

## Correlation of Nasal Endoscopy and Computed Tomography Scan Findings in Adult Patients With Chronic Rhinosinusitis

### Abstract

**Background:** The diagnosis of chronic rhinosinusitis (CRS) is usually based on appropriate clinical features. However, confirmation is based on the evidence of features of inflammation on nasal endoscopy and/or computed tomography (CT) scan of the paranasal sinuses. Though CT scan is the gold standard, studies have found nasal endoscopy equally helpful and sometimes complementary to CT scan in the diagnosis of CRS. **Aims and Objectives:** The aim of this study is to assess and correlate the findings on nasal endoscopy and CT scan of adult patients with CRS. **Materials and Methods:** Consecutive adult patients clinically diagnosed with CRS were enrolled. Those who did both nasal endoscopy and CT scan of the paranasal sinuses within 3 months' interval were studied. The findings were correlated. **Results:** The commonest symptoms were rhinorrhea and nasal obstruction seen in 95% and 92.5% of the patients. Purulent discharge in the middle meatus was the commonest finding on nasal endoscopy seen in 56.7% of the patients. There was pathology of at least one paranasal sinus in 71.7% of the patients on CT scan. Maxillary sinus was most commonly affected. Obstruction of the osteomeatal complex was present in 51.7% of the patients. The sensitivity, specificity, positive, and negative predictive values of nasal endoscopy were 73.3%, 85.3%, 92.7%, and 55.8%, respectively. **Conclusion:** The presence of cream-coloured discharge in the middle meatus on nasal endoscopy is a good predictive index in the diagnosis of CRS, whereas sinus intraluminal lesions are better elucidated by CT scan.

**Keywords:** Chronic rhinosinusitis, computed tomography, middle meatus, nasal endoscopy, osteomeatal complex

### Introduction

Chronic rhinosinusitis (CRS) is inflammation of mucosa of the nose and paranasal sinuses of 12 or more consecutive weeks' duration.<sup>[1]</sup> It is a global disease that is common worldwide. CRS significantly impacts the quality of life of its sufferers.<sup>[2,3]</sup> The recommended diagnostic criteria by the American Academy of Otolaryngology (AAO)–Head and Neck Surgery (HNS) Foundation of CRS are based on positive clinical features with either positive features of inflammation on nasal endoscopy and/or computed tomography (CT) scan of the paranasal sinuses.<sup>[1]</sup>

Nasal endoscopy allows a detailed evaluation by providing a well-illuminated and magnified view of the nasal cavity, meati, and nasopharynx.<sup>[4,5]</sup> CT scan, however, documents both intranasal and intraluminal sinus anatomy and pathologies. Conflicting results of levels of correlation between nasal endoscopic findings and CT scan of paranasal

sinus findings in CRS patients have been documented.<sup>[6-9]</sup> These data were mainly from developed countries where endoscopy and CT scan have been in use for many decades. However, in resource-limited countries of Sub-Saharan Africa and Nigeria in particular, nasal endoscopy is relatively new and so there is paucity of published data on its findings in patients with CRS. Out-of-pocket payment for medical services among our patients informed the need for this comparative study of the findings from these two diagnostic tools and the determination of the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of nasal endoscopy compared with CT scan in our environment. The result will serve as a guide in the choice of investigation in CRS patients, particularly among patients with limited resources.

This study thus assessed and correlated the findings on diagnostic nasal endoscopy and CT scan paranasal sinuses in adult patients with CRS.

Sylvia C. Uwaneme<sup>1</sup>,  
Chinyere N.  
Asoegwu<sup>2,3</sup>,  
Vincent A. Adekoya<sup>1</sup>,  
Clement C.  
Nwawolo<sup>2,3</sup>

<sup>1</sup>Department of Ear Nose and Throat Surgery, Lagos State University Teaching Hospital,  
<sup>2</sup>Department of Surgery, College of Medicine, University of Lagos,  
<sup>3</sup>Department of Ear Nose and Throat Surgery, Lagos University Teaching Hospital, Lagos, Nigeria

Received: 24-Jan-2022  
Accepted: 01-Apr-2022  
Published: 08-Jun-2022

**Address for correspondence:**  
Dr. Chinyere N. Asoegwu,  
Department of Surgery, College of Medicine, University of Lagos, Lagos, Nigeria.  
E-mail: casoegwu@unilag.edu.ng

