



Evaluation of Routine Ear, Nose, and Throat Screening in Heart Transplant Candidates: A Retrospective Cohort Study

Lidewij L. Vroonhof^a, Stefan Roest^{b,c}, Frank R. Datema^a, Olivier C. Manintveld^{b,c}, and Andries P. Nagtegaal^{a*}

^aDepartment of Otorhinolaryngology, Erasmus MC, Rotterdam, the Netherlands; ^bDepartment of Cardiology, Thorax Center, Erasmus MC, Rotterdam, the Netherlands; and ^cErasmus MC Transplant Institute, Erasmus MC, Rotterdam, the Netherlands

ABSTRACT

Background. Patients with end-stage heart failure refractory to medication can be treated with a heart transplant (HTx). These patients are subjected to a preoperative screening procedure according to International Society for Heart and Lung Transplantation guidelines. Additionally, in our hospital, a routine ear, nose, and throat (ENT) screening is performed, directed toward the identification of asymptomatic infections and head and neck neoplasms. There are no studies demonstrating that this screening has additional value in these patients.

Methods. To investigate the yield of protocolled ENT screening in candidates for HTx, we retrospectively reviewed the medical records of patients who were subjected to the screening procedure between 2012 and 2020.

Results. The study population consisted of 251 patients of whom 177 (70.5%) were male with a median age of 52 years (IQR, 45-59 years). Ten patients (4.0%) were diagnosed with an infection (sinus) or a neoplasm, resulting in a number needed to screen of 25. In all cases, ENT consultation or sinus radiography did not influence the decision to list patients for HTx. Furthermore, no major ENT infections or occurrence of de novo head and neck malignant neoplasm were observed during follow-up after HTx.

Conclusions. The clinically relevant yield of protocolled ENT screening in candidates for HTx is low. Based on these findings, we believe that only patients with abnormal findings on a routine sinus computed tomography scan and/or specific ENT complaints should be referred to an otorhinolaryngologist.

PATIENTS with end-stage heart failure refractory to medication can be treated with a heart transplant (HTx) or the implantation of a left ventricular assist device (LVAD) as a bridge to transplant (BTT) [1]. In our center, these procedures have been performed since 1984 and 2006, respectively. Before being placed on the waiting list, all patients are subjected to a thorough screening procedure in accordance with the guidelines of the International Society for Heart and Lung Transplantation [2–4]. In these guidelines, dental examination [2], screening of systemic chronic infectious diseases [2–4], and a general recommendation to treat localized infections [4] are mentioned. However, routine ear, nose, and throat (ENT) screening is not specifically recommended.

A consultation by an ENT specialist and conventional sinus radiography are both included in the screening protocol at our center. These are performed to detect asymptomatic infections

and neoplasms, which may flare up under a treatment regimen of immunosuppressive drugs after transplant. However, we do not know the yield of ENT screening in patients with end-stage heart failure listed for HTx because specific studies are missing. The yield of ENT screening in liver and kidney transplant candidates has been explored before. The screening of chronic rhinosinusitis in liver transplant candidates resulted in better survival if sinusitis treatment preceded transplant but did not prevent infectious complications [5]. In contrast, ENT screening in kidney transplant candidates revealed no additional benefit

*Address correspondence to Andries Paul Nagtegaal, MD, PhD, Department of Otorhinolaryngology, Erasmus MC, University Medical Center Rotterdam, Rotterdam, the Netherlands, Doctor Molewaterplein 40, 3015 GD Rotterdam, the Netherlands. Tel: +31107040120. E-mail: a.nagtegaal@erasmusmc.nl

[6]. The aim of our current study was to evaluate the results of ENT screening in a large cohort of candidates for HTx.

MATERIALS AND METHODS

All patients who were screened between 2012 and 2020 for either HTx or LVAD as a BTT >18 years were included in this study. The electronically stored medical records were retrospectively reviewed. The ENT screening consisted of a visit to the outpatient clinic, including history taking and physical examination (with nasal endoscopy when indicated), combined with conventional sinus radiography. When a patient had multiple ENT screenings, data from the last screening procedure were used. After completing the full screening procedure, all patients were discussed in a multidisciplinary team of cardiologists and thoracic surgeons to decide whether patients were eligible for listing for HTx or LVAD as a BTT. To compare pretransplant and post-transplant findings, all visits of patients to the ENT outpatient clinic after HTx were also reviewed.

