

Nasal secretion tissue plasminogen activator: A novel effective predictor of nasal polyp recurrence

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Clinical Implications

This study demonstrates that the concentration of tissue plasminogen activator in nasal secretions predicts postsurgical nasal polyp recurrence more efficiently than type 2 biomarkers.

Nasal polyps (NPs) are heterogeneous and occur in chronic rhinosinusitis, a complex disorder with high rates of postoperative recurrence.¹ Identification of predictors for recurrence is useful for improved personalized and holistic disease management. To date, previous attempts to predict NP recurrence are limited by the invasive nature of surgical tissue sample acquisition and the small number of biomarkers analyzed, which have been mostly related to type 2 (T2) and eosinophilic inflammation.^{2,3} The predictive value of T2 biomarkers may be impaired by the heterogeneous feature of NPs, and other biomarkers such as neutrophils may be more effective in predicting prognosis in patients with noneosinophilic NPs.² In addition, few studies have investigated the potential value of tissue remodeling markers as predictors of NP recurrence, although they are crucial for NP pathogenesis.⁴ Reduced production of tissue plasminogen activator (tPA) and subsequent excessive fibrin deposition have recently been implicated in the formation of NPs associated with both eosinophilic and noneosinophilic inflammation, making it a potential biomarker for NPs with diverse endotypes.^{5,6} This study aims to evaluate the efficiency of tPA as a biomarker, in comparison with 40 other inflammatory biomarkers, in nasal secretions as well as clinical characteristics to predict postoperative NP recurrence.

The study was approved by the Ethics Committee of Tongji Hospital. The NPs were diagnosed according to EPOS 2020,¹ and 187 Chinese Han patients with NPs were enrolled. Endoscopic sinus surgery was performed by fellowship-trained rhinologists in accordance with the extent of the disease and commonly accepted principles.⁷ After surgery, patients were routinely given intranasal glucocorticoids and nasal irrigation in combination with systemic glucocorticoids and antibiotics when needed.^{1,2} All patients were followed up for 12 months after surgery.¹ The definition of recurrence was as follows: endoscopic evidence of recurrence, together with at least 1 symptom even after receiving appropriate therapy.³ More information is provided in Appendix 1 (available in this article's Online Repository at www.jaci-inpractice.org).

Nasal secretion samples were collected before surgery.³ Thirty-nine inflammatory mediators including type 1, type 2 (T2), and type 17 cytokines, pro-inflammatory cytokines, chemokines, and immunoglobulins (Igs) were detected by Bio-Plex suspension chip method, and tPA and Charcot-Leyden crystal (CLC) were measured by enzyme-linked immunosorbent assay (ELISA). Data are shown as medians and interquartile ranges unless specifically stated. A logistic regression model was applied to identify predictors of outcome. These models were adjusted for confounding factors including age, sex, and comorbidities. Predictive abilities of the parameters were evaluated by using the area under receiver operating characteristic (ROC) curve (AUC). *P* values less than .05 were considered statistically significant. More information is provided in Appendix 1.

Fifty-four patients were excluded from the final analysis owing to being lost to follow-up, incomplete clinical data, or inadequate quantity of sample. There was no significant difference between excluded and finally analyzed subjects (*n* = 133). After completing 1 year follow-up, 38 of 133 patients (28.57%) had relapse of NPs (Table E1; available in this article's Online Repository at www.jaci-inpractice.org). Univariate regression analysis showed that the scores of nasal obstruction, loss of smell, total symptom and NPs, bilateral total computed tomography and endoscopic scores, upregulated levels in nasal secretion of CLC, thymic stromal lymphopoietin (TSLP), macrophage inflammatory protein (MIP)-1 β , chemokine (C-C motif) ligand 17 (CCL17) and IgE, and downregulated levels in nasal secretion of tPA were associated with recurrence of NPs (Table I). There was no significant difference in the extent of surgery between patients with and without polyp recurrence (Table E1). Patients with recurrent NPs received more courses of glucocorticoid (1 [1–1] courses vs 0 [0–0] courses; *P* < .001) and antibiotic treatment (1 [1–1] courses vs 0 [0, 0] courses; *P* < .001) than patients with recurrence-free NPs.