### Access this article online

#### Website:

www.jwacs-jcoac.org

DOI: 10.4103/jwas.jwas\_21\_22

#### Quick Response Code:



**How to cite this article:** Uwaneme SC, Asoegwu CN, Adekoya VA, Nwawolo CC. Correlation of nasal endoscopy and computed tomography scan findings in adult patients with chronic rhinosinusitis. J West Afr Coll Surg 2020;10:11-5.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

## Materials and Methods

This is a hospital-based prospective study conducted at the outpatient clinic of the Department of Otorhinolaryngology of the Lagos State University Teaching Hospital (LASUTH), Ikeja, Lagos, Nigeria. Ethical approval for this study was obtained from the Health Research and Ethics Committee of the LASUTH (LREC/10/06/574).

About 140 consecutive adult patients aged 18 to 83 years who had a clinical diagnosis of CRS and gave written consent were recruited. Those who did both nasal endoscopy and paranasal sinus CT scan within 3 months' interval were studied. The clinical diagnosis of CRS was based on the AAO–HNS Foundation Clinical practice guideline on adult rhinosinusitis 2015 recommendation<sup>[1]</sup> [Table 1].

Exclusion criteria included those younger than 18 years, history of previous sinonasal surgery, presence of sinonasal tumour, and refusal to give consent. Those who were recruited but were either unable to perform both nasal endoscopy and CT scan of the paranasal sinuses or had interval of more than 3 months between CT scan and nasal endoscopic examination were further excluded.

A structured questionnaire was used to obtain information on the biodata, clinical history, and physical examination findings. Nasal endoscopy was performed in the clinic under topical anesthesia with a 0° and 30° Medtronic 4 mm rigid endoscope by a Senior Resident Doctor. The nasal endoscopic findings were recorded on a compact disc. This was reviewed and rated by a Consultant Otorhinolaryngologist who was blinded on the CT scan finding. The expected significant findings included purulent (cream-coloured) discharge, mucosal oedema in the middle meatus or anterior ethmoid region, and polyps in the nasal cavity or the middle meatus.

CT scan of the paranasal sinuses was performed within 12 weeks of nasal endoscopy. This was reported by a Consultant Radiologist who was blinded to the findings on nasal endoscopy. The expected significant findings included mucosal thickening/opacification of the sinuses, presence of air–fluid level in the sinuses, obstruction of the osteomeatal complex (OMC), and presence of polyps and bone changes. The findings suggestive of polyps include enlarged sinus ostia, rounded masses within nasal cavity, expanded sinus or portions of nasal cavity, and thinning of bony trabeculae. Mucosal thickening of the sinus was denoted as thickening of two or more walls within the

sinus, whereas opacification of the sinus was denoted as partial or complete opacification within the sinus. Involvement of all four sinuses on one side is denoted as either right or left pansinusitis, whereas the involvement of all four sinuses on both sides is denoted as bilateral pansinusitis.

The CT machine used for this study was the Philips Brilliance 64 slices model manufactured in 2007. This is the CT scan machine owned by the hospital. About 2 mm cuts of coronal, sagittal, and axial views were done.

The data were analyzed using the Statistical Package for Social Sciences (SPSS) IBM version 23. Mean and standard deviation of numeric variables were determined. Percentages of categorical variables were also determined. *P*-value less than 0.05 was assumed to be significant at a 95% confidence interval. The nasal endoscopy findings were compared with the CT scans of the paranasal sinuses. The sensitivity, specificity, and PPV and NPV of nasal endoscopy in relation to the CT scan findings were determined.

## Results

About 296 adult patients seen at the Otorhinolaryngology outpatient department during the 1-year (November 2016 to October 2017) study period were diagnosed with CRS. One hundred and forty of these patients were consecutively recruited into the study. One hundred and twenty (85.7%) were studied, whereas the remaining 20 (14.3%) were further excluded for inability to perform both the nasal endoscopy and CT scan within 3 months' interval. The age range of the study participants was 18–83 years, with a mean age of 43.4±15.6 years. There were 41 (34.2%) males and 79 (65.8%) females with M: F of 1:1.9. Majority (46.7%) of the subjects were in the age group of 25–44 years. The duration of symptoms ranged from 1 to 50 years with a mean duration of 6.8±2.9 years.