Statistical Analysis

All continuous data were first checked for normal distribution (Shapiro-Wilk test). Normally distributed data are displayed as mean (SD), whereas non-normally distributed data are shown as a median (IQR; 25th and 75th percentiles). The categorical data are presented as numbers with percentages. The proportions were compared with χ^2 test. The threshold for statistical significance was set at $P < .05$. Data were analyzed using SPSS statistics 25 (IBM SPSS, Inc, Armonk, NY, United States). This study was approved by the Medical Ethics Committee of the Erasmus Medical Center (MEC-2020-0717) and carried out conforming to the Declaration of Helsinki.

RESULTS

Patient Characteristics

In total, 251 candidates for HTx were analyzed, of whom 70.5% were male (Table 1). The median age at screening was 52 years (IQR, 45-59 years). The screening procedure was performed in our hospital in 192 patients (76.5%), whereas 59 patients (23.5%) were screened at other institutions. Screening through only a conventional sinus radiograph occurred in 11 patients (4.4%). Another 3 patients (1.2%) did not receive a conventional sinus radiograph or visit the ENT outpatient clinic. Occasional alcohol consumption was reported by 12 patients (4.8%), whereas 4 patients (1.6%) actively smoked. The indications for HTx were nonischemic cardiomyopathy in 162 patients (64.5%), ischemic heart disease in 70 patients (27.9%), congenital heart disease in 16 patients (6.4%), valvular heart disease in 2 patients (0.8%), and graft failure requiring retransplant in 1 patient (0.4%).

Pretransplant evaluation

When also including minor complaints, ENT symptoms were present during the screening consultation in 88 patients (35.1%). Every abnormal finding during physical examination was noted, which was observed in 116 patients (46.2%), the majority related to nasal crusting (Table 2).

Table 1. Patient Characteristics and Overview of Findings From Routine ENT Screening

Age, median (IQR), y	52 (45-59)
Sex, No. (%), male	177 (70.5)
Screening institution, No. (%)	192 performed at our institution (76.5) 59 elsewhere (23.5)
Current alcohol/tobacco use, No. (%)	12 alcohol (4.8)/4 tobacco (1.6)
ENT complaints, No. (%)	88 (35.1)
Sinus radiograph performed, No. (%)	221 (88.0), 14 results were abnormal
Sinus CT performed, No. (%)	10 (4.0), 4 were abnormal
Treatment advice given, No. (%)	64 (25.5)
Follow-up consultation, No. (%)	18 (7.2)
Listing decision, No. (%)	191 HTx or LVAD as a BTT (76.1) 60 rejected (23.9)
Follow-up time, median (IQR), y	4.8 (2.7-6.6)
Survival, No. (%)	193 alive at end of follow-up (76.9)

Total study group consists of 251 participants with end-stage heart failure. Nos. refer to individual patients. The continuous variables are displayed as medians (25th and 75th percentiles in parentheses).

BTT, bridge to transplant; CT, computed tomography; ENT, ear, nose, and throat; HTx, heart transplant; LVAD, left ventricular assist device.

A conventional sinus radiograph was made in 221 patients (88.0%), of which 14 (5.6%) showed varying degrees of sinus opacification. Subsequently, in 10 (4.0%) of those 18 patients a computed tomography (CT) of the sinuses was performed, of which 4 (1.5%) showed signs of an infection (sinus) or neoplasm (detailed in paragraph below and Table 3). Eighteen patients (7.2%) had a follow-up consultation, in which no new findings arose that contraindicated HTx.