We further analyzed sensitivity and specificity of nasal secretion of CLC, TSLP, MIP-1 β , CCL17, IgE and tPA as well as clinical characteristics associated with NP recurrence in predicting NP recurrence. As shown in Figure 1, the ROC curve analysis showed that the most nasal secretion biomarkers had higher AUC values than clinical characteristics, and the levels of tPA had the highest predictive value (AUC = 0.896) for NP recurrence in total NP patients. The best cutoff point for tPA levels was determined as 1.845 ng/mg by using the Youden index with a sensitivity of 83.20% and specificity of 89.50%. Patients with low tPA levels (≤ 1.845 ng/mg) had a noticeably higher recurrence rate (33 of 52; 63.46%) than those with high tPA levels (5 of 81; 6.17%; *P* < .05). We found no statistical difference in recurrence time between patients with low tPA levels (3 mo [1–6 mo]) and patients with high tPA levels (3 mo [2–9 mo]), which may be due to the limited number of relapsed patients (*n* = 5) in the high tPA level group. Compared with those with high tPA levels, patients with low tPA levels also had higher nasal obstruction, facial pain, and loss of smell scores (Table E2; available in this article's Online Repository at www.jaci-inpractice.org).

The CLC, TSLP, IgE, and CCL17 are elevated and involved in T2 inflammation, whereas tPA is downregulated in all T2,

TABLE I. Univariate logistic analysis of mediators in nasal secretions and clinical characteristics associated with recurrence of NPs*

