2021 年美國消化疾病週

(Digestive Disease Week)

心得報告

報 告 人：臺中榮民總醫院胃腸肝膽科主治醫師 連漢仲

會議時間：2021 年 05 月 21 日之 2021 年 05 月 23 日

會議地點：美國。線上會議

目　　錄

出國報告提要

出國報告名稱	2021 年美國消化疾病週(Digestive Disease Week)
出國人員姓名	連漢仲
服務機關	行政院退輔會臺中榮民總醫院
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出國類別	參加會議發表論文
出國地點	美國。線上會議
活動日期	2021 年 05 月 21 日之 2021 年 05 月 23 日
發表論文	Validation of pharyngeal acid reflux criteria using hypopharyngeal multichannel intraluminal impedance-pH 使用多管腔食道內阻抗-酸度檢測儀驗證咽喉胃酸逆流的診斷標準

內容摘要

我發表之論文摘要：

背景及目的：目前缺乏使用經過驗證的雙酸度檢測(dual-pH monitoring)的咽酸逆流(pharyngeal acid reflux, PAR)標準。本研究目的為使用下咽多管腔阻抗-酸度檢測 (hypopharyngeal multichannel intraluminal impedance-pH, HMII-pH)咽喉 pH 值下降作為驗證 PAR 診斷標準。

方法：在疑似咽喉逆流(laryngopharyngeal reflux, LPR)的患者中，進行兩個世代研究，分別為開發組(development sets) (n = 68)及驗證組(validation sets) (n = 22)。另外健康受試者(n = 28)作為對照組。每位受試者在停用胃酸抑製劑時，進行 24 小時 HMII-pH 檢測下咽和食道的 pH 值和阻抗。PAR 候選者標準是食道及下咽 pH 突然下降，在食道酸化(pH<4)時，下咽 pH 下降至少 1 個單位，並在 30 秒內到達低於 pH5 的最低點。隨後根據 HMII-pH 阻抗的描述取得共識，並參考標準診斷對 PAR 候選者進行驗證。同時也評估 PAR 候選者的診斷效率及不同觀察者間的一致性。

結果：在開發組、驗證組和健康對照組分別有 73、60 和 3 個 PAR 候選者，確定為 PAR 事件的數量分別為 57(78%)、39(65%)和 3(100%)。疑似 LPR 患者的 PAR 事件明顯多於健康對照組(中位數(範圍)0 (0, 36) vs. 0 (0, 3)，P = 0.04)。開發組確定的最佳 PAR 事件診斷標準，即下咽 pH 下降至少 2 個單位及最低點低於 pH 5，在驗證組中得到確認(敏感度 85%~92%和特異性 56%~100%)。PAR 候選者在觀察者間一致性很高（kappa = 0.90）。

結論：PAR 診斷標准定義為在食道酸化期間，下咽 pH 下降至少 2 個單位及在 30 秒內最低點到達低於 pH 5，對於使用 HMII-pH 診斷 PAR 的敏感度很好。

發表之海報如下：

DDW 2021
May 21-23 | VIRTUAL™

Validation of Pharyngeal Acid Reflux Criteria Using Hypopharyngeal Multichannel Intraluminal Impedance-pH

Han-Chung Lien[1,2,3], Yen-Yang Chen[1], Chen-Chi Wang[2,4,5], Chun-Yi Chuang[6,7], Yung-An Tsou[8], Hong-Zen Yeh[1,2], Chi-Sen Chang[1,7]

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PURPOSE / OBJECTIVES

- There is a lack of validated pharyngeal acid reflux (PAR) criteria using dual-pH monitoring.
- We proposed and validated retrograde esophagopharyngeal pH decreases as PAR criteria using hypopharyngeal multichannel intraluminal impedance-pH (HMII-pH) techniques.

