

VOLUME 50 SUPPLEMENT 3 October 2018
ISSN 1590-8658

Digestive and Liver Disease

An International Journal of Gastroenterology and Hepatology



Abstracts of the A.I.S.F. - Italian Association for the
Study of the Liver - Monothematic Conference
“The autoimmune diseases of the liver and the biliary system”
Bologna, October 4th- 5th, 2018

Digestive and Liver Disease

An International Journal of Gastroenterology and Hepatology

Vol. 50 Supplement 3 (2018)

Official Journal of:

Italian Association for Hospital Gastroenterologists and Digestive Endoscopists
(AIGO)
Italian Association for the Study of the Liver (AISF)
Italian Association for the Study of the Pancreas (AISP)
Italian Association for Digestive Endoscopy (SIED)

Italian Society of Gastroenterology (SIGE)
Italian Society of Pediatric Gastroenterology and Hepatology (SIGENP)
Italian Group for the Study of Inflammatory Bowel Disease (IG-IBD)
Fédération Francophone de Cancérologie Digestive (FFCD)

Editors Emeriti

Mario Angelico, *Rome, Italy*
Gabriele Bianchi-Porro, *Milan, Italy*

Editor-in-Chief

Roberto de Franchis, *Milan, Italy*

Managing Editor

Silvia Malosio, *Milan, Italy*

Co-Editors

Savino Bruno, *Milan, Italy*
Silvia Fargion, *Milan, Italy*
Maurizio Vecchi, *Milan, Italy*

Editorial Assistant

Brenda Dionisi, *Milan, Italy*

ASSOCIATE EDITORS DESIGNATED BY THE AFFILIATED SOCIETIES

Carlo Agostoni (SIGENP), *Milan, Italy*
Carolina Ciacchi (SIGE), *Naples, Italy*

Edoardo Giannini (AISF), *Genoa, Italy*
Gioacchino Leandro (AIGO), *Castellana Grotte, Italy*
Raffaele Pezzilli (AISP), *Bologna, Italy*

Franco Radaelli (SIED), *Como, Italy*
Fernando Rizzello (IG-IBD), *Bologna, Italy*

SECTION EDITORS

General Gastroenterology

Colm O'Morain, *Dublin, Ireland*
Ambrogio Orlando, *Palermo, Italy*
Edoardo Savarino, *Padua, Italy*
Marco Soncini, *Milano, Italy*
Radu Tutuian, *Bern, Switzerland*
Umberto Volta, *Bologna, Italy*
Angelo Zullo, *Roma, Italy*

Imaging

Annalisa Berzigotti, *Bern, Switzerland*
Cristina Bezzio, *Garbagnate Milanese, Italy*
Federica Furfaro, *Rozzano, Italy*
Giovanni Maconi, *Milan, Italy*

Infectious Disease

Antonella d'Arminio Monforte, *Milan, Italy*

Inflammatory Bowel Disease

Alessandro Armuzzi, *Rome, Italy*
Emma Calabrese, *Rome, Italy*
Steve Collins, *Hamilton, ON, Canada*
Peter Lakatos, *Budapest, Hungary*

Liver Disease

Pietro Andreone, *Bologna, Italy*
Alessia Ciancio, *Turin, Italy*

Liver Disease

Jaime Bosch, *Barcelona, Spain*
Maurizia Brunetto, *Pisa, Italy*
Patrizia Burra, *Padua, Italy*
Alessandra Dell'Era, *Milan, Italy*
Maria Francesca Donato, *Milano, Italy*
Rafael Esteban Mur, *Barcelona, Spain*
Anna Fracanzani, *Milan, Italy*
Vincenzo La Mura, *San Donato Milanese, Italy*
Ana Lleo, *Milan, Italy*
Valerio Nobili, *Rome, Italy*
Salvatore Petta, *Palermo, Italy*
Fabio Piscaglia, *Bologna, Italy*
Ashwani K Singal, *Birmingham, AL, USA*

Pancreatic Disease

Gabriele Capurso, *Rome, Italy*
Alberto Malesci, *Milan, Italy*

Pediatric Gastroenterology

Salvatore Cucchiara, *Rome, Italy*

Surgery

Massimo Falconi, *Milan, Italy*
Gianluca Matteo Sampietro, *Milan, Italy*
Roberto Santambrogio, *Milan, Italy*

Statistical Consultant

Federico Ambrogio, *Milan, Italy*

EDITORIAL BOARD

Domenico Alvaro, *Rome, Italy*
Waddah Alrefai, *Chicago, Illinois, USA*
Angelo Andriulli, *Foggia, Italy*
Paolo Angeli, *Padua, Italy*
Adolfo Francesco Attili, *Rome, Italy*
Gabrio Bassotti, *Perugia, Italy*
Laurent Beaugerie, *Paris, France*
Robert Benamouzig, *Bobigny, France*
Antonio Benedetti, *Ancona, Italy*
Marc Benninga, *Amsterdam, Netherlands*
Marina Berenguer, *Valencia, Spain*
Roman Bogorad, *Cambridge, Massachusetts, USA*
Jean-Pierre Bronowicki, *Vandoeuvre-les-Nancy, France*
William Brugge, *Boston, Massachusetts, USA*
Elisabetta Buscarini, *Crema, Italy*
Carlo Catassi, *Ancona, Italy*
Umberto Cillo, *Padua, Italy*
Agostino Colli, *Lecco, Italy*
Rita Conigliaro, *Modena, Italy*
Dario Conte, *Milan, Italy*
Gino Roberto Corazza, *Pavia, Italy*
Enrico Corazziari, *Rome, Italy*
Antonio Craxi, *Palermo, Italy*
Gianfranco Delle Fave, *Rome, Italy*
Anthony Demetris, *Pittsburgh, Pennsylvania, USA*
Sharon DeMorrow, *Temple, Texas, USA*
Philippe Ducrotte, *Rouen, France*
Amal Dutta, *Dallas, Texas, USA*