Markers	Recurrent (n = 38)	Recurrence-free (n = 95)	Odds ratio (95% CI)	Adjusted <i>P</i> value
tPA (ng/mg)	1.13 (0.72–1.70)	3.81 (2.26–5.22)	0.214 (0.108–0.425)	<.001
CLC (ng/mg)	40.17 (10.04–78.19)	8.14 (4.24–15.31)	1.036 (1.019–1.054)	<.001
IL-1 β (pg/mg)	11.89 (3.09–48.86)	9.36 (4.21–28.42)	1.010 (1.000–1.020)	.059
IL-1R α (pg/mg)	404.87 (258.67–814.21)	577.31 (314.16–847.06)	0.999 (0.999–1.000)	.110
IL-2 (pg/mg)	0.76 (0.55–1.34)	0.88 (0.62–1.26)	0.965 (0.857–1.085)	.550
IL-4 (pg/mg)	0.76 (0.54–1.34)	0.67 (0.29–1.00)	0.914 (0.694–1.205)	.525
IL-5 (pg/mg)	1.04 (0.42–3.01)	1.16 (0.63–2.28)	0.936 (0.848–1.032)	.186
IL-6 (pg/mg)	22.81 (10.45–74.89)	18.83 (6.99–37.29)	1.002 (0.998–1.006)	.239
IL-7 (pg/mg)	8.47 (5.30–12.66)	7.44 (4.86–11.45)	0.979 (0.940–1.020)	.305
IL-8 (ng/mg)	0.75 (0.43–1.58)	0.70 (0.36–1.37)	1.048 (0.846–1.297)	.670
IL-9 (pg/mg)	4.60 (2.31–8.93)	3.54 (1.50–7.30)	0.982 (0.947–1.017)	.310
IL-10 (pg/mg)	5.77 (3.95–8.73)	6.21 (3.89–9.90)	0.999 (0.984–1.014)	.916
IL-12 (pg/mg)	13.36 (8.55–28.60)	19.62 (10.46–33.83)	0.985 (0.963–1.008)	.196
IL-13 (pg/mg)	6.54 (2.34–11.74)	5.29 (3.01–8.00)	1.000 (0.990–1.011)	.933
IL-15 (pg/mg)	5.11 (3.37–6.86)	4.92 (3.35–6.69)	0.987 (0.952–1.024)	.494
IL-17A (pg/mg)	5.52 (3.86–8.35)	4.76 (3.01–8.43)	0.994 (0.977–1.011)	.498
Eotaxin (pg/mg)	17.65 (4.36–46.61)	16.80 (6.80–38.60)	1.001 (0.992–1.010)	.772
bFGF (pg/mg)	29.31 (16.82–50.10)	31.11 (15.43–66.47)	1.001 (1.000–1.002)	.180
G-CSF (ng/mg)	0.57 (0.18–3.81)	0.59 (0.15–2.42)	1.112 (0.966–1.280)	.138
GM-CSF (pg/mg)	36.37 (18.30–72.03)	49.54 (19.60–83.34)	1.131 (0.803–1.594)	.480
IFN- γ (pg/mg)	22.00 (16.16–36.69)	26.51 (17.63–36.93)	0.997 (0.985–1.008)	.558
IP-10 (ng/mg)	17.54 (4.09–42.67)	21.01 (8.00–41.75)	0.995 (0.984–1.007)	.418
MCP-1 (pg/mg)	19.24 (10.40–37.86)	12.60 (5.84–24.00)	1.009 (0.998–1.020)	.114
MIP-1 α (pg/mg)	3.83 (1.13–11.63)	3.22 (1.14–10.48)	1.038 (1.008–1.069)	.072
PDGF-BB (pg/mg)	10.78 (3.79–27.04)	8.68 (1.26–21.07)	0.999 (0.995–1.003)	.521
