

## Light microscopy is useful to better define NERD and functional heartburn

We read with great interest the well done pathophysiological study by Woodland *et al*<sup>1</sup> showing that an impaired oesophageal mucosal integrity, expressed by low baseline impedance values, is likely due to repeated acid reflux episodes, which contribute also to slow recovery after this challenge. The above alterations are associated with increased acid sensitivity and thus mucosal integrity, recovery capacity and symptom perception seem to be strictly linked.

The study demonstrates that Non-Erosive Reflux Disease (NERD) patients have a lower baseline impedance and a slower postacid impedance recovery than patients with functional heartburn (FH), as a further confirmation that they represent clearly separate entities. It is noteworthy that this is one of the few studies performed by evaluating the variables of interest in the two well-distinguished groups of NERD and FH on the basis of data deriving from impedance-pH monitoring, as we have recently recommended.<sup>2,3</sup> However, the figure related to individual baseline impedance values illustrates the presence of a great overlap between NERD and FH and, more importantly, a consistent subgroup of patients with FH has been shown to have an increased acid sensitivity similar to patients with NERD, despite having normal reflux evaluation and no reflux-symptom correlation. The authors acknowledge this overlap and suggest that it may be due to a no clear-cut definition of NERD patients who could partially be patients with erosive oesophagitis falsely classified as NERD because of previous proton pump inhibitor therapy. However,

it cannot be excluded that the FH group also could have been contaminated by the presence of true NERD patients due to a false-negative impedance-pH study and this can explain the increased acid sensitivity observed in some of them. A more precise differentiation would have been possible by the assessment of histological abnormalities visible in the mucosa of patients enrolled in the study. It is true that a better subgrouping of both NERD and FH populations would have been achieved by using electron microscopy for evaluating the presence or not of dilated intercellular spaces, as suggested by the authors themselves, but we would like to stress that nowadays it is possible to use the more practical and cheaper light microscopy, which has also the advantage to assess and score all the histopathological alterations characterising microscopic oesophagitis and not only the dilation of intercellular spaces.<sup>4</sup> We showed in a recent study<sup>5</sup> that histological abnormalities evaluated by light microscopy are absent in almost all cases with FH, whereas they are present in the majority of patients with NERD, including both those with abnormal oesophageal acid exposure and those with oesophagus hypersensitivity to both acid and weakly acidic reflux episodes. These data have been further confirmed by a very recent investigation by German authors.<sup>6</sup>

So, we believe that the assessment of this rapidly achievable morphological marker should be adopted in all studies aimed at evaluating pathophysiological or clinical differences between NERD and FH patients in order to guarantee that these two groups are separated as completely as possible.

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