MATERIAL & METHODS

- Two cohort sets (development (n = 68) and validation (n = 22) were performed in patients with suspected laryngopharyngeal reflux (LPR).
- Healthy subjects (n = 28) serve as controls.
- Twenty-four-hour HMII-pH catheters configured to detect pH and impedance simultaneously in both hypopharynx and esophagus were used when off acid suppressants.
- PAR candidates defined as an abrupt retrograde esophagopharyngeal pH drop, that is, a pharyngeal pH decrease ≥1 unit that reached a nadir pH below 5 within 30 s during esophageal acidification, were subsequently validated against consensus of 3 experts diagnosed by HMII-pH tracings.
- The diagnostic performance and interobserver agreement of PAR candidates were assessed.

RESULTS

- There were 73, 60, and 3 PAR candidates in the development, validation and control sets, of which numbers of PAR events were 57 (78%), 39 (65%), and 3 (100%), respectively.
- Patients with suspected LPR had more PAR events than healthy controls (median (95%): 0 (4) vs. 0 (0), P < 0.05).
- Optimal PAR criteria (a pharyngeal pH decrease ≥2 units and a nadir pH ≤5) identified in the development set, were confirmed in the validation set (sensitivity 85%~92% and specificity 56%~100%).
- The concordance rate between 2 independent observers was 82.2% and 98.3 % in the development and validation sets, respectively.

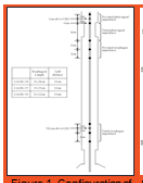


Figure 1. Configuration of the HMII-pH catheter to detect PAR. The catheter was selected according to participants' esophageal length. The impedance electrode pairs were located in the hypopharynx, proximal and distal esophagus. The 2 pH probes were located at 1 cm above UES and 5 cm (+/- 1 cm) above LES.

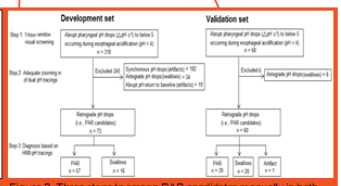


Figure 2. Three steps to screen PAR candidates manually in both development and validation sets. In step 1, using 1-hour-window visual screening, pharyngeal pH drops were selected based on Williams' method with exclusions of meal periods, isolated pharyngeal pH drops, pH out of range, and pharyngeal drift (pH drop to nadir pH > 30s). In step 2, Under the assumption that genuine PAR can only occur in retrograde esophagopharyngeal pH drops, synchronous or antegrade pH drops were excluded during adequate zooming in of dual pH tracings. Among the retrograde pH drops, tracings with abrupt pH return to baseline which often occurred simultaneously in both pH channels were also likely due to artifacts from equipment errors. All the artifacts and swallows in step 2 were subsequently proven by impedance tracings in step 3. In step 3, true PAR events were confirmed based on impedance-pH tracings.

Table 1. Prediction of presence of PAR by PAR candidates criteria based on the magnitude and nadir of pharyngeal pH drops in the development and validation sets.