Sixty-four patients (25.5%) received treatment (advice) after ENT consultation, of which most was deemed irrelevant with respect to the decision to list a patient for HTx (Table 2). Specifically, most of these cases involved advice on nasal hygiene. One patient was diagnosed with polypoid tissue in the nose, for which local and systemic corticosteroids were prescribed. The

Table 2. Overview of ENT Diagnoses and Treatment in Screening of Patients Before HTx

Diagnosis	Treatment	No. of Patients
Nasal crusting, (mild) epistaxis	Nasal hygiene, ie, rinsing with NaCl, nasal ointment, coagulation of epistaxis	47
Reduced hearing	Hearing test	3
Impaction of cerumen	Removal of cerumen	2
External otitis	Gauze with ointment (hydrocortisone/oxytetracycline/polymyxin B)	1
Chronic rhinosinusitis with polyps	Local and systemic corticosteroids	1
Granular myringitis	Antibiotic ear drops (hydrocortisone/colistin/bacitracin)	1

All these diagnoses were not deemed relevant with respect to the listing decision.

ENT, ear, nose, and throat; HTx, heart transplant.

Table 3. Overview of All 10 Patients Diagnosed With an Infection or Neoplasm During Screening

Case	Age/Sex	Complaints	Physical Examination	Radiology	Other Diagnostics	ENT Treatment	Listing Decision	Outcome
1	60/F	None	Normal	X: AFL rt maxilla CT: AFL both maxillae	-	Fluticasone propionate nasal spray, nasal rinsing	HTx	HTx
2	35/F	None	Normal	X: AFL lt maxilla	-	None	HTx	Deceased on waiting list
3	56/M	Nasal congestion	Normal	X: opacification rt maxilla	-	None	Rejected, very high risk	Deceased
4	62/M	Unknown	Unknown	X: MT lt maxilla	-	Unknown	HTx or LVAD BTT	HTx, died 2 mo post operation
5	60/M	Unknown	Normal	X: opacification rt maxilla CT: MT rt maxilla	-	Antibiotics (amoxicillin) and nasal rinsing	HTx or LVAD BTT	LVAD BTT, afterward HTx
6	63/M	Rhinorrhea	White rhinorrhea	X: opacification rt maxilla	-	Nasal rinsing	HTx or LVAD BTT	LVAD BTT, died 2 mo post operation
7	43/M	None	Normal	X: AFL rt maxillary CT: no air-fluid level in right maxilla. Dental element in lt maxilla with extensive MT, no AFL	-	Dental surgery	HTx	Died on waiting list
8	60/F	None; history of sinus surgery	Purulent mucus in left middle meatus	X: MT both maxillae CT: MT both maxillae, suspicion of left odontogenic origin	-	Nasal rinsing, dental surgery	HTx	Currently on waiting list
9	59/F	Stable lump in the neck since 10 y	Lump in neck level II, ~1-2 cm	X: normal	USG FNAC: pleomorphic adenoma, Milan 4a	Watchful waiting	HTx	HTx
10	40/M	None	Fleshy pedunculated polyp near left middle turbinate, purulent rhinorrhea	X: normal CT: soft tissue swelling near lt middle turbinate, opacification lt maxilla	Biopsy: inflammatory polyp with severe dysplasia/CIS of the squamous epithelium	Endoscopic sinus surgery Histology: moderate dysplasia of the squamous epithelium, no malignant neoplasm	HTx	HTx

AFL, air-fluid level; Age, age at screening; BTT, bridge to transplant; CIS, carcinoma in situ; CT, CT of sinuses; ENT, ear, nose, and throat; F, female; USG FNAC, ultrasound-guided fine needle aspiration cytology; HTx, heart transplant; lt, left; LVAD, left ventricular assist device; M, male; MT, mucosal thickening; rt, right; X, conventional sinus radiography.

patient had a follow-up consultation at our institution, at which no nasal polyps were observed anymore.

After completing the full screening procedures and review by the multidisciplinary team, 191 patients (76.1%) were accepted for HTx or LVAD implantation as a BTT, whereas 60 patients (23.9%) were rejected. In all cases, ENT consultation or sinus radiography did not influence the listing decision.