MIP-1 β (pg/mg)	64.13 (31.82–164.49)	32.31 (14.59–50.92)	1.011 (1.003–1.018)	.006
RANTES (pg/mg)	58.54 (28.06–190.16)	184.02 (91.87–322.95)	1.000 (1.000–1.001)	.140
TNF- α (pg/mg)	5.57 (2.67–13.71)	6.08 (2.23–11.07)	1.001 (1.000–1.003)	.154
VEGF (pg/mg)	299.18 (120.69–759.87)	387.78 (173.63–640.13)	1.000 (0.999–1.000)	.820
CCL17 (pg/mg)	0.84 (0.34–1.84)	0.32 (0.20–0.54)	5.977 (2.448–14.591)	<.001
TSLP (pg/mg)	1.41 (0.74–2.31)	0.78 (0.51–1.27)	2.051 (1.211–3.474)	<.001
IL-25 (pg/mg)	0.14 (0.07–0.28)	0.16 (0.08–0.31)	1.007 (0.976–1.039)	.663
IL-33 (ng/mg)	1.58 (0.82–3.24)	1.37 (0.63–2.08)	0.991 (0.866–1.135)	.900
IL-22 (pg/mg)	2.21 (1.32–3.71)	2.14 (1.25–3.44)	0.876 (0.679–1.129)	.306
IgG1 (ng/mg)	28.23 (16.91–41.34)	27.65 (16.93–32.86)	0.997 (0.981–1.013)	.705
IgG2 (ng/mg)	18.13 (12.14–27.20)	17.10 (10.52–21.54)	1.045 (1.003–1.097)	.064
IgG3 (ng/mg)	3.68 (2.44–12.23)	4.98 (2.16–9.68)	1.019 (0.970–1.070)	.460
IgG4 (ng/mg)	3.23 (1.64–7.57)	2.16 (0.78–5.30)	0.995 (0.980–1.011)	.532
IgA (ng/mL)	14.16 (9.00–25.88)	11.85 (8.63–21.03)	1.029 (0.996–1.063)	.083
IgM (ng/mg)	4.36 (2.91–7.84)	3.78 (1.81–6.42)	1.003 (0.985–1.022)	.744
IgE (pg/mg)	0.47 (0.10–2.37)	0.11 (0.033–0.307)	1.483 (1.021–2.154)	.003
Blood eosinophil count ($\times 10^9/L$)	0.40 (0.15–0.57)	0.19 (0.12–0.34)	2.561 (0.444–14.785)	.293
Blood eosinophil percent (%)	5.51 (2.04–9.32)	3.14 (1.66–5.21)	1.035 (0.931–1.151)	.527
Nasal obstruction VAS score	9.00 (6.80–10.00)	7.00 (5.00–8.00)	1.380 (1.126–1.692)	.002
Rhinorrhea VAS score	5.50 (2.00–8.00)	5.00 (2.00–7.00)	1.055 (0.918–1.213)	.447
Facial pain VAS score	0.50 (0–5.00)	0 (0–2.00)	1.135 (0.976–1.319)	.101
Loss of smell VAS score	10.00 (4.80–10.00)	6.00 (2.00–9.00)	1.242 (1.070–1.441)	.004
Total symptom VAS score	25.50 (19.00–32.00)	20.00 (14.00–27.00)	1.066 (1.016–1.119)	.009
Nasal polyp score	4.00 (4.00–6.00)	3.00 (2.00–4.00)	1.919 (1.386–2.658)	<.001
Bilateral CT score	18.00 (13.80–23.00)	14.00 (9.00–20.00)	1.094 (1.016–1.178)	.017
Endoscopic score	10.00 (8.00–12.50)	8.00 (6.00–10.00)	1.447 (1.206–1.736)	<.001

