



Small-Bowel Capsule Endoscopy in Clinical Practice: Has Anything Changed Over 13 Years?

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Received: 3 February 2018 / Accepted: 25 April 2018 / Published online: 16 May 2018
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Abstract

Background In Lombardia, one of the 20 Italian administrative Regions, small-bowel capsule endoscopy (SBCE) was introduced in 2001. In January 2011, the Regional Health Authorities established a reimbursement for outpatient SBCE.

Aim To prospectively record data on SBCE between 2011–2013 and compare them to similar data retrospectively collected from the same geographical area (covering the period 2001–2008) and published in 2008.

Methods Consecutive SBCEs performed between January 2011 and December 2013 in Lombardia were prospectively collected.

Results In 3 years, 3142 SBCEs were collected; the diagnostic yield (DY) and the overall complication rate were 48.4 and 0.9%, respectively. The main indication was suspected small-bowel bleeding (76.6% of patients); complete small-bowel inspection was achieved in 2796 (89.0%) patients. SBCE was performed as an outpatient procedure in 1945 patients (61.9%). A significant increase in the rate of patients undergoing SBCE for suspected small-bowel bleeding was observed from 2001–2008 to 2011–2013 (67.3 vs. 76.1%; $p < 0.001$). There was an increase in the number of complete small-bowel examinations (81.2 vs. 89.0%; $p < 0.001$) and of outpatient SBCEs (6.7 vs. 61.9%; $p < 0.001$). Conversely, both the retention rate (2.1 vs. 0.8%; $p < 0.001$) and the rate of patients undergoing SBCE for Crohn's disease (11.5 vs. 5.5%; $p < 0.001$) decreased significantly. The overall DY remained stable (50.6 vs. 48.4%; $p = 0.089$).

Conclusion Our study shows that, over 13 years, the SBCE safety profile and completion rate significantly improved over time; a change in the spectrum of clinical indications was also observed.

Keywords Small-bowel capsule endoscopy · Reimbursement policy · Capsule retention · Diagnostic yield

Background

Studies focused on the role of small-bowel capsule endoscopy (SBCE) in clinical practice are often single center and/or frequently include small numbers of patients [1–4]. On the other hand, the available multicenter studies are generally retrospective, include heterogeneous centers that operate in different countries and usually cover long intervals of time [5–8].

In Lombardia (one of the twenty administrative Regions of Italy, located in Northern Italy, consisting of 12 provinces, with an area of 23,844 square kilometers and about 10 million inhabitants), SBCE was introduced in clinical practice in 2001. A collaborative/scientific network (SBCE Lombardia study group), linking centers and gastroenterologists interested in SBCE, has been established since. Based on the active collaboration among the network members,

Members of the “SBCE Lombardia study group” are listed in “Appendix”.

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periodic meetings, as well as continuous quality improvement programs, were implemented [9]. Moreover, a survey on SBCE performed over 7 years (from 2001 to 2008) was published in 2010 [8]. In January 2011, based mainly on an economic analysis of data collected by the SBCE network members [8–11], the Regional Health Authorities granted reimbursement for the performance of SBCE as an outpatient procedure, with a reimbursement of 850.00 euros per procedure [12]. Thereafter, in order to prospectively monitor the activity of the centers, the institution of a Prospective Regional Register has been suggested and encouraged by the Regional Health Authorities.

The primary aim of the present study is to describe the extent of use, indications, results, complications, and practical issues related to the use of SBCE, in a large cohort of consecutive patients in a clinical practice setting, by means of a dedicated Prospective Regional Register. The secondary aim was to compare the prospective data (recorded in 2011–2013) to those retrospectively collected in a previous similar survey performed in the same geographical area before the introduction of the reimbursement (retrospective survey performed in 2008, covering the period of time 2001–2008) [8].

