Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Digestive and Liver Disease 52 (2020) 816–818

Contents lists available at ScienceDirect

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld

Correspondence

Lights and shadows of SARS-CoV-2 infection risk assessment in endoscopy

Dear Editor

The literature related to endoscopy during the SARS-CoV-2 pandemic makes for interesting reading. The current advice and guidelines proposed by Scientific Societies are unfortunately based on low-grade evidence (expert opinions/observational studies) [1]. Moreover, no studies provide a true estimate of the infection risk in the Endoscopy Unit (EU), but the limited evidence available concludes that SARS-CoV-2 transmission in EUs is low risk, if all the preventive measures are adopted [2,3]. However, this assumption is based on surveys conducted in centers not homogeneously involved in the SARS-CoV-2 pandemic [2,3]. Furthermore, regarding the methodology of the administered questionnaires, some of the information was collected using only the personal impression of the physicians about both the risk of infection and the possible transmission route [2]. During the pandemic, routine endoscopic procedures have been mostly cancelled or postponed and restricted to urgent cases [4]. Hence, after the first "pandemic wave", the topic of re-opening the EU to outpatients and to routine procedures is a matter of debate. Therefore, we believe that the limitations of both available studies and guidelines should be accurately examined. This is mandatory in order to properly assess the SARS-CoV-2 infection risk in EUs and accurately plan their re-opening to outpatients. To date, the only papers that focused on this topic, although very interesting, are mainly descriptive [5] and base their observation solely on the aforementioned low-grade evidence [6].

Firstly, little is known about the biology of the virus and its infection routes (e.g. fecal-oral route). The risk estimation is difficult considering that the diagnosis of SARS-CoV-2 infection is currently based on throat swab testing, with overall sensitivity ranging from 56 to 83%: 66.7% in the first week of the infection and lower in the following weeks [7]. Moreover, the test represents only a "single frame" over a long period, as undetectable viral load could be present in the different stages of the infection. The low accuracy of throat swab testing could be related to improper collection or contamination of samples, inappropriate sites of the throat, inexperienced staff, improper laboratory equipment or storage [8].

The general transmission risk of an infectious disease is strictly related to its prevalence in the population. While the rate of spread was especially high in northern Italian regions, each province showed a very different official disease prevalence (Table 1). At the time of the conducted surveys, the risk both inside and outside the enrolled centers was very different, thus 3 out of 41 centers accounted for almost 55% of all Health Care Worker (HCW) infections [2]. The authors attributed these differences to suboptimal preventive measures, and did not consider the different rates of disease prevalence. It would have been interesting to extend the survey period, in order to make the evaluation more reliable, as the illness prevalence became more homogeneous after the first weeks, and COVID-19 patients were more equally distributed within the different centers after saturation of first line hospitals.

Moreover, the re-organization of hospitals and activities during the pandemic strongly influenced the infection risk assessment among operators and patients. At the beginning of the pandemic, many public hospitals were almost completely converted into COVID-19 facilities, whereas other Institutes were only partially dedicated to it. Furthermore, EU personnel in northern Italy was redeployed to COVID-19 direct assistance roles. Hence, there is no possible way to definitively understand where HCW infections happened: in EUs, in COVID-19 dedicated Units or outside the hospitals, since the surveys were conducted temporally close to the Italian lockdown date.

Lastly, the studies stating a low risk of infection in EUs evaluated only the development of clinically relevant COVID-19 [2,3]. However, no definitive data is available to predict who could develop a severe disease versus who could remain asymptomatic but infectious. Moreover, recent evidence from Wuhan highlighted that more than 59% of infections were not confirmed by tests, thus asserting the presence of potentially contagious asymptomatic subjects [9]. The viral load in asymptomatic patients was also found to be similar to that of symptomatic ones. On this basis, coupling more diagnostic tests (e.g. serology) could be useful.

Accounting for these factors and for the lack of real prevalence data, the estimation of the general risk of acquiring SARS-CoV-2 in the population and consequently in the hospital and EUs is challenging. Our province of Cremona has, up to now, the highest Italian prevalence of SARS-CoV-2 infections (1/65 people) and our Institute admitted almost 3000 COVID-19 inpatients during the first two months of the European pandemic. After three months, in our hospital, we reported overall 355 infected HCWs out of 1650 (21.5%). In our EU 6 out of 25 (24%) HCWs were infected, despite the adoption of recommended preventive measures; whereas in the Internal Medicine division (where 120 beds were entirely dedicated to COVID-19 assistance) 11 out of 51 HCWs were infected (21.5%). These limited figures did not show any statistically significant difference between the prevalence of infection within EUs, COVID-19 s department and overall hospital settings in an high risk area ($p = 0.99$). To our knowledge, no study has methodologically calculated the infection risk in EUs, while taking into consideration the disease prevalence inside and outside the hospital.