bFGF, Basic fibroblast growth factor; CT, computed tomography; G-CSF, granulocyte colony-stimulating factor; GM-CSF, granulocyte-macrophage colony-stimulating factor; IFN- γ , interferon gamma; IL, interleukin; IL-1Ra, IL-1 receptor antagonist; IP-10, interferon gamma-induced protein-10; MCP-1, monocyte chemoattractant protein-1; PDGF-BB, platelet-derived growth factor-BB; RANTES, regulated on activation, normal T-cell expressed and secreted; TNF- α , tumor necrosis factor alpha; VAS, visual analog scale; VEGF, vascular endothelial growth factor.

*For continuous variables, data are expressed by medians and interquartile ranges. The *P* values in bold < .05.

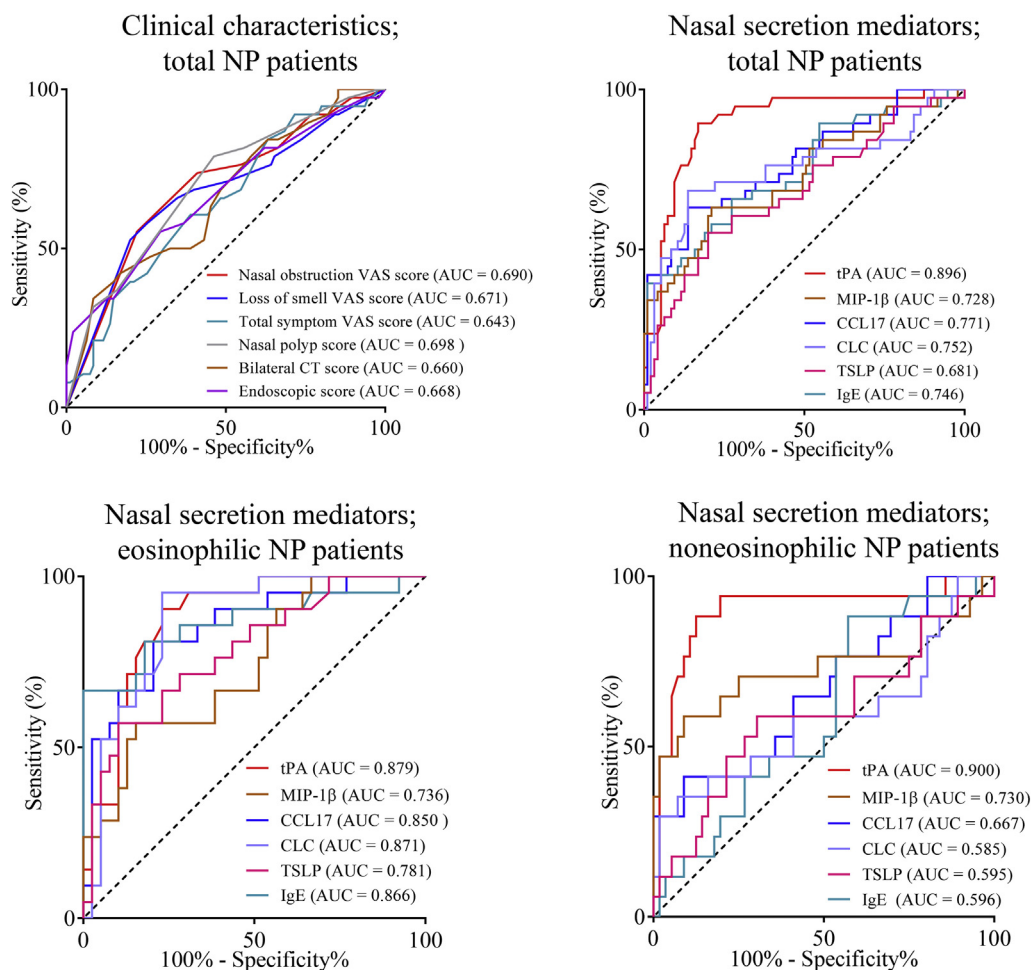


FIGURE 1. The concentrations of tPA in nasal secretions can predict the postoperative recurrence of NPs. The ROC curves are shown for clinical characteristics and nasal secretion biomarkers in predicting NP recurrence in total NP patients and for nasal secretion biomarkers in predicting NP recurrence in patients with eosinophilic or noneosinophilic NPs. CT, Computed tomography; VAS, visual analog scale.

type 1, and type 3 inflammation.^{5,6} We divided NP patients into those with eosinophilic ($n = 60$; 21 [35%] having recurrence) and noneosinophilic disease ($n = 73$; 17 [23.29%] having recurrence),⁸ and found that the biomarkers CLC, TSLP, IgE, and CCL17 all had greater AUCs, indicating a higher predictive capacity, in eosinophilic NPs than in noneosinophilic NPs, whereas tPA and MIP-1 β levels demonstrated comparable capacity in eosinophilic and noneosinophilic NPs (Fig 1). This may explain, at least in part, the higher predictive capacity of tPA than T2-related markers in the total group. Of note, in both eosinophilic and noneosinophilic NPs, the tPA had the highest predictive capacity.

The advantage of our study is that tPA in nasal secretions can be detected in the outpatient department and, hence, can be used to guide the surgical approach and postsurgical treatment selection. The patients with low tPA levels may benefit from more aggressive surgery and postoperative medical treatment, such as high-volume steroid irrigation or biologics, when suitable to the specific endotype. In this study, there was no significant difference in the extent of surgery between patients with recurrent and nonrecurrent NPs, suggesting that the extent of surgery would not bias our results.⁹ There are several limitations in our current

study, including short follow-up period after surgery, single-center study design, and the absence of validation in an independent cohort. In addition, to generalize the application of tPA in nasal secretions in the clinic, standard procedures for collection of nasal secretions and measurement of tPA should be established. Although our study was conducted in Chinese Han patients, tPA may also have potential predictive value in White patients in Western countries given a similar reduction of tPA discovered in those patients.⁵ However, more studies are needed to confirm our current findings in other populations.

In summary, our study has shown that measurement of levels of tPA in nasal secretion is a promising noninvasive predictor for NP recurrence, with a higher power than T2 biomarkers.

