

Response to Editorial comments and Reviewers

Authors names and departments etc have been corrected.

Authors contributions have been listed.

Methods section lengthened and symptoms added.

DTPA has been defined

Conclusion shortened

Heading revised

Comments added

References changed and PMID and DOI included

I cannot change Figure 1 as it was directly derived from Statistica as a complete and uneditable file. Happy to delete the figure if you would like.

Reviewer 1

Q wondering if the scintigraphy test would help decide on decision making process as to who to offer surgery with goal of treating LPR symptoms.

A1 This paper was undertaken to test the veracity of the scintigraphic test compared to the current accepted reference standards of pH, manometry and less frequently, impedance studies. Scintigraphy is the only test that assesses LPR and lung aspiration reliably and reproducibly. We have found in a second series of 225 patients that scintigraphy reliably picks up LPR and aspiration in 30% of 225 patients without symptoms of LPR.

Q2 All or majority of patients had classical reflux symptoms with path reflux on pH monitoring and would have undergone a fundoplication even if they did not have LPR symptoms. The utility of a new test should either be : a) identify patients pre-op who are likely to have resolution of LPR symptoms in addition to their GERD symptoms .. i.e can the test help predict whose LPR would get better. did the 17 aspiration and 27 pharyngeal patents have better resolution than the ones who did not have these findings. b) pick up LPR in patients with no classical symptoms (outside the purview of this paper

A2a Yes the test did identify who would respond to fundoplication, especially if there was lung aspiration or a rising time-activity curve over the pharyngeal

region of interest. This has been stated more explicitly in the manuscript. Interestingly, the test can also predict failure of fundoplication. WE have just shown in a series of 750 cases that delayed liquid gastric emptying which is now a routine part of the scintigraphic assessment is highly predictive of surgical failure.

A2b Yes the scintigraphic test does pick up LPR in asymptomatic patients with symptoms of GERD alone. We have found this in 30% of cases with GERD, which has just been submitted in another paper from this group.

Reviewer 2

Q1 still under evaluation but certainly promising, are not mentioned in the discussion: the Dx-pH measurement system, which is increasingly being used in patients with LPR, is easy to the patients and minimally invasive; the detection of salivary pepsin, that may be an alternative simple tool to detect LPR. The real clinical role of these tests in patients with LPR is unknown but they should not be omitted in a discussion.

A1 This has been done and two references added to the discussion

Q2 Reappearance of cough on stopping PPI occurred in two patients after FP. Why and for which symptoms these patients were on PPI treatment shortly (3 months) after surgery? This was due to disease recurrence by symptoms, pH monitoring and scintigraphy. Patients were kept on anti-reflux medications for 6 weeks post-op and then ceased before review at 3 months. This has been added into the methods section. Further information on the 5 patients re-studied due to recurrent symptoms has also been added.

Q3 The total percentage of patients on PPI after surgery should be specified.

A3 This has already been addressed in the Methods section.

Q4 Moreover, in one other patient no symptom resolution was observed despite normalisation of scintigraphy and 24-hour pH monitoring. These findings may rise some doubts about the reliability of scintigraphy, taking into account that functional components to the symptoms may not be negligible in patients

classified as having LPR, thus making more difficult a correct diagnosis, even in case of a positive scintigraphy test.

A5 This has been addressed in the results and discussion section. This patient had no evidence of reflux by either scintigraphy or 24 hour pH monitoring. Added into the discussion is the statement

" The one patient that had no response to surgery had no definable reflux by pH monitoring or scintigraphy on follow-up. It does demonstrate the complexity of the disease where there may be a mixed pathology of both GERD and primary respiratory disease or a behavioral component."

Q5. Accordingly, a limitation of the study is that there is not objective evaluation after surgery, whose outcome is mainly assessed on clinical symptoms. Consequently, any conclusion about efficacy of surgery in patients with LPR evaluated by scintigraphy may be questioned.

A5 Conclusion has been changed to

"The findings of the current study indicate that reflux scintigraphy utilising the current protocol is a potential screening tool for pharyngeal contamination and lung aspiration if GERD is suspected in patients with cough or other LPR symptoms. This requires further study in a more mixed and less selected group of patients. Subsequent assessment in over 700 patients has shown further utility in predicting response to surgical intervention and more importantly, factors that may predict surgical failure."

Q6 In one patient only it is cited a normalization of scintigraphy and 24-hour pH monitoring. Were these tests performed in all patients? If not, how many patients underwent objective outcome evaluations?

A6 This is the patient who had recurrent symptoms after surgery but no evidence of reflux by either 24 hour pH monitoring or scintigraphy.

Q7 Giong in some small details: At page 8, in the 6th line from below, p has been reported as $p=0.000$, is it correct?

A7 This is correct.

Q8 At page 13, in the 5th line from below “variable” should be substituted by “variables” In conclusion, the study is certainly worth of publication but needs some revision especially regarding the true possible diagnostic role of scintigraphy in LPR, which might not be so straightforward as hypothesized, and will need more evaluations.

A 8 Corrected and the conclusion has been modified to reflect this.