Stefano Fagioli, *Bergamo, Italy*
Pietro Familiari, *Roma, Italy*
Massimo Fantini, *Rome, Italy*
Piero Marco Fisichella, *Boston, Massachusetts, USA*
Heather Francis, *Temple, Texas, USA*
Mirella Fraquelli, *Milan, Italy*
Dennis Freshwater, *Birmingham, UK*
Lorenzo Fuccio, *Bologna, Italy*
Pietro Fusaroli, *Bologna, Italy*
Armando Gabbrielli, *Verona, Italy*
Giovanni Battista Gaeta, *Naples, Italy*
Giuseppe Galloro, *Naples, Italy*
Antonio Gasbarrini, *Rome, Italy*
Eugenio Gaudio, *Rome, Italy*
Shannon Glaser, *Temple, Texas, USA*
Michael Gschwantler, *Vienna, Austria*
Pietro Invernizzi, *Milan, Italy*
Robert Jensen, *Baltimore, USA*
Michel Kahaleh, *Charlottesville, New York, USA*
David Laharie, *Pessac, France*
René Laugier, *Marseille, France*
Astrid Lievre, *Saint-Cloud, France*
Patrick Maisonneuve, *Milan, Italy*
Gianpiero Manes, *Rbo, Italy*
Riccardo Marmo, *Salerno, Italy*
Marco Marzioni, *Ancona, Italy*
Carlo Merkel, *Padova, Italy*
Filomena Morisco, *Naples, Italy*

Massimiliano Mutignani, *Milano, Italy*
David Mutimer, *Birmingham, UK*
Matteo Neri, *Milan, Italy*
Mattijs Numans, *Leiden, Netherlands*
Maria Caterina Parodi, *Genoa, Italy*
Jean-Marc Phelip, *Saint-Etienne, France*
Paola Piccolo, *Rome, Italy*
Antonio Pinna, *Bologna, Italy*
Massimo Puoti, *Milano, Italy*
Alessandro Repici, *Milan, Italy*
Oliviero Riggio, *Rome, Italy*
Mario Rizzetto, *Turin, Italy*
Renato Romagnoli, *Turin, Italy*
Massimo Rugge, *Padua, Italy*
Tilman Sauerbruch, *Bonn, Germany*
Jean-Cristophe Saurin, *Pierre-Bénite, France*
Vincenzo Savarino, *Genoa, Italy*
Laurent Siproudhis, *Rennes, France*
Etienne Sokal, *Brussels, Belgium*
Mario Strazzabosco, *New Haven, Connecticut, USA*
Giacomo Carlo Sturniolo, *Padua, Italy*
Pier Alberto Testoni, *Milan, Italy*
Giuseppe Tisone, *Rome, Italy*
Gian Eugenio Tontini, *Milan, Italy*
Michael Trauner, *Vienna, Austria*
Vincenzo Villanacci, *Brescia, Italy*
Frank Zerbib, *Bordeaux, France*
Huiping Zhou, *Richmond, Virginia, USA*

© 2018 Editrice Gastroenterologica Italiana S.r.l. All rights reserved.

This journal and the individual contributions contained in it are protected under copyright by Editrice Gastroenterologica Italiana S.r.l. and the following terms and conditions apply to their use:

Photocopying

Single photocopies of single articles may be made for personal use as allowed by national copyright laws. Permission of the Publisher and payment of a fee is required for all other photocopying, including multiple or systematic copying, copying for advertising or promotional purposes, resale, and all forms of document delivery. Special rates are available for educational institutions that wish to make photocopies for non-profit educational classroom use.

For information on how to seek permission visit www.elsevier.com/permissions or call: (+1) 800-523-4069 x 3808.

Derivative Works

Subscribers may reproduce tables of contents or prepare lists of articles including abstracts for internal circulation within their institutions. Permission of the Publisher is required for resale or distribution outside the institution.

Permission of the Publisher is required for all other derivative works, including compilations and translations (please consult www.elsevier.com/permissions).

Electronic Storage or Usage

Permission of the Publisher is required to store or use electronically any material contained in this journal, including any article or part of an article (please consult www.elsevier.com/permissions).

Except as outlined above, no part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, without prior written permission of the Publisher.

Notice

No responsibility is assumed by the Publisher for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products, instructions or ideas contained in the material herein. Because of rapid advances in the medical sciences, in particular, independent verification of diagnoses and drug dosages should be made.

Although all advertising material is expected to conform to ethical (medical) standards, inclusion in this publication does not constitute a guarantee or endorsement of the quality or value of such product or of the claims made of it by its manufacturer.

Digestive and Liver Disease is a monthly journal published by Elsevier Ltd and printed by Henri Ling, Dorchester, UK.