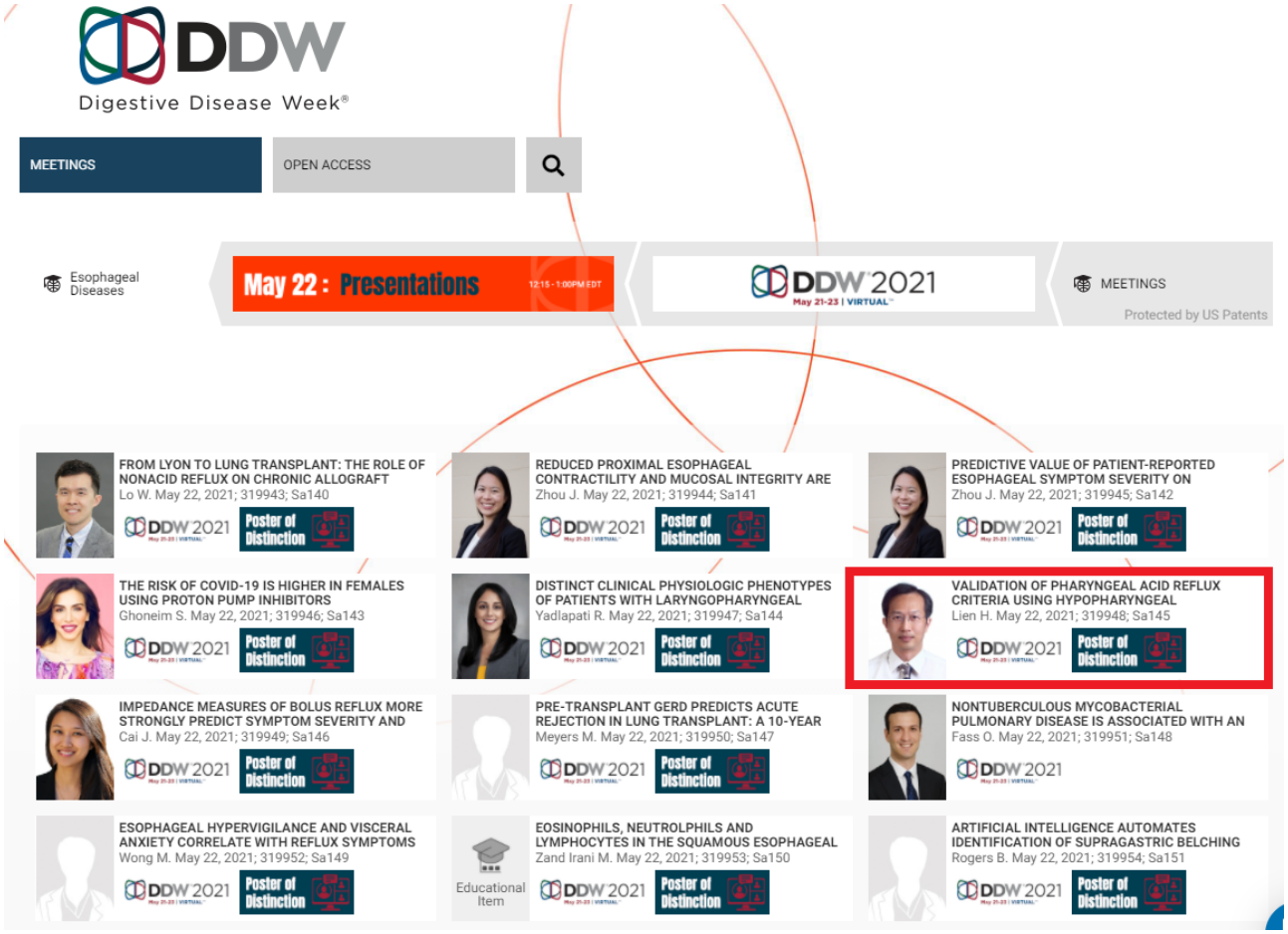
	Sensitivity	Specificity	PPV	NPV	Youden index
Development set (73 PAR candidates)					
pH drop ≥1 unit, nadir pH <5	1.00 (57/57)	0.00 (0/16)	0.78 (57/73)	--	--
pH drop ≥2 unit, nadir pH <5	**0.88 (50/57)**	**0.56 (9/16)**	**0.88 (50/57)**	**0.56 (9/16)**	**0.44**
pH drop ≥1 unit, nadir pH <4	0.70 (40/57)	0.38 (6/16)	0.80 (40/50)	0.26 (6/23)	0.08
pH drop ≥2 unit, nadir pH <4	0.68 (39/57)	0.63 (10/16)	0.87 (39/45)	0.36 (10/28)	0.31
Validation set (60 PAR candidates)					
pH drop ≥1 unit, nadir pH <5	1.00 (39/39)	0.00 (0/21)	0.65 (39/60)	--	--
pH drop ≥2 unit, nadir pH <5	**0.92 (36/39)**	**1.00 (21/21)**	**1.00 (36/36)**	**0.88 (21/24)**	**0.92**
pH drop ≥1 unit, nadir pH <4	0.87 (34/39)	0.57 (12/21)	0.79 (34/43)	0.71 (12/17)	0.44
pH drop ≥2 unit, nadir pH <4	0.85 (33/39)	1.00 (21/21)	1.00 (33/33)	0.78 (21/27)	0.85

PPV, positive predictive value; NPV, negative predictive value.