Importantly, the number of potentially asymptomatic infections could be even higher than recognised. In our Institute HCWs were tested for high specific and early anti-SARS-COV2 neutralizing antibodies IgG3, a subclass usually associated with viral infections (the same antibodies used as treatment in COVID-19 patients) [10]. This test was offered to identify potentially asymptomatic but infected

https://doi.org/10.1016/j.dld.2020.06.013

Table 1
Prevalence of SARS-CoV-2 infected subjects in the northern Italian provinces at the end of the periods considered in the surveys (1,2] (data from Italian National Health Institute).

Provinces	Population	Infected (N.) on 13 th March	Infected (%)	Infected (N.) on 23 th March	Infected (%)
Milano	3,197,000	1307	0,040	5326	0,166
Cremona	359,000	1344	0,374	2925	0,814
Monza	876,000	143	0,016	1130	0,128
Pavia	546,000	482	0,088	1444	0,264
Bergamo	1,116,000	2369	0,212	6471	0,579
Brescia	1,266,000	1784	0,140	5905	0,466
Como	599,000	118	0,019	581	0,096
Lecco	337,000	237	0,070	934	0,277
Varese	891,000	125	0,014	421	0,047
Lodi	230,000	1133	0,490	1817	0,790
Piacenza	287,000	710	0,247	1885	0,656
Bologna	1,003,000	155	0,015	833	0,083
Rimini	339,000	363	0,107	1035	0,305
Forlì-Cesena	395,000	49	0,012	380	0,096
Ravenna	389,000	55	0,014	342	0,087
Ancona	471,000	158	0,033	702	0,149
Pesaro	359,000	496	0,138	1312	0,365
Novara	368,000	48	0,013	420	0,114
Verona	929,000	210	0,022	1099	0,118

HCWs. Throat swab testing was then performed and assessed, if the serology resulted positive. From this, we observed that 1 out of 25 HCWs in EU and 2 out of 51 HCWs in the Internal Medicine COVID-19 Unit, with no clinical history, had positive antibodies and subsequently a negative swab test result (4 vs 3.9%, respectively $p = 0.99$). From this data we could hypothesize that several HCWs could have increased the infection risk as asymptomatic carriers and have since recovered.

Hence, we think that considering EUs as low-risk areas for SARS-CoV-2 infection could be a premature assumption. Further studies are needed to investigate the real risk, above all in light of the re-opening of endoscopic activity to outpatients.

CreSCoV Working Group (Gruppo Cremonese di studio clinico su COVID-19)

Collaborators:

Abruzzi Luciano†, UO Neurologia ASST di Cremona

Bosio Giancarlo, UO Pneumologia ASST di Cremona

Buffoli Federico UO Gastroenterologia e Endoscopia digestiva ASST di Cremona

Buselli Paolo, UO Riabilitazione specialistica ASST di Cremona

Barletta Giovanna, UO Anestesia e Rianimazione ASST Cremona

Cammelli Lorenzo Direzione Medica ASST di Cremona

Canino Rosario Direzione Sanitaria ASST di Cremona

Caresana Gioacchino, UO Dermatologia ASST di Cremona

Cavalli Claudio, UO Pediatria ASST di Cremona

Coluccello Antonio, UO Anestesia e Rianimazione ASST di Cremona

Coppeta Giovanni Paolo, UO Pronto Soccorso ASST di Cremona

Crotti Massimo, UO Immunoematologia e Medicina Trasfusionale ASST di Cremona

D'Anna Mauro, UO Medicina del Lavoro ASST di Cremona

Danzi Gian Battista, UO Cardiologia ASST di Cremona

De Gennaro Fabio; UO Medicina Interna ASST di Cremona

Faliva Alessio, UO Terapia del dolore ASST di Cremona

Fioravanti Antonio, UO Neurochirurgia ASST di Cremona

Foramitti Marina, UO Nefrologia ASST di Cremona

Fornabaio Chiara, UO Malattie Infettive ASST di Cremona

Fornaciari Margherita, UO Medicina Legale e Rischio Clinico

Generali Daniele, UO Patologia Mammaria e ricerca traslazionale ASST di Cremona

Giannotti Guglielmo, UO Chirurgia Generale ASST di Cremona

Giorgi Pierfranceschi Matteo, UO Medicina Generale ASST di Cremona

Giossi Alessia, UO Neurologia ASST di Cremona

Machiavelli Andrea Marco, UO Farmacia ASST di Cremona

Malberti Fabio, UO Nefrologia ASST di Cremona

Molteni Alfredo, UO Ematologia ASST di Cremona

Nardecchia Anna Laura, UO Medicina Generale ASST di Cremona

Paoletti Oriana, UO Centro Emostasi e Trombosi ASST di Cremona

Pan Angelo UO Malattie Infettive ASST di Cremona, Cremona, Italy

Pasin Federico, UO Medicina Generale ASST di Cremona

Pasquali Nicola, UO Chirurgia Generale ASST di Cremona

Passalacqua Rodolfo, UO Oncologia ASST di Cremona

Pezzarossa Enrico, UO Dermatologia ASST di Cremona

Pezzetti Federica, Direzione Medica ASST di Cremona

Pianta Luca, UO Otorinolaringoiatria ASST di Cremona

Romanini Laura, UO Radiologia ASST di Cremona

Ruggeri Patrizia, Centro Diabetologico ASST di Cremona

Silla Alberto, UO Gestione Operativa ASST di Cremona

Soro Sara, UO Gastroenterologia ed Endoscopia Digestiva ASST di Cremona

Tonoli Sandro, UO Radioterapia e Medicina Nucleare ASST di Cremona

Ungari Marco, UO Anatomia Patologica ASST di Cremona

Viola Erika Maria, UO Ortopedia ASST di Cremona

Zoncada Alessia, UO Malattie Infettive ASST di Cremona

Declaration of Competing Interest

The authors declare they do not have any conflict of interest

Acknowledgement

None

References

[1] Gralnek IM, Hassan C, Beilenhoff U, et al. ESGE and ESGENA position statement on gastrointestinal endoscopy and the COVID-19 pandemic. Endoscopy 2020 Apr 17 Online ahead of print.

[2] Repici A, Pace F, Gabbiadini R, et al. Endoscopy units and the COVID-19 outbreak: a multi-center experience from Italy. Gastroenterology 2020 Apr 10 S0016-5085(20)30466-2.

[3] Repici A, Aragona G, Cengia G, et al. Low risk of covid-19 transmission in GI endoscopy. Gut 2020 Apr 22 gutjnl-2020-321341. Online ahead of print.

[4] Maida M, Sferrazza S, Savarino E, et al. Impact of the COVID-19 pandemic on gastroenterology divisions in Italy: a national survey. Dig Liver Dis 2020 May 16.
[5] Elli L, Raimondi A, Scaramella L, et al. Endoscopy during the COVID-19 outbreak: experience and recommendations from a single center in a high-incidence scenario. Dig Liver Dis 2020 Apr 27;52(6):606–12.
[6] Cennamo V, Bassi M, Landi S, et al. Redesign of a GI endoscopy unit during the COVID-19 emergency: a Practical Model. Dig Liver Dis 2020 May 16 Online ahead of print. doi:10.1016/j.dld.2020.05.007.
[7] Zou L, Ruan F, Huang M, et al. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. N Engl J Med 2020 Mar 19;382(12) 1177–117.
[8] Mungroo MR, Khan NA, Siddiqui R, et al. Novel Coronavirus: current understanding of clinical features, diagnosis, pathogenesis, and treatment options. Pathogens 2020 Apr 17;9(4):E297.
[9] Ozma MA, Maroufi P, Khodadadi E, et al. Clinical manifestation, diagnosis, prevention and control of SARS-CoV-2 (COVID-19) during the outbreak period. Infez Med. 2020;28(2):153–65 Ahead of print Jun 1.
[10] Chen L, Xiong J, Bao L, Shi Y. Convalescent plasma as a potential therapy for COVID-19. Lancet Infect Dis 2020 Feb 27 [Epub ahead of print].

Roberto Grassia on behalf of The CreSCoV Working Group
Gastroenterology and Digestive Endoscopy Unit, ASST Cremona, Cremona, Italy

Sophie Testa
Department of Laboratory Medicine, Haemostasis and Thrombosis Center, ASST Cremona, Italy

Annalisa De Silvestri
Biometry and Clinical Epidemiology, Scientific Direction, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy

Andrea Drago, Fabrizio Cereatti, Clara Benedetta Conti*
Gastroenterology and Digestive Endoscopy Unit, ASST Cremona, Cremona, Italy

*Corresponding author.
E-mail address: benedetta.conti1@gmail.com (C.B. Conti)