Reduced rate for members of Italian Scientific Societies AISF, AISP, IG-IBD, SIED, SIGE, SIGENP, and for the French FFCD members. Further information (orders, claims and journal enquiries) are available on the Journal website (<http://www.dldjournalonline.com/>). Annual subscriptions will include all the issues and any supplements for the year. Claims for missing issues should be made within six months of the dispatch date.



Member of the Italian Association Periodical Press.

The paper used in this publication meets the requirements of ANSI/NISO Z39.48-1992 (Permanence of Paper)

Periodico Mensile. Registrazione Tribunale di Roma n. 17221/1978

⊗ Direttore Responsabile: Gianluca Svegliati Baroni

Digestive and Liver Disease

Contents

Vol. 50 Supplement 3 (October 2018)

*Index Medicus (MEDLINE), Current Contents/Clinical Practice,
Science Citation Index and EMBASE/Excerpta Medica
Sociedad Iberoamericana de Información Científica (SIIC)*

Associato alla Unione Stampa Periodica Italiana

Abstracts of the A.I.S.F. - Italian Association for the Study of the Liver - Monothematic Conference "The autoimmune diseases of the liver and the biliary system" Bologna, October 4th - 5th, 2018

**Abstracts of the A.I.S.F. - Italian Association for the Study of the Liver -Monothematic Conference "The autoimmune
diseases of the liver and the biliary system" Bologna, October 4th- 5th, 2018**

e353



Abstracts of the A.I.S.F. - Italian Association for the Study of the Liver - Monothematic Conference “The autoimmune diseases of the liver and the biliary system” Bologna, October 4th - 5th, 2018

P-1

From guidelines to uniform pan-healthcare professional practice: development of an international consensus Care Pathway for the diagnosis and management of Primary Biliary Cholangitis (PBC)

G.M. Hirschfield¹, M. Carbone², H. Cortez-Pinto³,
G. Macedo⁴, V. de Lédighen⁵, F. Adekunle⁶,
O. Chazouilleres⁷

¹ Centre for Liver Research, University of Birmingham, Birmingham, UK

² Division of Gastroenterology, University of Milan-Bicocca, Milan, Italy

³ Departamento de Gastroenterologia, CHLN, Laboratório de Nutrição, Faculdade de Medicina, Universidade de Lisboa, Portugal

⁴ Gastroenterology Department, Centro Hospitalar São João, and Porto World Gastroenterology Organization Training Center, University of Porto Medical School, Porto, Portugal

⁵ Investigation Centre of Liver Fibrosis, Haut-Lévêque Hospital, Bordeaux University Hospital, Pessac, France

⁶ Intercept Pharmaceutical, London, UK

⁷ Hépatologie, AP-HP Hôpital Saint Antoine, Paris, France

PBC is an infrequent but important, lifelong autoimmune cholestatic liver disease that leads to liver fibrosis, cirrhosis and, ultimately, the need for liver transplantation. Its clinical course is heterogeneous, making it difficult for clinicians to diagnose and risk stratify patients with confidence. Patient management is frequently shared across primary and secondary care, and between physicians, nurse specialists and physician assistants. A key recommendation of recent EASL treatment guidelines was the development of a Care Pathway, to facilitate standardized approaches to management based on current practice. Evidence-based guidelines are critical but do not readily translate into a patient care flow: the objective of this exercise was to leverage clinical expertise to develop this practical translation.

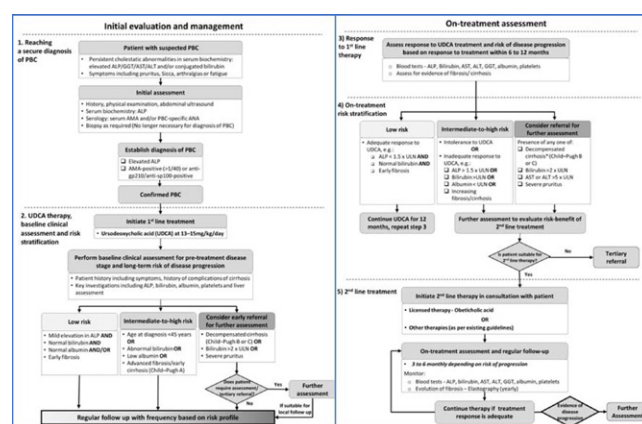


Figure 1. Consensus Care Pathway for the diagnosis and management of PBC.

Twelve PBC specialists convened (with transparent financial support from industry) with the aim of drafting a Care Pathway to support all clinicians in the day-to-day management of PBC patients. It was concluded that the Care Pathway should give practical advice on: confirming PBC diagnosis, performing baseline clinical and risk assessments, initiating first-line treatment, performing on-treatment risk stratification, identifying patients who require second-line treatment and/or further assessments. The experts debated the assessments and criteria that should be included and formed subsequent consensus.

Based on the consensus, a working group of six of the experts further developed and completed the Care Pathway. The working group reached added-consensus on a five-part structure for the Care Pathway based on EASL guidelines alongside their clinical experience (Figure 1).

As an exemplar for all clinicians involved in the care of patients with chronic liver disease, this consensus Care Pathway for the management of PBC, builds on recently-published guidelines to support patient care. It provides an opportunity for more uniform practice, and for safe and timely adoption of varied models of care provision to PBC patients, which go beyond classical physician-lead only management.