Figure 3 Examples of representative artifacts, swallows, and PAR events based on visual analyses of 1-hour-window screening (step 1) and adequate zooming (step 2) of the dual pH tracings. Final diagnosis was made based on HMII-pH tracings.
(A) Synchronous pH drops characterize as onset of pH drops occurs simultaneously in both pharyngeal and esophageal channels (solid vertical line in step 2), which are most likely due to equipment errors. Besides, abrupt pH return to baseline (arrowhead) also occurs simultaneously in both channels. (B) Antegrade pH drops characterize as pharyngeal pH drops followed by esophageal pH drops, in which an acidic liquid swallowing event outside of meals was diagnosed by antegrade impedance change (step 3). (C) Retrograde pH drops characterize as pharyngeal pH drops (vertical line) were proceeded by esophageal pH drops. However, simultaneous abrupt pH return to baseline (arrowhead) in both channels (step 2) suggests artifacts, which were subsequently proved by HMII-pH tracings in step 3. (D) Retrograde pH drops typically occur in a PAR event when an esophageal pH drop is followed by a pharyngeal pH drop. (E) Retrograde pH drops could also occur in a PAR event during a prolonged or pre-existing esophageal acidification. (F) Retrograde pH drops due to acidic liquid swallows (arrowhead) may occur immediately after a PAR event, and can only be diagnosed by HMII-pH tracings.

SUMMARY / CONCLUSION

PAR criteria defining a pharyngeal pH decrease ≥2 units, reaching a nadir pH ≤5 within 30s during esophageal acidification are sensitive in diagnosing HMII-pH-based PAR.



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心得報告

由於新冠肺炎(COVID-19)的關係，2021 年美國消化疾病週(Digestive Disease Week, DDW)於 5 月 21 日至 23 日在美國時間以線上會議方式進行，並且至 8 月 31 日前有 100 次額度可於 DDW 網頁觀看本次會議內容。DDW 是全球消化系內、外、小兒科最大的會議，全球上萬名消化系內、外、小兒科專家學者皆會參與此盛事。本次論文傑出海報，台灣有慈濟陳健麟教授、翁銘彣助理教授及本人在「食道疾病(Esophageal Diseases)」的議題中發表，並在 5 月 22 日 12:15 PM 到 1:00 PM (美東時間 UTC-4)進行線上會議。在準備論文傑出海報發表時，經歷了製作 E 海報、錄製 4 分鐘語音宣傳海報內容及當天的線上會議室，練習線上會議的操作，是個很好的學習經驗。

本會議主要提供消化道疾病臨床最新的回顧與討論及臨床指引。消化道疾病患者多需要侵入性檢查才能確定診斷，尤其目前在新冠肺炎大流行期間，醫護及檢查空間的防護裝備顯得重要，本會議特別有新冠肺炎相關議題，提供指引給予醫護們遵循。另外，新冠肺炎本身及相關治療對於消化道的影響及相關處置也有專家提供意見等。

精準醫療是目前全人醫療的趨勢，人工智慧扮演了重要的角色，此次會議也有人工智慧運用在消化道各疾病上的相關議題。例如「使用數字技術和人工智慧改善您的 GI 工作(Improving your GI practice with digital technologies and artificial intelligence)」、「人工智慧和內視鏡：現狀和未來(AI and Endoscopy: Current State of Affairs and Future)」、「深度神經網絡用於巴瑞氏食道針對性切片定位早期腫瘤(Deep neural network for the localisation of early neoplasia in Barrett's esophagus with targeted biopsies)」、「疾病中的腸道微生物群：確定診斷和臨床管理中的個人化方法(Gut microbiota in disease: Identifying personalized approaches in diagnosis and clinical management)」等等議題，便是可嘗試運用在本科患者。