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ONLINE REPOSITORY

APPENDIX 1

Methods

Subjects. This study was approved by the Ethics Committee of Tongji Hospital and conducted with written informed consent. The study included 187 adult patients with bilateral nasal polyps (NPs). The NPs were diagnosed according to European Position Paper on Rhinosinusitis and Nasal Polyps 2020. Atopic status was assessed by using skin prick test with a panel of 19 common inhalant allergens in our region (Macro-Union Pharmaceutical Co., Beijing, China), and/or specific immunoglobulin E (IgE) against common inhalant allergens detected by using the ImmunoCAP (Phadia, Uppsala, Sweden). The diagnosis of allergic rhinitis was based on concordance of atopic status and allergic symptoms. The diagnosis of asthma was made according to the Global Initiative for Asthma guideline. Symptoms including nasal obstruction, rhinorrhea, facial pain, and loss of smell were scored by visual analog scale (VAS) from 0 to 10, with 0 for no symptom and 10 for the worst. Endoscopic physical findings were scored according to the Lund-Kennedy scoring system. Computed tomography (CT) scans were graded based on the Lund-Mackay scoring system. Two to 3 days before surgery, CT, VAS, and endoscopic scores were collected or determined. Patients with an acute upper respiratory tract infection or acute asthma episode within 4 weeks of entering the study and patients undergoing immunotherapy were excluded. In addition, this study excluded patients who had fungal sinusitis, cystic fibrosis, primary ciliary immobility syndrome, immunodeficiency, systemic vasculitis, or choanal polyps. Blood was drawn and leucocytes were counted 2 to 3 days before surgery at the Department of Clinical Laboratory at Tongji Hospital using a routine method (CELL-DYN Sapphire Hematology Analyzer; Abbott Diagnostics, Santa Clara, CA).

Postoperative NP recurrence assessment. Patients were followed up at 1, 2, 3, 6, and 12 months after endoscopic sinus surgery, and additional visits to the physician were allowed. After surgery, patients were given fluticasone propionate nasal spray 200 µg and saline irrigation, twice-daily continuously for at least 6 months until patients achieved good clinical control. When polyps or mucosal edema were noted after surgery, intranasal steroid treatment was commenced. Subjects with uncontrolled symptoms and tissue edema were given 20 days of oral prednisone tablets (30 mg daily on days 1–5, 20 mg daily on days 6–10, 10 mg daily on days 11–15, and 5 mg daily on days 16–20), and/or 1 to 2 weeks of broad-spectrum antibiotics for those with mucous purulent secretions. The definition of recurrence was as follows: endoscopic evidence of recurrence,

together with at least 1 symptom even after receiving appropriate therapy including systemic glucocorticoids and antibiotics.

Fifty-four patients were excluded from the final analysis owing to loss to follow-up, incomplete clinical data, or inadequate quantity of samples, and there was no significant difference in demographic and clinical characteristics between excluded and finally analyzed subjects ($n = 133$).

Measurement of biological markers in nasal secretions. Nasal secretion samples were collected with the patient under general anesthesia and just before surgical procedure. Briefly, a sinus sponge pack was inserted into each nasal cavity and removed after 5 minutes, and put in an Eppendorf tube containing 2 mL of sterile 0.9% sodium chloride for 30 minutes on ice to mobilize the nasal secretions. Sponges were transferred into a syringe and liquid was squeezed out into Eppendorf tube, which was centrifuged (1,500 g, 10 min) at 4°C. Secretions were collected in another Eppendorf tube and scored at –80°C for further use.

Levels of tissue plasminogen activator (tPA; Biotechnology, Wuhan, China) and Charcot-Leyden crystal (CLC) protein (Cloud-Clone Corp., Wuhan, China) were measured by using the commercial enzyme-linked immunosorbent assay (ELISA) kits according to the manufacturer's instructions. Protein levels of additional 39 biological mediators in nasal secretions were measured by using the Bio-Plex suspension chip method (Bio-Rad, Hercules, CA). Cytokine values below the level of detection were replaced by the values representing one-tenth of the detection limit.

Statistical analysis. Statistical analysis was performed using Graphpad Prism 7.0 (GraphPad Software, La Jolla, CA) and SPSS 27.0 statistical software (IBM SPSS, Armonk, NY). For continuous variables, results are represented as medians and interquartile ranges. Categorical variables are shown as percentages. For continuous variables, a Mann-Whitney U 2-tailed test was used for between-group comparison. For categorical variables, a χ^2 test or Fisher exact test was performed to determine the difference between groups. P less than .05 was considered statistically significant.