Materials and Methods

In January 2011, at least one doctor from each center performing SBCE in Region Lombardia was invited to participate in the data collection by e-mail and by telephone call from the Prospective Regional Register coordinator (MS). The centers, which started performing SBCE within the period of time 2011–2013, were invited to join in the data collection, as soon as they owned the equipment. For the purpose of data collection, participating centers were asked to fill in a dedicated questionnaire for each SBCE performed, from January 2011 to December 2013. The questionnaire, developed by a Scientific Committee of SBCE experts (MS, CMG, ER), collected information on: (I) patient demographics; (II) clinical indication for SBCE; (III) organizational issues (i.e., referring physician and inpatient/outpatient setting); (IV) technical issues (i.e., type of preparation and type of device used); (V) assessment of the clinical risk of capsule retention and any procedure performed to evaluate the patency of the small-bowel before SBCE; (VI) SBCE results (according to Saurin's classification [13]); (VII) complications (recorded within 3 months from the SBCE ingestion); (VIII) other investigations scheduled after SBCE.

The Prospective Regional Register coordinator (MS) collected questionnaires quarterly (last collection: March 2014); he also tabulated and analyzed the data. Data collected through the 2011–2013 prospective questionnaires were compared, when possible, to data retrospectively

collected in the same geographical area in the previous survey (2001–2008) [8].

Categorical variables were summarized using frequencies and percentages. Quantitative variables were summarized using means and standard deviation or median and interquartile range as appropriate. Fisher's exact test or Chi-squared test were used to compare categorical variables, as appropriate; Student's *t* test was used to compare continuous variables. A *p* value < 0.05 was considered statistically significant. Wilcoxon rank-sum tests for unpaired data were performed for statistical evaluation of the significant difference between inpatient and outpatient groups. The descriptive statistical analyses were carried out with Excel software (Office package V.2016; Microsoft® Co. Redmonton, Washington, USA), whereas other analyses were performed through the Vassarstat Statistical Computation website available online at www.vassarstat.net.

Results

Prospective Regional Register Data (Period of Time 2011–2013)

Overall, 30 out of 32 invited centers (93.7%) agreed to participate in the data collection from 1 January 2011 to 31 December 2013. All the gastroenterologists participating in the data collection are listed in “Appendix”. Overall data on 3142 SBCEs were collected: 1038 (33.0%) SBCEs were carried out in 2011, 1109 (35.3%) in 2012, and 995 (31.7%) in 2013. The SBCE examinations performed in each District of the Region Lombardia in the period of time 2011–2013 are reported in Table 1. The patients' mean age was 62.3 ± 17.7 years; patients > 65 y. o. represented 55.5% of the whole population, with a male prevalence (53.3%). The indications for the procedure were: suspected small-bowel bleeding in 76.1%, suspected Crohn's disease in 4.5%, Familial Adenomatous Polyposis (FAP) and Peutz–Jeghers syndrome in 4.4%, unexplained diarrhea in 3.0%, Celiac Disease in 2.9%, suspected small-bowel tumor in 1.8%, confirmation of findings identified with other procedures in 1.4%, known Crohn's Disease in 1.0% and unexplained abdominal pain 0.8%. The overall capsule endoscopy diagnostic yield (i.e., the rate of patients with at least one P3 lesion according to Saurin's classification [13]) was 48.4% (1521/3142). In the 1521 patients with a positive SBCE examination, the main findings were: vascular lesions (44.6%), inflammatory changes (erosions or ulcers: 25.2%), polyps or masses (17.2%), active bleeding in the small-bowel lumen (11.1%), and stenosis (1.9%). The overall number of patients receiving a complete small-bowel evaluation via SBCE was 2796 (2796/3142: 89.0%).

Table 1 Number of SBCEs performed in the 12 districts of Region Lombardia in the period 2011–2013

District	No. of centers participating in the data collection	Percentage of inhabitants (%)	Number of capsules performed in 2011–2013 (%)
Bergamo	1	11.2	122 (3.9)
Brescia	3	12.7	596 (19.0)
Como	1	6.0	121 (3.9)
Cremona	2	3.7	125 (3.9)
Lecco	1	3.5	27 (0.8)
Lodi	0	2.3	0 (0.0)
Monza-Brianza	2	8.7	415 (13.2)
Milano	14	31.3	1162 (37.0)
Mantova	1	4.2	134 (4.2)
Pavia	1	5.5	115 (3.7)
Sondrio	1	1.9	42 (1.4)
Varese	3	9.0	283 (9.0)
Region Lombardia	30	100	3142 (100)