<https://doi.org/10.1016/j.dld.2018.07.020>

P-2

Hepatobiliary and non-hepatobiliary malignancies in PSC patients from Southern Europe: a comparative study in two European centers

F. Simionato¹, N. Cazzagon¹, L. Llovet²,
P. Furlan³, V. Baldo³, P. Angeli⁴, M.C. Londono²,
A. Pares², A. Floreani¹

¹ Dpt of Surgery, Oncology and Gastroenterology - University of Padova, Padova, Italy

² Liver Unit, Hospital Clínic, IDIBAPS, CIBERehd, University of Barcelona, Barcelona, Spain

³ Hygiene and Public Health Unit, Dpt of Cardiac, Thoracic and Vascular Sciences, University of Padova, Padova, Italy

⁴ Dpt of Medicine - DIMED, University of Padova, Padova, Italy

Primary Sclerosing Cholangitis is a risk factor for the development of hepatobiliary malignancies (HPB) and non-HPB.

Aim: To calculate the risk of malignancies in two Southern European cohorts of PSC and in the general population of the same geographical areas.

Methods: The study was performed in PSC patients from Padova (Italy) and Barcelona (Spain). The cancer incidence was compared with the standardized incidence ratio (SIR) calculated using the Veneto Tumor Registry and the Tarragona Cancer Registry.

Results: We included 165 patients (58% males), 106 from Padova and 59 from Barcelona with a median age at diagnosis of 31 and 40 years, a median follow-up of 8.5 [3.8-15.5] and 9.61 [5.9-15.4] years. Association with IBD was observed in 54% and 63% of cases respectively. During follow-up, 22 patients (13%) developed malignancies, (4% HPB 9% non-HPB malignancies). The overall prevalence of malignancies was not significantly different in the two centres (11 vs. 17%, $p=ns$). The overall cancer incidence in Padova cohort was increased compared to the general population (SIR=1.91 [95%CI=1.03-3.24]), this was not the case in the Barcelona cohort (SIR=1.41 [95%CI 0.72-2.51]). An increased incidence of HPB malignancies was observed in both cohorts (SIR=23.37 in Padova and 14.3 in Barcelona), due to an increased incidence of biliary malignancies (SIR=67.58 [95%CI 11.33-223.2] in Padova and 34.44 [95%CI 5.77-113.7] in Barcelona). Among the non-HPB malignancies, we noted an increased incidence of CRC in Padova (SIR=5.78 [95%CI 1.47-15.73]), of small intestine cancer in Barcelona (SIR=60.43 [95%CI 3.01-297.1] and of cervical cancer in both cohorts (SIR=19.84 [95%CI 0.99-97.86] and 22.66 [95%CI 1.14-111.8], respectively).

Conclusions: PSC patients from Southern Europe have an increased risk for HPB and intestinal malignancies, although this risk is lower in respect to previous published data. Moreover, there was an increased risk of cervical cancer compared to the general population of the same geographical area.

<https://doi.org/10.1016/j.dld.2018.07.021>



P-3

Epidemiology of primary biliary cholangitis in Italy: novel insights on gender and comorbidities

A. Gerussi^{1,2}, V. Manno³, M. Carbone¹,
G. Minelli³, D. Taruscio⁴, S. Conti³, P. Invernizzi¹

¹ UOC Gastroenterologia e Centro per le Malattie Autoimmuni del Fegato, Ospedale San Gerardo, Dipartimento di Medicina e Chirurgia, Università degli studi di Milano-Bicocca, Monza

² Clinica Medica, Dipartimento di Area Medica, Università degli studi di Udine, Udine

³ Servizio Tecnico Scientifico di Statistica, Istituto Superiore di Sanità

⁴ Centro Nazionale Malattie Rare, Istituto Superiore di Sanità

Primary biliary cholangitis (PBC) is a rare autoimmune liver disease, that mostly affects females. Usually associated with other autoimmune diseases, very little is known about non-autoimmune comorbidities.

The aim of our study was to evaluate the epidemiology of PBC in Italy by administrative data, and to estimate incidence, prevalence, F:M and presence of comorbidities, from 2011 to 2015.

The national hospital discharge database (NHDD) has been used to identify incident and prevalent cases. The study included adult subjects diagnosed with biliary cirrhosis (ICD9-CM: 571.6) as a primary or secondary diagnosis, from 2011 to 2015. Incident rate and prevalence have been estimated by direct standardization method. Main comorbidities have been studied, from 2006 to 2015, and the Standardized Hospitalization Ratio (SHR) has been estimated by indirect standardization method, using the comorbidities of hospitalized (for any cause) Italian population as a reference (SHR = 100).

In the study period (2011-15), we identified 5533 PBC cases, 3790 of them were females (68.5%, F:M 2.2:1). Prevalent cases were 9664 (74.6% females, F:M 2.9:1). F:M was stable during the study period. Incident rate was 1.03×100.000 in males and 1.92 in females; prevalence was 1.89 for male individuals and 4.75×100.000 in female ones. Both measures reduced, with a more significant drop in women. For both genders, an excess in infectious diseases, neoplasms of the liver and biliary tract, endocrine disease, kidney and urinary tract diseases and autoimmune diseases was found in PBC cohort. The most relevant comorbidity was tumors of the liver and biliary tract (SHR = 1250 in males and 791 in females).

To conclude, PBC showed a reduction in incidence and prevalence of hospitalization for PBC from 2011 to 2015; F:M was less than 3. Novel insights on comorbidities have come up from this national study.