Univariate logistic regression was used to evaluate variables associated with NP recurrence. These models were adjusted for confounding factors, including age, sex, and comorbidities. Receiver operating characteristic curves were created with the best cutoff value for predicting NP recurrence. The area under the curve was calculated and a value close to 1 indicates an excellent ability to discriminate. The best cutoff value with optimal sensitivity and specificity was identified as that yielding the maximum Youden index.

TABLE E1. Baseline demographic, clinical characteristics, and surgical procedures of patients with recurrent or recurrence-free NPs*

Characteristics	Recurrent (n = 38)	Recurrence-free (n = 95)	P value
Gender, male, n (%)	29 (76.32)	60 (63.15)	.147
Age, y, median (interquartile range)	43.00 (27.30–50.00)	42.00 (29.00–52.00)	.725
Patients with atopy, n (%)	19 (50.00)	39 (41.05)	.349
Patients with AR, n (%)	10 (26.32)	14 (14.73)	.118
Patients with asthma, n (%)	7 (18.42)	8 (8.42)	.101
AERD, n (%)	1 (2.63)	2 (2.11)	.854
Nasal obstruction VAS score	9.00 (6.80–10.00)	7.00 (5.00–8.00)	.001
Rhinorrhea VAS score	5.50 (2.00–8.00)	5.00 (2.00–7.00)	.465
Facial pain VAS score	0.50 (0–5.00)	0 (0–2.00)	.085
Loss of smell VAS score	10.00 (4.80–10.00)	6.00 (2.00–9.00)	.002
Total symptom VAS score	25.50 (19.00–32.00)	20.00 (14.00–27.00)	0.010
NP score	4.00 (4.00–6.00)	3.00 (2.00–4.00)	<.001
Bilateral CT score	18.00 (13.80–23.00)	14.00 (9.00–20.00)	.004
Endoscopic score	10.00 (8.00–12.50)	8.00 (6.00–10.00)	.002
Blood leukocyte count ($\times 10^9/L$)	6.25 (5.36–7.58)	5.97 (5.01–7.18)	.124
Blood neutrophil count ($\times 10^9/L$)	3.33 (2.89–4.09)	3.05 (2.38–4.04)	.100
Blood neutrophil percent (%)	52.90 (48.07–61.98)	51.45 (46.45–57.00)	.161
Blood lymphocyte count ($\times 10^9/L$)	1.99 (1.49–2.50)	2.12 (1.67–2.52)	.582
Blood lymphocyte percent (%)	31.00 (25.75–36.98)	35.35 (29.67–41.10)	.012
Blood eosinophil count ($\times 10^9/L$)	0.40 (0.15–0.57)	0.19 (0.12–0.34)	.008
Blood eosinophil percent (%)	5.51 (2.04–9.32)	3.14 (1.66–5.21)	.019
Blood monocyte count ($\times 10^9/L$)	0.45 (0.36–0.56)	0.43 (0.36–0.57)	.556
Blood monocyte percent (%)	7.00 (5.97–8.55)	7.35 (6.37–9.05)	.251
Surgical procedures†	n = 76 sides	n = 190 sides	
Maxillary antrostromy, n (%)	76 (100)	190 (100)	
Total ethmoidectomy, n (%)	76 (100)	190 (100)	
Sphenoidotomy, n (%)	54 (71)	115 (61)	.315
Middle turbinate resection, n (%)	20 (26)	59 (31)	.631
Inferior turbinate resection, n (%)	54 (71)	150 (79)	.500
Frontal sinusotomy Draf 1, n (%)	16 (21)	45 (24)	.707

(continued)

TABLE E1. (Continued)

Characteristics	Recurrent (n = 38)	Recurrence-free (n = 95)	P value
Frontal sinusotomy Draf 2a, n (%)	24 (32)	68 (36)	.729
Frontal sinusotomy Draf 2b, n (%)	19 (25)	25 (13)	.081
Surgical procedures†	n = 38 persons	n = 95 persons	
Septoplasty, n (%)	18 (47)	45 (47)	.937

AERD, Aspirin-exacerbated respiratory disease; AR, allergic rhinitis; CT, computed tomography; VAS, visual analog scale.

Bold indicates statistically significant ($P < .05$).