Outcome of ENT Screening Protocol

Based on 10 patients (4.0%) diagnosed with sinusitis or a neoplasm (Table 3), the number needed to screen was 25. Most of these patients did not have matching symptoms. In 8 of these cases (3.2% of total study group), opacification of the paranasal sinuses (indicative for sinusitis) was observed on radiologic examination. Nasal rinsing with saline or a nasal spray was advised in half of the patients. Two patients were referred to the maxillofacial surgeon on suspicion of an odontogenic origin, antibiotics were prescribed in 1 patient, 2 patients did not receive any treatment at all, and in 1 patient treatment is unknown. None of the patients with sinusitis received endoscopic sinus surgery.

Two patients (0.8% of total study group) were diagnosed with a neoplasm. One had a pleomorphic adenoma in the parotid gland, which is a benign tumor but has the potency of malignant transformation over time [7]. Surgical resection was not chosen at that time because of comorbidity, and afterward this patient successfully underwent transplant. In follow-up the adenoma showed no growth, and the patient did not give any complaints. The other patient had a unilateral nasal polyp on the left side. The biopsy specimen showed severe dysplasia of the squamous epithelium and additional resection was acquired through endoscopic sinus surgery. After resection, pathology showed moderate dysplasia in which no invasive growth was seen.

Post-transplant Evaluation

During the study period, a total of 126 patients (42.6%) received HTx; 40 of those had previously been implanted with an LVAD as a BTT. In this group, 34 patients were referred to the ENT surgeon because of specific complaints after HTx (Table 4). None of these complaints correlated with the screening data prior to surgery or in any way influenced the postoperative course.

Only 1 patient developed chronic rhinosinusitis (in combination with otitis media with effusion) after HTx. Despite immunosuppressive medication, the course was mild, and the patient was treated with nasal steroids only. Another patient, who missed out on the ENT screening presented with a beginning cholesteatoma. The disease stabilized after cleaning and could be handled conservatively.

At the time of the data review, 193 of all screened patients (76.9%) were still alive. Mortality was significantly higher in the group of 10 patients diagnosed with sinusitis or a neoplasm (50% vs 22%; $P = .04$, χ^2 test), but the causes of death were not related to any ENT pathology. The median follow-up time was

Table 4. Diagnoses in All ENT Consultations in Study Cohort After HTx

ENT Diagnoses After HTx	No. of Patients
Epistaxis	7
Vocal cord paresis/paralysis	5
Tracheostomy care	3
Aphthous stomatitis/candida	3
Otitis media with effusion	2
Chronic rhinosinusitis	1
Tracheal stenosis	1
PTLD (diagnosed after tonsillectomy)	1
Cholesteatoma	1
Other ENT diagnosis*	11

A total of 126 patients received HTx, 40 of whom had previously been implanted with an LVAD as a BTT. After HTx, 34 patients were referred to the ENT outpatient clinic because of specific complaints.

BTT, bridge to transplant; ENT, ear, nose, and throat; HTx, heart transplant; LVAD, left ventricular assist device; PTLD: post-transplant lymphoproliferative disease.

* Other ENT diagnoses were (nos. between brackets) functional dysphonia (2), cerumen impaction (2), tinnitus (2), undiagnosed throat complaints (1), eustachian tube dysfunction (1), common cold (1), laryngitis after gastroscopy (1), transient oral hyperkeratosis (1). None of the listed diagnoses were present at the time of screening, before HTx.

4.8 years (IQR, 2.7-6.6 years), counted from the date of the listing decision, after completing the total screening procedure.

DISCUSSION

We evaluated the outcome of standard ENT screening in patients with end-stage heart failure who were candidates for HTx. The screening consisted of a visit to the ENT outpatient clinic combined with conventional sinus radiography. In the majority of patients, the findings during ENT screening were deemed irrelevant and did not influence the decision to list patients for HTx. Only 10 of a total of 251 patients were diagnosed with sinusitis or a neoplasm, resulting in a number needed to screen of 25. ENT findings did not influence the decision to list patients for HTx or LVAD implantation in any of the cases. In addition, ENT infections after HTx or LVAD implantations were rare and no malignant neoplasms were detected.