<https://doi.org/10.1016/j.dld.2018.07.022>



P-4

Epidemiology and clinical impact of non-viral acute hepatitis in a tertiary unit of Hepatology in Italy

F. Rizzi, A. Adriani, A. Morgando, C. Alessandria, B. Imperatrice, G. Saracco, A. Marzano

Unit of Gastro-Hepatology, San Giovanni Battista Hospital, University of Torino, Turin, Italy

Introduction and Aims: Autoimmune hepatitis have a variable occurrence, clinical phenotype and outcome, and the factors contributing to this variability are uncertain. The goal of this study is to evaluate, through a retrospective analysis, data of severe acute hepatitis (SAH) requiring hospital admission between 1/2017 and 6/2018 in a tertiary inpatient Hepatological Unit. Incidence, clinical impact and outcome of non-viral/autoimmune acute hepatitis (AAH) were analyzed. AAH diagnosis was made using AAH scoring: definite diagnosis when AAH score was >15 pre-treatment and >17 post-treatment, or probable diagnosis when it was <15 and <17 respectively. SAH and Acute-on-Chronic Liver Disease (ACLD) were defined as presence of jaundice, hepatomegaly and/or coagulation alteration (showed by an increased INR) and presence of a previous chronic liver disease, respectively.

Results: Among 1302 patients admitted to the Unit in the period, 723 were transferred, from the hospital emergency unit, and the remaining patients were scheduled for diagnostic or oncologic procedures and therapies.

SAH was the admission diagnosis in 29/723 (4%) inpatients; among them 13 (45%) had HBV (3) or HAV (10)-related acute hepatitis and 16/29 were AAH (55%); of them only 9 (56%) were definite and 7 probable with different aspects. Among the 16 patients ACLD was diagnosed in 5 cases.

All the AAH patients were treated with high dose steroid e.v. (prednisolone 1 mg/kg/die) and in 4 cases azathioprine was added. During the follow-up, lasted at most 18 months, we observed a complete response in 14 patients (87.5%).

Conclusions: An increase of admission for SAH in a non-infective disease/hepatological tertiary inpatient unit was observed in the analyzed period and more than half of them were non-viral/AAH, in a large part (44%) with not definite but probable diagnosis and with comorbidities. This new scenario requires a careful attention in diagnosis and probably a new approach to the long-term immunosuppressive therapy.

<https://doi.org/10.1016/j.dld.2018.07.023>

P-5

Two simple magnetic resonance scores are able to predict survival in patients with Primary Sclerosing Cholangitis

N. Cazzagon^{1,2,3}, S. Lemoine^{2,3}, S. El Mouhadi⁴, P. Trivedi⁵, A. Dohan^{6,7,8}, A. Kemgang Fankem^{2,3}, C. Housset^{2,3}, Y. Chretien^{2,3}, C. Corpechot^{2,3}, G. Hirschfield⁵, A. Floreani¹, R. Motta⁹, B. Gallix⁶, A. Barkun¹⁰, J. Barkun¹¹, O. Chazouilleres^{2,3}, L. Arrivé⁴

¹ Department of Surgery, Oncology and Gastroenterology, DiSCOG, Gastroenterology Unit, University of Padova, Padova, Italy

² Reference Centre for Inflammatory Biliary Disease (MIVB), French Network for Rare Liver Diseases in Adults and Children (FILFOIE) Saint Antoine Hospital, Assistance Publique-Hôpitaux de Paris (APHP), Paris, France

³ Inserm-Umr.S938, Sorbonne University, Paris, France

⁴ Department of Radiology, Saint-Antoine Hospital, Assistance Publique-Hôpitaux de Paris (APHP), Paris, France

⁵ Institute of Immunology & Immunotherapy, University of Birmingham, Birmingham, UK

⁶ Department of Radiology, McGill University Health Centre, Montreal, QC, Canada

⁷ Department of Radiology, Cochin Hospital, Assistance Publique-Hôpitaux de Paris (APHP), Paris, France

⁸ Inserm, Umr U965, Lariboisiere Hospital, Paris, France

⁹ Department of Medicine - DIMED - Institute of Radiology, University of Padova, Padova, Italy

¹⁰ Department of Gastroenterology, McGill University Health Center, Montreal, QC, Canada

¹¹ Department of Surgery, McGill University Health Centre, Montreal, QC, Canada

Background: Primary sclerosing cholangitis (PSC) has a variable course. To predict clinical outcome in a single patient is a major need. Magnetic resonance (MR) imaging with 3D-MR cholangiography is the modality of choice for diagnosis. Two MR scores are able to predict radiologic progression of PSC.

Aim: to assess the clinical prognostic value of these two MR scores.

Methods: This retrospective multicentric study included two cohorts of large duct PSC patients with at least one 3D-MRC: a derivation cohort composed by patients from Paris and an external validation cohort composed by patients from Birmingham, Padova and Montreal. All first available MR examinations were reevaluated by two radiologists and the two MR scores were calculated: MR score without gadolinium = (1xdilatation of intrahepatic bile ducts) + (2xdysmorphism) + (1xportal hypertension), MR score with gadolinium = (1xdysmorphism) + (1xparenchymal enhancement heterogeneity). Primary endpoint was survival without liver transplantation (LT) and cirrhotic decompensation. Survival was assessed by Cox regression model.