The symptoms of CRS and its frequencies in the subjects were anterior and posterior nasal discharge 114 (95%), nasal blockage 111 (92.5%), headache 81 (67.5%), facial pain/pressure/fullness 65 (54.2%), hyposmia/anosmia 52 (43.3%), cough 45 (37.5%), halitosis 39 (32.5%), epistaxis (32.5%), and dental pain 22 (18.3%). Allergy symptoms of excessive sneezing and itching of the ear nose and throat were noted in 57 (47.5%) and 48 (40.0%) of the subjects, respectively.

Purulent (cream-coloured) discharge in the middle meatus was the commonest sign noted in 68 (56.7%) subjects on nasal

**Table 1: Diagnostic criteria for chronic rhinosinusitis**

Signs and symptoms	Endoscopic findings	CT scan finding
Mucopurulent anterior and/or posterior nasal drainage	Purulent mucus/oedema in the middle meatus/anterior ethmoid region	Inflammation of the paranasal sinuses
Nasal obstruction/congestion	Polyps in the nasal cavity/middle meatus	
Facial pain/pressure/fullness		
Decreased sense of smell		

Twelve weeks or more of two or more symptoms and signs plus one or more endoscopic or CT scan finding of signs of inflammation are diagnostic of CRS

**Table 2: Distribution of type of pathology and sinuses involved on CT scan**

Sinuses	Opacification No. of patients (%) <i>n</i> = 120	Mucosal thickening No. of patients (%) <i>n</i> = 120	General pathology No. of patients (%) <i>n</i> = 120
Maxillary	50 (41.7)	57 (47.5)	81 (67.5)
Ethmoid	32 (26.7)	32 (26.7)	61 (50.8)
Frontal	24 (20.0)	16 (13.3)	37 (30.8)
Sphenoid	21 (17.5)	15 (12.5)	34 (28.3)
Pansinusitis	13 (10.8)	3 (2.5)	14 (11.7)

**Table 3: Nasal endoscopy findings and computed tomography scan findings among the study subjects**

Findings	Nasal endoscopy No. of patients (%)	CT scan No. of patients (%)
Middle meatal discharge	68 (56.7)	—
Middle meatal mucosal oedema	46 (38.3)	34 (28.3)
Obstruction of osteomeatal complex	—	62 (51.7)
Polyps	39 (32.5)	17 (14.2)
Inflammation of sinuses	—	86 (71.7)
Anatomic variations	25 (20.8)	45 (37.5)

endoscopy. Middle meatal oedema and nasal polyps were noted in 46 (38.3%) and 39 (32.5%) of the subjects, respectively.

On CT scan, oedema of the middle meatus, obstruction of the OMC, polyps and mucosal thickening, and opacification of the sinuses were noted. Inflammation of at least one paranasal sinus was noted in 86 (71.7%) subjects, and maxillary sinus was the most commonly involved in 81 (67.5%) subjects. The details of the findings in the sinuses on CT scan are shown in Table 2.

A comparison of the findings on nasal endoscopic and CT scan in the subjects was made in Table 3. CRS diagnosis by nasal endoscopy was in 68 (56.7%) and in 86 (71.7%) patients on CT scan.

Positive endoscopic findings were noted in 68 (56.7%) patients, whereas 54 (43.3%) had negative findings. Positive findings on CT scan were recorded for 86 (71.7%) patients, whereas 34 (28.3%) were negative. Positive findings on both endoscopy and CT scan were noted in 63 of the 68 patients who had positive endoscopic findings. Twenty-nine of the 54 patients who had negative findings on endoscopy also had negative CT scan findings. The sensitivity, specificity, PPV, and NPV of nasal endoscopy in diagnosing CRS in patients compared with CT scan was 73.3%, 85.3%, 92.7%, and 55.8%. The result is shown in Table 4.

## Discussion

The age range of patients in this study was 18–83 years with female preponderance. CRS diagnosis by nasal endoscopy was in 68 (56.7%) and 86 (71.7%) patients on CT scan. Sixty-three of the 68 patients who had positive endoscopic findings also had positive CT scan findings.