另有如「胃腸道疾病流行病學的重要見解(Important Insights in the Epidemiology of Gastrointestinal Disease)」，「胃食道逆流疾病的發病機制、診斷和治療進展(Advances in the Pathogenesis, Diagnosis and Treatment of Gastroesophageal Reflux Disease)」，「治療逆流疾病及其併發症的新方法(Novel Approaches in Management of Reflux Disease and Its Complications)」，「難以治療胃食道逆流疾病 2021 (Difficult to Treat GERD 2021)」，「巴瑞氏食道篩檢及診斷的最新進展(Updates in Screening and Diagnosis of Barrett's Esophagus)」，「2020 年以後的願景：巴瑞氏食道目前的管理(Beyond 2020 Vision: Current Management of Barrett's Esophagus)」，「Castell 醫學博士講座：食道疾病的爭議(Donald O. Castell, MD, Lecture: Controversies in Esophageal Disorders)」，「胃腸神經疾病與動力學(Grand Rounds: Neurogastroenterology & Motility)」，「神經胃腸病學和運動學的更新：基礎和轉譯科學(Updates in Neurogastroenterology and Motility: Basic and Translational Science)」，「胃腸動力學的複雜臨床事件：關注管理(Complex Clinical Scenarios in GI Motility: A Focus on Management)」，「胃腸神經疾病與動力學

(NGM)部分傑出摘要全體會議(Neurogastroenterology & Motility (NGM) Section Distinguished Abstract Plenary)」,「功能性消化不良、噁心及嘔吐(Functional Dyspepsia, Nausea and Vomiting)」,目前最夯的腸道菌議題,如「沿腦-腸軸對胃腸功能進行細胞及迴路的神經調節(Cells and Circuits in the Neural Regulation of GI Functions Along the Brain-Gut Axis)」,「微生物組和微生物療法(Grand Rounds: Microbiome & Microbial Therapy)」,「名牌飲食和減肥營養素:炒作還是幫助?(Brand-Name Diets and Nutrients for Weight Loss: Hype or Help?)」,「腸道微生物和腸道上皮細胞在健康和疾病中的相互作用(Gut Microbe and Intestinal Epithelial Cell Interactions in Health and Disease)」,「微生物組在腸道炎症中的作用(The Role of the Microbiome in Gut Inflammation)」,「營養和胃腸道(Grand Rounds: Nutrition and GI)」,「Frances 及 Powell 醫學博士講座:小腸微菌、代謝物與腸道疾病(Frances and Don W. Powell, MD, Lecture: Small Intestinal Microbes, Metabolites and GI Disease)」,「Josephine 和 Camilleri 醫學博士講座—食物、微生物和功能性胃腸疾病:炒作背後的科學(Josephine and Michael Camilleri, MD, Lecture — Food, Microbes and Functional GI Disease: The Science Behind the Hype)」等等議題內容包裹萬象。美國的 Vaezi MF 教授則對於胃食道逆流檢測的新技術"黏膜完整性測試(Mucosal Integrity Testing)"精闢的演說。此次會議傑出海報從基礎到臨床的消化道疾病共有 17 大議題(如附件一),每個議題有若干傑出海報的呈現,讓人目不暇給,亦可參考其研究方法。

建議事項

在本次 E 海報的發表中,有一篇是美國聖地牙哥加利福尼亞大學(University of California, San Diego, UCSD) 年輕醫師 Rena Yadlapati 發表的傑出海報(Distinct clinical physiologic phenotypes of patients with laryngopharyngeal reflux symptoms: A prospective multi-center study),與本人 2020 年在 *Clin Gastroenterol Hepatol* 發表的文章題目(Distinct physiological characteristics of isolated laryngopharyngeal reflux symptoms)類似。由於咽喉胃酸逆流症狀的獨特生理特徵與臨床表現各異是新的概念,相隔一年便有先進國家跟進並發表,說明先進國家積極提供財務及人力投入相關研究發展。相對於台灣健保低價及高服務量,使得年輕醫師對相關領域的投入度不高,發展不易且將來恐有人才斷層的問題,相較亞洲各國已漸失去優勢。臺中榮總為公立醫學中心,負有研發責任,但先決條件需有足夠財務及人力,加以長期規劃努力,培育年輕醫師才能提升水準。這點值得思考、檢討,以期改進突破。另外,也建議院方多加鼓勵年輕醫師積極參加國際會議,不僅能開啟眼界,更能啟發有興趣的研究發想及計畫可能執行的研究方式。

附件一：傑出海報議題

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