Results: 238 PSC patients were included, equally distributed in derivation and validation cohort. Median age at diagnosis was 37(25-52) years, 66% of patients were males and 72% had IBD. Gadolinium chelates were injected in 64% of patients. During the median follow-up of 4.4(2.6-6.4) and 3.8(1.5-6.2) years, 20 and 25 patients underwent LT, 9 and 5 patients died and 18 and 24 patients

developed cirrhotic decompensation in derivation and validation cohorts, respectively. In univariate analysis total bilirubin, AST, ALT, GGT, albumin, MR score without and with gadolinium were associated with event-free survival. Predictive performances of MR scores without and with gadolinium assessed by c-statistic were 0.89 IC95%(0.84–0.95) and 0.75 IC95%(0.64–0.87), respectively. Independent prognostic factors identified by multivariate analysis were MR scores and total bilirubin. The prognostic value of MR scores was confirmed in the validation cohort.

Conclusion: MR risk scores without and with gadolinium accurately predict clinical outcome in PSC patients.

<https://doi.org/10.1016/j.dld.2018.07.024>

P-6

Magnetic resonance cholangiography and biochemical predictive criteria of response to endoscopic treatment of severe strictures in patients with primary sclerosing Cholangitis



N. Cazzagon^{1,2}, O. Chazouilleres¹, C. Corpechot¹, S. El Mouhadi³, E. Chambenois³, B. Desaint¹, S. Lemoine¹, U. Chaput¹, L. Arrivé³

¹ Reference Centre for Inflammatory Biliary Disease and Autoimmune Hepatitis (MIVB), Saint-Antoine Hospital, APHP, Paris, France

² Department of Surgery, Oncology and Gastroenterology, University of Padova, Padova, Italy

³ Department of Radiology, Saint-Antoine Hospital, APHP, Paris, France

Background: The aim of this study was to assess whether magnetic resonance cholangiography (MRC), clinical and biochemical criteria are able to predict improvement after endoscopic treatment (ET) for dominant stenosis (DS) in patient with primary sclerosing cholangitis (PSC).

Methods: Patients with large ducts PSC with at least one ET for DS were included. MRC were evaluated according to the standard model by Ruiz et al. and a qualitative score of improvement was built. Score 3 (improvement likely) was given in severe common bile duct (CBD) stricture with marked dilatation without severe stenosis of upstream duct, score 1 (improvement unlikely) in case of severe multiple stenosis of secondary ducts without biliary dilatation and score 2 (indeterminate) to an intermediate pattern. Response to ET, assessed at 12 months from inclusion, was defined by the presence of at least one clinical or biochemical criteria.

Results: We included 31 patients who underwent at least one ET for DS. At MRC all patients had a severe ($\leq 75\%$ of the duct diameter) CBD stricture and half had a severeright (RHD) and/or left hepatic duct (LHD) stricture. According to the qualitative score, 16 patients were scored 3, 7 patients were scored 1 and 9 patients were scored 2. Intraobserver variability of the score was 74%, $k=0.6$ (substantial agreement) and interobserver variability between the three radiologists was 60%, $k=0.40$ (fair agreement). Response to ET was obtained in 52% of patients. By univariate analysis short LHD strictures, higher bilirubin, transaminase, pruritus and qualitative score 3 were associated to response to ET. Total bilirubin and AST were independent predictive factors of response (HR24.0, 95%CI:3.4–170.4, $p=0.001$ and 23.8, 95%CI3.4–169.4, $p=0.002$).

Conclusion: In PSC patients with severe strictures of extrahepatic bile duct, MRC may contribute to identify patients likely to improve after ET as well as biochemical features. A validation in a larger cohort is warranted to confirm these results.

<https://doi.org/10.1016/j.dld.2018.07.025>

P-7

Non-invasive B-cell clonality markers may help in the rational approach to HCV SVR cryoglobulinemic patients with persisting manifestations



S. Lorini¹, L. Gagnani¹, V. Santarlasci¹, M. Monti¹, U. Basile², L. Petraccia¹, F. Madia¹, S. Marri¹, L. Martini¹, E. Carradori¹, A. Xheka¹, P. Caini¹, A.M. Pellicelli³, L. Cosmi⁴, F. Annunziato⁴, A.L. Zignego¹, on behalf of the Special Interest Group on the Systemic Manifestations of hepatitis viruses of the Italian Association for the Study of the Liver (AISF)

¹ Masve Center, Department of Clinical and Experimental Medicine, University of Florence, Florence, Italy

² Catholic University of the Sacred Heart, Rome, Italy

³ Azienda Ospedaliera San Camillo Forlanini, Rome, Italy

⁴ Department of Clinical and Experimental Medicine, University of Florence, Florence, Italy

Background: Mixed cryoglobulinemia (MC), a both autoimmune and lymphoproliferative disorder (LPD), is characterized by the clonal expansion of B-cell populations, mostly in the liver and, less frequently, in the bone marrow or blood. DAAs can improve or heal MC vasculitis, but persistence or recurrence may be observed after SVR. Rituximab (RTX) is the first-choice therapy in such cases. However, MC persistence may also be due to other causes, including the occurrence of irreversible organ/tissue damage. Consequently, the evaluation of B-cell clonality may consistently help for a correct clinical, prognostic and therapeutic approach.

Methods: The following patients were consecutively enrolled: Group A: DAA-treated SVR MC patients with complete clinical response; Group B: DAA-treated SVR MC patients maintaining symptoms. B-cell clonal expansion was evaluated, after DAA-therapy, by flow-cytometry, Free Light Chains ratio (κ/λ) and t(14;18).