*For continuous variables, results are expressed as medians and interquartile ranges. Categorical variables are shown as percentages. For continuous variables, a Mann-Whitney U 2-tailed test was used for between-group comparison. For categorical variables, a χ^2 test or Fisher exact test was performed to determine the difference between groups.

†The surgical procedures in 2 sides of the nasal cavity were summed except for septoplasty, which was calculated as procedure per person.

TABLE E2. Baseline demographic and clinical characteristics of patients with low tPA and high tPA levels*

Characteristics	Low tPA (n = 52)	High tPA (n = 81)	P value
Gender, male, n (%)	31 (59.62)	58 (71.60)	.153
Age, y, median (interquartile range)	43.00 (28.00–51.30)	41.50 (25.00–48.00)	.458
Patients with atopy, n (%)	25 (48.08)	33 (40.74)	.407
Patients with AR, n (%)	13 (25.00)	11 (13.58)	.096
Patients with asthma, n (%)	9 (17.31)	6 (7.41)	.079
AERD, n (%)	1 (1.92)	2 (2.46)	.837
Nasal obstruction VAS score	8.70 (5.50–10.00)	7.00 (4.30–8.80)	.036
Rhinorrhea VAS score	5.00 (3.00–8.00)	4.00 (2.00–7.00)	.136
Facial pain VAS score	1.50 (0–5.00)	0 (0–2.00)	.012
Loss of smell VAS score	9.50 (5.00–10.00)	5.00 (2.00–8.00)	.002
Total symptom VAS score	25.50 (18.80–34.25)	20.00 (13.30–26.00)	.002
NP score	4.00 (2.00–6.00)	4.00 (2.00–4.00)	.231
Frontal sinuses CT score	2.00 (0–4.00)	2.00 (1.00–4.00)	.656
Anterior ethmoidal sinuses CT score	3.00 (2.00–4.00)	3.00 (2.00–4.00)	.818
Posterior ethmoidal sinuses CT score	3.00 (2.00–4.00)	2.50 (1.00–4.00)	.249
Maxillary sinus CT score	3.00 (2.25–4.00)	3.00 (2.00–4.00)	.722
Sphenoidal sinus CT score	2.00 (0–3.00)	1.00 (0–3.00)	.450
OMC CT score	4.00 (2.00–4.00)	4.00 (2.00–4.00)	.984
Total CT score	15.50 (11.50–22.00)	16.00 (8.30–20.80)	.523
Blood leukocyte count ($\times 10^9/L$)	6.52 (5.31–7.78)	6.10 (5.24–7.38)	.402
Blood neutrophil count ($\times 10^9/L$)	3.31 (2.81–4.03)	3.33 (2.64–4.24)	.821
Blood neutrophil percent (%)	51.89 (48.14–56.22)	52.74 (46.89–57.84)	.862
Blood lymphocyte count ($\times 10^9/L$)	2.14 (1.81–2.65)	2.24 (1.65–2.52)	.282
Blood lymphocyte percent (%)	34.4 (28.4–40.8)	33.5 (28.6–41.1)	.921
Blood eosinophil count ($\times 10^9/L$)	0.24 (0.13–0.51)	0.22 (0.14–0.46)	.679
Blood eosinophil percent (%)	3.82 (1.45–8.23)	3.53 (2.24–5.72)	.952
Blood monocyte count ($\times 10^9/L$)	0.45 (0.44–0.61)	0.50 (0.42–0.61)	.592
Blood monocyte percent (%)	7.02 (5.91–7.90)	7.52 (6.41–8.20)	.056

AERD, Aspirin-exacerbated respiratory disease; AR, allergic rhinitis; CT, computed tomography; VAS, visual analog scale.

Bold indicates statistically significant ($P < .05$).

*For continuous variables, results are expressed as medians and interquartile ranges. Categorical variables are shown as percentages. For continuous variables, a Mann-Whitney U 2-tailed test was used for between-group comparison. For categorical variables, a χ^2 test or Fisher exact test was performed to determine the difference between groups.