The commonest presenting clinical features from this study were rhinorrhea and nasal obstruction. This is similar to the findings in other studies on CRS.<sup>[3,10,11]</sup> A study found

**Table 4: Sensitivity, specificity, and positive and negative predictive values of nasal endoscopy**

Parameters	Middle meatus pathology/OMC obstruction or inflammation of the sinuses No. of patients (%)
TP	63 (52.5)
TN	29 (24.2)
FP	5 (4.2)
FN	23 (19.2)
Sensitivity	73.3
Specificity	85.3
PPV	92.7
NPV	55.8

TP: true positive, TN: true negative, FP: false positive, FN: false negative, PPV: positive predictive value NPV: negative predictive value

headache as the commonest symptom, whereas another study recorded ear pressure and halitosis as part of the commonest symptoms.<sup>[12,13]</sup> The commonest findings on nasal endoscopy in this study were cream-coloured discharge in the middle meatus (56.7% of the subjects), followed by oedema of the mucosa of the middle meatus (38.3%). This is corroborated with studies done by Mishra and Verma,<sup>[14]</sup> Sharada and Gopalan,<sup>[15]</sup> and Tyagi *et al.*,<sup>[16]</sup> in which purulent discharge in the middle meatus was the commonest findings reported. Other studies also showed that mucosal oedema in the middle meatus was a common finding on nasal endoscopy.<sup>[17,18]</sup> Contrary to our result, some studies noted polyps in the middle meatus as the commonest finding on endoscopy.<sup>[18,19]</sup>

CT scan evidence of OMC obstruction was found in 51.7% of the study participants. Buruah *et al.*<sup>[20]</sup> and Neto *et al.*,<sup>[21]</sup> however, recorded 61.2% and 65%, respectively, of OMC obstruction in their studies. Intraluminal sinus pathology involving at least one paranasal sinus was observed in 71.7%

of the patients in this study. Paranasal sinus involvement of 60–98.3% has been reported in other studies.<sup>[17,18]</sup> The maxillary sinus was the most commonly involved followed by the ethmoidal sinus, whereas the sphenoid was the least as in other studies.<sup>[17,18,22]</sup> This can be explained by the fact that these studies were carried out in adults. Pansinusitis (unilateral or bilateral) was associated more with opacification of the sinuses than mucosal thickening (10.8% vs. 2.5%). Pansinusitis (unilateral or bilateral) is therefore associated with increased severity of the disease. Polyps were detected more by nasal endoscopy than CT scan in 39 (32.5%) and 17 (14.2%) of the subjects, respectively, as in some studies.<sup>[23,24]</sup> The difference can be attributed to the ability of the endoscope to identify small polyps in the middle meatus, which may not have been seen on CT scan. Also, polyps are known to have non-specific features on coronal CT scan unlike nasal endoscopy.<sup>[18]</sup> A study, however, found that nasal polyposis was equally detected by both CT scan and nasal endoscopy.<sup>[13]</sup>

In this study, the sensitivity of 73.3%, specificity of 85.3%, PPV of 92.7%, and NPV of 55.8% for nasal endoscopy were recorded. The high PPV, specificity, and sensitivity recorded in this study mean that accurate diagnosis of CRS can be based on nasal endoscopic findings of middle meatal purulent (cream-coloured) discharge, mucosal oedema, and/or polyps in patients with positive symptoms based on the AAO–HNS guidelines. The NPV of 55.8% means that negative findings on nasal endoscopy may not accurately rule out CRS in the patients. Bhattacharyya and Lee<sup>[25]</sup> studied the diagnosis of CRS based on clinical guidelines and endoscopy with CT findings as gold standard. They noted that the addition of endoscopy to symptom-based diagnosis significantly increased overall accuracy from 42.8% to 69.1%, odds ratio from 1.1 to 4.6, PPV from 39.9% to 66.0%, NPV from 62.5% to 70.3%, and specificity from 12% to 84.1%. They concluded that in patients who met symptom criteria for CRS, addition of endoscopy significantly improved diagnostic accuracy for CRS and that endoscopy may help reduce CT utilization in making the diagnosis of CRS in select patients. Ferguson *et al.*<sup>[26]</sup> evaluated the association between symptom-based criteria with specific findings of mucopurulence on endoscopy and CT results in CRS. Subjective symptom compared with CT had low predictive accuracy. Endoscopic finding of mucopurulence, however, correlated well with positive CRS on CT and was absent in patients with negative CT findings. Specificity of nasal endoscopic findings of mucopurulence in OMC compared with CT was 100%, whereas the sensitivity was 24%. They concluded that endoscopy can confirm CRS diagnosis but cannot rule it out. So CT should be performed in cases of suspected CRS even if mucopurulence is absent on endoscopy. Sriprakash and Sisodia<sup>[19]</sup> noted a 95.6% sensitivity, 80% specificity, 97.7% PPV, and 66.7% NPV and concluded that nasal endoscopy is as good as CT in diagnosing CRS. Hussein and Jaf<sup>[13]</sup> in their study which compared nasal endoscopy with CT scan in the diagnosis of CRS recorded sensitivity of 78.9%, specificity 100%, PPV