Results: We evaluated 84 patients: 47 group A and 37 group B (mean FU 15.5 months). B-cell clonality markers were not observed in group A. At least one clonality marker was detected in 27/37 (73%) of group B patients, including all (six) patients with lymphoma, in hematological regression after DAAs. Three positive patients had systemic symptoms suggestive of an LPD evolution. Patients negative for B-cell clonality were generally characterized by persisting arthralgia and/or sicca syndrome, and/or neuropathy. κ/λ ratio was altered in 47% of cases, flow cytometry in 16% and t(14;18) in 43%. In >20% of cases more than a marker was detected.

Conclusion: Clonality markers were associated with more severe pre-therapy MC. This suggests the hypothesis of having gone beyond the LPD point of no return and the rationale for RTX treatment. The κ/λ ratio, may be an useful marker in MC patients with persisting symptoms, in the light of a more rational clinical and therapeutic approach to these patients.

<https://doi.org/10.1016/j.dld.2018.07.026>

P-8

A chromosome X-wide association study in primary biliary cholangitis allowed the identification of 5 novel susceptibility loci

R. Asselta¹, E. Paraboschi¹, M. Carbone²,
A. Gerussi², V. Ronca², L. Cristofori²,
F. Malinverno², S. Duga¹, P. Invernizzi²

¹ Department of Biomedical Sciences - Humanitas University, Via Rita Levi Montalcini, 4, 20090, Pieve Emanuele (Milano), Italy

² Division of Gastroenterology and Center for Autoimmune Liver Diseases, San Gerardo Hospital, Department of Surgery and Medicine, University of Milan Bicocca, Milan, Italy

Genome-wide association studies (GWAS) in primary biliary cholangitis (PBC) failed to find X chromosome genetic variants associated with the disease, but analytical problems arising from X unique mode of inheritance were not taken in account. Aim of our study was to explore the specific contribution of the X chromosome to the genetic architecture of PBC by performing a chromosome X-wide association study (XWAS).

Genotype data on X chromosome derived from 5 GWAS studies (cohorts coming from Italy, UK, Canada, China, Japan), for a total of 5,244 cases and 11,875 controls, were included. Genotype data were quality checked, corrected for population stratification, and imputed by using the IMPUTE2 software. A total of 110,000 single-nucleotide polymorphisms (SNPs), common to all cohorts, were then used for association analyses. These were performed by using the PLINK-XWAS software. A subsequent meta-analysis was performed using METAINTER.

In the single-SNP association analysis we found 11 population-specific loci associated with PBC at a suggestive $p < 5 \times 10^{-5}$, the most significant being a signal mapping within the OTUD5 gene ($p = 4.80 \times 10^{-6}$; OR = 1.39 CI = 1.03–1.58; Japanese cohort). This gene codes for a protein that was demonstrated to suppress the type-I interferon-dependent innate immune response.

A meta-analysis was hence performed separately for Caucasian and East Asian populations. This analysis revealed 7 novel loci, 5 of which (i.e. GRIPAP1, PIM2, OTUD5, LLOXNC01, KCND1) below the threshold for X-wide significance. Finally, we performed a gene-ontology enrichment analysis, evidencing a significant enrichment for genes involved in immune system ($p = 8.4 \times 10^{-11}$).

In this study, by applying a XWAS analysis, we were able to evidence novel association signals with PBC risk, shedding light on the genetic contribution of the “neglected” X chromosome to this immune-mediated disorder.

<https://doi.org/10.1016/j.dld.2018.07.027>

P-9

Ageing-related expression of Twinfilin-1 regulates cholangiocyte biological response to injury

C. Pinto¹, L. Maroni¹, D.M. Giordano¹,
S. Saccomanno^{1,2}, J.M. Banales³, M.C. Albertini⁴,
F. Orlando⁵, M. Milkiewicz⁶, E. Melum^{7,8,9},
I.L. Ciriza³, P. Milkiewicz¹⁰, C. Rychlicki¹,
L. Trozzi¹, M. Scarpelli², A. Benedetti¹,
G. Svegliati Baroni¹, M. Marziani¹

¹ Department of Gastroenterology and Hepatology, Università Politecnica delle Marche, Ancona, Italy

² Institute of Pathological Anatomy and Histopathology, Università Politecnica delle Marche, Ancona, Italy

³ Department of Liver and Gastrointestinal Diseases, Biodonostia Health Research Institute – Donostia University Hospital, Ikerbasque, CIBERehd, University of the Basque Country (UPV/EHU), San Sebastian, Spain

⁴ Department of Biomolecular Sciences, Università degli Studi di Urbino “Carlo Bo”, Urbino, Italy

⁵ Advanced Technology Center for Aging Research, Experimental Animal Models for Aging Unit, Scientific Technological Area, IRCCS-INRCA, Ancona, Italy

⁶ Department of Medical Biology, Pomeranian Medical University, Szczecin, Poland

⁷ Norwegian PSC Research Center, Department of Transplantation Medicine, Division of Surgery, Inflammatory Diseases and Transplantation, Oslo University Hospital, Rikshospitalet, Oslo, Norway

⁸ Research Institute of Internal Medicine, Division of Surgery, Inflammatory Diseases and Transplantation, Oslo University Hospital, Rikshospitalet, Oslo, Norway

⁹ K.G. Jebsen Inflammation Research Centre, Institute of Clinical Medicine, University of Oslo, Oslo, Norway

¹⁰ Liver and Internal Medicine Unit, Department of General, Transplant and Liver Surgery, Medical University of Warsaw

Background and Aims: Ageing is a complex biological process that affects the functional capacity of multiple organs and is associated to the development of many diseases. Disorders affecting the biliary tree develop and progress differently according to the patient age. The aim of the study was to identify molecular pathways associated to cholangiocytes ageing and to verify their effects in the biological response to injury of biliary epithelial cells.