Pretransplant Screening

In solid-organ transplant recipients, the incidence of rhinosinusitis is reported to range between 1.3% and 11.0% [8,9], which is in line with the general population [10]. Specifically in HTx recipients, the occurrence of sinusitis ranges from 0.5% to 37% [11–13]. In our study, 8 of the 10 cases showed signs of an infection, all of them involving the paranasal sinuses, which adds up to a prevalence of 3.2%.

In the general population, malignant neoplasms of the head and neck area constitute 3% of all cancers and strongly relate to tobacco use and alcohol intake [14]. We did not identify any malignant neoplasms in our study cohort because the 2 neoplasms we found were both benign. Even in screening of liver transplant candidates, who commonly have a risk profile that includes a history of smoking and daily alcohol use, few cases

of head and neck cancer are detected, ranging from 0.17% to 1.3% [15,16]. This demonstrates that pretransplant screening for ENT malignant neoplasms, even in high-risk patients, has a low yield. In liver transplant candidates, it has been suggested to screen all patients with a significant history of smoking [15]. However, the current data set does not provide any evidence to warrant an extrapolation of this recommendation to our population of HTx candidates.

Post-transplant Evaluation

Of a total of 126 patients who underwent HTx, only 1 patient developed chronic rhinosinusitis afterward, resulting in a prevalence of 0.8%. None of the 10 patients diagnosed with sinusitis or neoplasm in the screening had a complicated course after HTx. Similar observations have been reported in literature: in a cohort of liver and kidney transplant recipients no complicated sinusitis was witnessed [17], and the presence of pretransplant chronic rhinosinusitis does not contribute to mortality after liver transplant [18].

Solid-organ transplant recipients have a 3- to 5-fold risk of developing a malignant neoplasms, probably owing to the effect of immunosuppressive therapy and the impact of pre-existing risk factors [19]. Specifically in HTx recipients, the risk of developing a malignant neoplasm 1 to 5 years after transplant has been estimated to be around 11%, of which (nonmelanoma) skin cancer is the most common subtype found [20]. The occurrence of ENT malignant neoplasms is generally limited to several cases in large cohort studies [21–23], which is a result of its low incidence. Of note, the relative risk of developing an ENT malignant neoplasms after transplant is markedly increased compared with the general population [24,25]. None of the patients in our cohort developed head and neck malignant neoplasms after transplant.

Adaptation of Screening Protocol

In aiming to minimize hospital visits for HTx candidates, we adjusted the screening protocol after reviewing the results of our data. The conventional sinus radiography has been replaced by a CT scan of the sinuses, and ENT screening is only needed in case of abnormal radiologic findings or specific complaints. Although radiation exposure is higher during a CT of the sinuses (0.12 mSv compared with 0.0044 mSv with conventional sinus radiography; averages calculated by a radiation expert in our hospital), we still consider this acceptable. In comparison, worldwide average annual exposure to radiation amounts to 2.4 mSv per individual [26].

Limitations

The retrospective nature of this study has several limitations that need to be addressed. First, not all patients with abnormal findings on sinus radiography were referred for a CT scan, which may have led to missing out on cases. Second, follow-up of treatment of pretransplant patients was not always performed, thereby incorrectly giving clearance for listing for HTx.

Furthermore, the diagnostic methods were suboptimal: most patients received anterior rhinoscopy, which is inferior to nasal endoscopy, and conventional sinus radiography is inferior to a CT scan with respect to detecting pathology. This may have resulted in an underestimation of the number of patients with pathologic ENT findings. Lastly, the follow-up period after transplant can be considered rather short when studying the occurrence of malignant neoplasms in transplant recipients. Because patients were not routinely screened after transplant, a malignant neoplasm in its preclinical stage could be overlooked.

CONCLUSIONS

In conclusion, the outcome of ENT screening in a cohort of candidates eligible for HTx was investigated. Of 251 patients, only 10 were diagnosed with an infection or a neoplasm, most without matching complaints. All of these cases would also have been detected on a CT of the sinuses, which is why we believe that this modality can replace the current ENT screening. Visiting the ENT outpatient clinic should only be necessary in case of abnormal CT scan results or in case of specific complaints.

DATA AVAILABILITY

The data that has been used is confidential.

DISCLOSURE

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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