100%, NPV 91.1%, and the total agreement of 93.3% for nasal endoscopy. Kappa statistics showed a significantly high level of agreement ( $\kappa = 0.837$ ,  $P < 0.001$ ). They concluded that diagnostic nasal endoscopy could have sensitivity and specificity almost as worthy as CT scanning, and being an outpatient procedure, it may lessen unjustified diagnostic CT scanning procedures.

Stankiewicz and Chow,<sup>[27]</sup> on the contrary, reported that nasal endoscopy had a 46% sensitivity, 86% specificity, 74% PPV, and 64% NPV and concluded that there was poor correlation between nasal endoscopy and sinus CT. Pokharel *et al.*<sup>[28]</sup> in their study recommended that either a CT scan or nasal endoscopy (preferably with photo or video documentation) should be a part of any prospective clinical trial, as it provides the majority of objective data used to diagnose CRS.

## Conclusion

In patients with positive clinical features, nasal endoscopic finding of purulent (cream-coloured) discharge and/or polyps in the middle meatus are adequate for the diagnosis of CRS. However, negative endoscopic finding does not rule out the diagnosis of CRS and may therefore require CT scan for confirmation of diagnosis.

## Limitations

Some patients who were included in this study came with CT scan done prior to presentation to the hospital, so all the CT scans were not done with the same machine.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

## References

1. Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, Brook I, Ashok Kumar K, Kramper M, *et al.* Clinical practice guideline (update): Adult sinusitis. *Otolaryngol Head Neck Surg* 2015;152:S1-39.
2. Gliklich RE, Metson R. The health impact of chronic sinusitis in patients seeking otolaryngologic care. *Otolaryngol Head Neck Surg* 1995;113:104-9.
3. Olowosusi OZ, Asoegwu CN, Olagunju AT, Nwawolo CC. A cross-sectional evaluation of the correlation between disease severity and quality of life in chronic rhinosinusitis patients in Nigeria. *Eur Arch Otorhinolaryngol* 2015;272:2341-6.
4. Lanza DC. Diagnosis of chronic rhinosinusitis. *Ann Otol Rhinol Laryngol Suppl* 2004;193:10-4.
5. Levine HL. The office diagnosis of nasal and sinus disorders using rigid nasal endoscopy. *Otolaryngol Head Neck Surg* 1990;102:370-3.
6. Sharp H, Rowe-Jones J, Mackay I. The outcome of endoscopic sinus surgery; correlation with computerized tomography score and systemic disease. *Clin Otolaryngol* 1999;24: 39-42.
7. Bhattacharyya T, Piccirillo J, Wippold FJ II. Relationship between patient-based descriptions of sinusitis and paranasal sinus computed tomographic findings. *Arch Otolaryngol Head Neck Surg* 1997;123:1189-92.