Materials and Methods: A panel of microRNAs (miRs) involved in ageing processes was evaluated in cholangiocytes of young and old-mice (2 and 22 months of age respectively), subjected to 3,5-diethoxycarbonyl-1,4-dihydrocollidine (DDC)-treatment, a model of sclerosing cholangitis. Intracellular pathways common to elevated microRNAs were identified by *in silico* analysis. Cell proliferation was evaluated in Twinfilin-1 (*Twf1*) knocked-down cells, assessed by sulforhodamine B (SRB) assay. Senescence and senescence-associated secretory phenotype (SASP) markers were evaluated *in vitro* by qPCR. *In vivo*, senescence-accelerated prone mice (SAMP8, a model for accelerated ageing), *Twf1*^{-/-} or their respective controls were subjected to DDC. mRNA expression level of *Twf1* was evaluated in PBC and PSC patients by qPCR.

Results: Cholangiocytes of DDC-treated mice showed up-regulation of a panel of ageing-related miRs. *Twf1* was identified by

in silico analysis as a common target of the up-regulated *miRs*. *Twf1* expression was increased both in aged and diseases cholangiocytes, and in human cholangiopathies. Knock-down of *Twf1* in cholangiocytes reduced cell proliferation. Senescence and SASP markers resulted increased in *Twf1* knocked-down cholangiocytes upon pro-proliferative stimulation compared to control. *In vivo*, SAMP8 mice with accelerated ageing showed increased biliary proliferation and fibrosis while *Twf1*^{-/-} had a tendency to lower biliary proliferation and fibrosis upon DDC administration compared to control animals.

Conclusions: We identified *Twf1* as an important mediator of both cholangiocyte adaptation to ageing processes and response to injury. Our data suggest that disease and ageing might share common intracellular pathways.

<https://doi.org/10.1016/j.dld.2018.07.028>

P-10

Autoimmune liver disease serology in acute hepatitis E virus infection



B. Terziroli Beretta-Piccoli¹, P. Ripellino²,
C. Gobbi², A. Cerny¹, A. Baserga¹,
C. Di Bartolomeo¹, F. Bihl³, G. Deleonardi⁴,
L. Melidona⁴, A.G. Grondona⁴, G. Mieli-Vergani⁵,
D. Vergani⁶, L. Muratori⁷, the Swiss Autoimmune
Hepatitis Cohort Study Group*

¹ Epatocentro Ticino, Lugano, Switzerland

² Neurocentro della Svizzera Italiana, Ospedale
regionale di Lugano, Lugano, Switzerland

³ Servizio di Epatologia EOC, Bellinzona, Switzerland

⁴ LUM Autoimmunity and Allergy AUSL Bologna, Italy

⁵ Paediatric Liver, GI and Nutrition Centre,
MowatLabs, King's College Hospital, London, UK

⁶ Institute of Liver Studies, MowatLabs, King's College
Hospital, London, UK

⁷ DIMEC, University of Bologna, Bologna, Italy

Introduction: Existing data show an increased seroprevalence of HEV among AIH patients, raising the question as to whether HEV as a role as a potential AIH trigger. Our aim was to investigate whether acute HEV infection is associated with the presence of AIH-relevant autoantibodies.

Material & Methods: Sera of adult patients with acute HEV infection were tested for autoimmune liver serology according to the International AIH Group recommendations.

Results: 48 patients were enrolled. 66% were men, median age at HEV infection was 53.5 years. Half of the patients had at least one serological positivity, 16% were positive for two autoantibodies. ANA were positive in one third, SMA in 20.8%, ANCA in 14.6%. AMA, Anti-SLA, anti-LKM1 and anti-LC1 were negative in all patients. At IIF on rat kidney tissue 2/10 SMA positive patients had the VG and VGT patterns, suggestive of AIH. SMA showed a trend toward association with female gender ($p=0.064$), and were associated with ALT < 500 U/l ($p=0.037$). There was no statistically significant association of autoantibodies positivity with age, presence of diabetes, cirrhosis, immunosuppression or extrahepatic HEV complications.

Follow-up serum from 7/26 seropositive patients was collected between 10 and 15 months later. Three patients were seronegative at follow-up, two showed the same specificities but at lower titres, and two had unchanged titres and specificities. The SMA-positive patient showing the VGT pattern, was still SMA-positive, but with the non AIH-specific V pattern. Follow-up serum from the SMA-positive patient with the VG pattern was not available. None of the followed-up patients developed AIH.

Conclusion: Our data show that ANA, anti-SMA and/or ANCA positivity is a frequent event in acute HEV infection, being found in about half of the cases. Two patients with coexisting extrahepatic autoimmune diseases had AIH-specific SMA, and deserve long-term follow up.

<https://doi.org/10.1016/j.dld.2018.07.029>