de etmoide, um provável pólipo antrocoanal e uma provável bola fúngica de frontal. Em avaliação de 41 TC de adultos com DCP, Bequignon et al., não identificaram mucoceles [7]. Por outro lado, Berlucchi et al., descreveram o caso de uma criança com DCP que apresentou recorrentes mucoceles etmoidais [34].

Os resultados do presente estudo comprovam a relevância de uma descrição completa da TC desses pacientes (além da pneumatização de seios paranasais e LM) pois demonstra que, além das alterações nasossinusais relacionadas ao transporte mucociliar, variações anatômicas e lesões podem agravar os sintomas destes pacientes e podem ser incluídas no planejamento terapêutico.

Em nossa amostra incluímos pacientes com diagnóstico confirmado de DCP com ou sem cirurgia prévia. Consideramos que, mesmo a cirurgia alterando variações anatômicas e podendo alterar o escore de LM, a presença de pacientes operados no estudo adicionou informações relevantes sobre a pneumatização dos seios paranasais e da evolução da RSC após a cirurgia.

O presente estudo possui como limitações o número de participantes e a ausência de um grupo controle. No entanto, é relevante por seu caráter inédito e por apresentar resultados exclusivamente de pacientes adultos e com diagnóstico confirmado de DCP.

3 Conclusões e Perspectivas Futuras

3 CONCLUSÕES E PERSPECTIVAS FUTURAS

No primeiro estudo, os resultados demonstraram que a ESS proporcionou uma melhora da qualidade de vida dos pacientes, associada a uma melhora dos achados da endoscopia nasal. No entanto, o estudo identificou que alterações do olfato não tiveram resposta perceptível, após a cirurgia.

Os resultados do segundo estudo demonstraram uma alta prevalência de alteração da pneumatização dos seios paranasais em adultos com DCP. Do mesmo modo, identificamos alterações anatômicas e lesões que podem estar associadas a um agravamento dos sintomas nasossinusais nesses pacientes. A identificação desses achados tomográficos é relevante para um planejamento cirúrgico seguro e possibilita diagnóstico e tratamento desses outros fatores que também podem interferir na qualidade de vida do paciente.

Os achados descritos nos auxiliam na avaliação dos pacientes com DCP. Assim, em pacientes com história e quadro clínico sugestivo de DCP essas alterações tomográficas podem auxiliar na suspeita diagnóstica, sobretudo no Brasil, onde o acesso a exames diagnósticos é difícil. Por fim, o presente estudo contribui para a melhor compreensão dos possíveis resultados esperados com a cirurgia endoscópica endonasal nesses pacientes.

Como perspectivas futuras, nossa equipe permanecerá descrevendo as tomografias de pacientes com DCP, seguindo os parâmetros adotados e sugeridos no presente estudo. Do mesmo modo, continuaremos registrando a evolução pré-operatória e pós-operatória dos pacientes com DCP para tentar confirmar os resultados encontrados no presente estudo, por meio de estudo com maior número de participantes e associando a avaliação da qualidade de vida por meio de questionário específico para DCP.

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Anexos

ANEXOS

Anexo A

Grupo de Rinologia do Hospital das Clínicas da USP
Nome: _____ Sexo: ___ Idade: ___
RGHC: _____ Telefone: (___) _____ - _____

Instrumento para Avaliação dos Sintomas da Obstrução Nasal NOSE

➔ Ao paciente: Pedimos que nos ajude a compreender melhor o impacto da obstrução nasal em sua qualidade de vida. **Por favor, dê suas respostas a esta pesquisa.** Obrigado!

Durante **o último mês** qual foi a intensidade em que as situações abaixo foram um **problema** para você?

Faça um círculo na resposta mais correta

	Não é um problema	Problema muito pequeno	Problema moderado	Problema razoavel-mente grave	Problema grave
1. Congestão nasal ou sensação de nariz cheio	0	1	2	3	4
2. Bloqueio ou obstrução nasal	0	1	2	3	4
3. Dificuldade para respirar pelo nariz	0	1	2	3	4
4. Dificuldade para dormir	0	1	2	3	4
5. Incapaz de respirar o suficiente pelo nariz durante exercício ou esforço	0	1	2	3	4

Bezerra, TFP; Padua, FGM; Pilan, R; Voegels, RL. Adapt. Stewart MG (2004)

ANEXO B

Grupo de Rinologia do Hospital das Clínicas da USP
Nome: _____ Sexo: __
RGHC: _____ Idade: __ Telefone: (___) _____ - _____

AVALIAÇÃO DE RESULTADOS NASOSSINUSAIS: SNOT-22 (Português-BR)

Você encontrará abaixo uma lista de sintomas e conseqüências sociais e emocionais da sua rinossinusite. Gostaríamos de saber mais sobre estes problemas e pedimos que respondesse às seguintes perguntas da melhor maneira possível. Não há respostas certas ou erradas e somente você pode nos dar essas informações. Por gentileza, dê uma nota para seus problemas conforme se apresentaram nas duas últimas semanas. Obrigado por sua participação. Caso tenha alguma dúvida, peça a nossa ajuda imediatamente.

Considerando a gravidade dos problemas, classifique a intensidade dos sintomas, circulando o número correspondente da escala:	Nenhum problema	Problema muito leve	Problema leve	Problema moderado	Problema grave	Pior problema possível
1. Necessidade de "assoar o nariz"	0	1	2	3	4	5
2. Espirros	0	1	2	3	4	5
3. Nariz "escorrendo"	0	1	2	3	4	5
4. Tosse	0	1	2	3	4	5
5. Secreção do nariz indo para garganta	0	1	2	3	4	5
6. Secreção grossa saindo do nariz	0	1	2	3	4	5
7. Sensação de ouvido cheio ou tampado	0	1	2	3	4	5
8. Tontura ou vertigem	0	1	2	3	4	5
9. Dor de ouvido	0	1	2	3	4	5
10. Dor ou pressão no rosto	0	1	2	3	4	5
11. Dificuldade para conseguir dormir	0	1	2	3	4	5
12. Acordar no meio da noite	0	1	2	3	4	5
13. Falta de uma boa noite de sono	0	1	2	3	4	5
14. Acorda cansado	0	1	2	3	4	5
15. Fadiga ou cansaço durante o dia	0	1	2	3	4	5
16. Diminuição do seu rendimento para realizar atividades do seu dia a dia	0	1	2	3	4	5
17. Diminuição da sua concentração para realizar atividades do seu dia a dia	0	1	2	3	4	5
18. Frustrado, agitado ou irritado	0	1	2	3	4	5
19. Tristeza	0	1	2	3	4	5
20. Sensação de vergonha	0	1	2	3	4	5
21. Dificuldade para sentir "cheiros" ou "gostos"	0	1	2	3	4	5
22. Nariz entupido	0	1	2	3	4	5

(Kosugi EM, Chen VG, Fonseca VM, Cursino MM, Mendes Neto JA, 2011)

Total:_____