8. Lund VJ, Kennedy DW. Staging for rhinosinusitis. *Otolaryngol Head Neck Surg* 1997;117:S35-40.
9. Ashraf N, Bhattacharyya N. Determination of the 'incidental' Lund score for the staging of chronic rhinosinusitis. *Otolaryngol Head Neck Surg* 2001;125:483-6.
10. Somefun OA, Nwawolo CC, Mazai AE. An evaluation of sinusitis in Lagos, Nigeria. *Niger Med J* 2005; 46:53-56.
11. Bhattacharyya N. The economic burden and symptom manifestations of chronic rhinosinusitis. *Am J Rhinol* 2003;17:27-32.
12. Deosthale NV, Singh B, Khadakkar SP, Harkare VV, Dhoke PR, Dhote KS, *et al.* Effectiveness of nasal endoscopy and CT scan of nose and paranasal sinuses in diagnosing sino-nasal conditions. *J Evol Med Dent Sci* 2014;3:3695-703. doi: 10.14260/jemds/2014/2346
13. Hussein RK, Jaf SMS. A comparative study of diagnostic nasal endoscopy and computed tomography in chronic rhinosinusitis. *Med J Babylon* 2019;16:199-202.
14. Mishra DK, Verma LR. Quality of life after functional endoscopic sinus surgery. *Napalese J ENT Head Neck Surg* 2010;1:2.
15. Sharada S, Gopalan VP. Clinical profile of patients having chronic rhinosinusitis: A descriptive study in tertiary care centre. *Acad Med J India* 2015;3:138-40.
16. Tyagi S, Srivastava M, Singh V. Diagnosis of chronic rhinosinusitis: Can nasal endoscopy be the new gold standard in developing countries? *Int J Otorhinolaryngol Head Neck Surg* 2016;2:30-4.
17. Lohiya SS, Patel SV, Pawde AM, Bokare BD, Sakhare PT. Comparative study of diagnostic nasal endoscopy and CT paranasal sinuses in diagnosing chronic rhinosinusitis. *Indian J Otolaryngol Head Neck Surg* 2016;68:224-9.
18. Shahizon AM, Suraya A, Rozmnan Z, Aini AA, Gendeh BS. Correlation of computed tomography and nasal endoscopic findings in chronic rhinosinusitis. *Med J Malaysia* 2008;63:211-5.
19. Sriprakash V, Sisodia SS. Correlation between nasal endoscopy and computed tomography in a tertiary care hospital. *Int J Otorhinolaryngol Head Neck Surg* 2020;6:181-5.
20. Baruah S, Vyas P, Srivastava A. CT scan vs nasal endoscopy findings in the diagnosis of chronic rhinosinusitis—Our experience. *Int J Otorhinolaryngol Head Neck Surg* 2019;5:739-45.
21. Neto SAA, Martins PSL, Souza AS, Baracat ECE, Nanni L. The role of osteomeatal complex anatomical variants in chronic rhinosinusitis. *Radiol Bras* 2004;39:227-32.
22. Amodu EJ, Fasunla AJ, Akano AO, Daud Olusesi A. Chronic rhinosinusitis: Correlation of symptoms with computed tomography scan findings. *Pan Afr Med J* 2014;18:40.
23. Gowda PRB, Kumar MVV. A comparative study of diagnostic nasal endoscopy and computerized tomography of paranasal sinus in diagnosing sino nasal disease. *Int J Otorhinolaryngol Head Neck Surg* 2019;5:140-4.
24. Kumar A, Kumar P, Kumar N. A comparative study of chronic sino-nasal diseases between diagnostic nasal endoscopy (DNE) and CT scan. *J Dent Med Sci* 2017;16:05-11.
25. Bhattacharyya N, Lee LN. Evaluating the diagnosis of chronic rhinosinusitis based on clinical guidelines and endoscopy. *Otolaryngol Head Neck Surg* 2010;143:147-51.
26. Ferguson BJ, Narita M, Yu VL, Wagener MM, Gwaltney JM Jr. Prospective observational study of chronic rhinosinusitis: Environmental triggers and antibiotic implications. *Clin Infect Dis* 2012;54:62-8.
27. Stankiewicz JA, Chow JM. Nasal endoscopy and the definition and diagnosis of chronic rhinosinusitis. *Otolaryngol Head Neck Surg* 2002;126:623-7.
28. Pokharel M, Karki S, Shrestha BL, Shrestha I, Ama tya RCM. Correlations between symptoms, nasal endoscopy, computed tomography and surgical findings in patients with chronic rhinosinusitis. *Kathmandu Univ Med J* 2013;43:201-5.