The overall complication rate was 0.89% (28/3142); the capsule was retained in 26 patients, and two patients aspirated it in the airways at the time of ingestion (both of them expelled the capsule by coughing). Capsule retention led to acute obstruction in seven patients (7/26); in five of them, an urgent surgical intervention was performed, whereas one patient underwent an urgent device-assisted enteroscopy (DAE) and another one an urgent EGD. (The capsule was retained in the stomach.) Details of patients experiencing capsule retention have been described elsewhere [14].

Among the 1621 patents with negative SBCE, 1123 (69.3%) did not receive any further diagnostic/therapeutic examination during a 3 month follow-up, but only a clinical monitoring was planned. Conversely among the 1521 patients with positive SBCE, 1037 (68.2%) received further diagnostic/therapeutic procedures, mainly based on SBCE findings.

In the period 2011–2013, SBCE was performed as an inpatient procedure in 1163 patients (37.0%), as an outpatient procedure in 1945 patients (61.9%) and in a day-hospital setting in 34 patients (1.1%). The use of SBCE in the outpatient setting has increased from 56.9% in 2011 to 63.6% in 2012 and to 65.0% in 2013 ($p=0.0003$). The outpatients were younger than the inpatients: 60.2 ± 17.2 vs. 65.9 ± 17.3 years, respectively ($p < 0.001$), whereas no differences were found between the two populations by gender, indication or SBCE prescriber. In outpatients, a lower diagnostic yield (45.90 vs. 52.46%; $p < 0.001$) was observed, as compared to the hospitalized patients; this data remained significant even when corrected for age and sex. The rate of patients with incomplete small-bowel examination was 9.0% (105/1163) in outpatients and 12.4% (241/1945) in inpatients ($p=0.003$), whereas the SBCE retention rate was comparable in both subgroups of patients (16/1945: 0.83% and 10/1163, respectively: 0.80%; $p=1.00$).

Comparison Between the Prospective Regional Register Data (Period of Time 2011–2013) and the Retrospective Survey (Period of Time 2001–2008) Data

In the period 2001–2008, an increase in the number of centers performing the procedure was observed (from 5 to 29), whereas from 2011 to 2013 the number of centers remained stable (32 centers) over the 3-year period of data collection. The participation rate in the data collection of centers performing SBCE was comparable in the two periods of time (23/29 in 2001–2008 and 30/32 in 2011–2013, $p=0.13$). There was a significant increase in the yearly number of SBCE performed over time (417/year in 2001–2008 vs. 1047/year in 2011–2013), but the total number of examinations in 2008 (840 examinations) was slightly lower than the mean number of tests carried out annually in the period 2011–2013. According to the number of inhabitants, 8.6 SBCE per 100,000 inhabitants were carried out in 2008 (840/9.742.676 inhabitants), while 10.5 SBCE per 100,000 inhabitants were performed in 2011 (1047/9.704.151 inhabitants).

Comparing the two periods of time with regard to the spectrum of indications, an increase was observed in the patients undergoing the examination for suspected small-bowel bleeding (67.3% in 2001–2008, 76.1% in 2011–2013; $p < 0.001$), while the number of patients undergoing SBCE for known or suspected Crohn's disease decreased significantly (11.5% in 2001–2007, 5.5% in 2011–2013; $p < 0.001$). Despite these differences, the overall diagnostic yield of SBCE remained stable (50.6% in 2001–2008, 48.4% in 2011–2013; $p=0.089$), as well as the spectrum of detected findings (prevalence of vascular lesions, followed by inflammatory lesions and last by neoplastic lesions). A statistically significant decrease was observed as far as the retention rate is concerned: 61 retentions were reported in the period 2001–2008 (61/2921: 2.1%)

and 26 retentions in the period 2011–2013 (26/3142: 0.8%) ($p < 0.001$). The rate of patients with incomplete small-bowel SBCE examination was significantly higher in the period 2001–2008 (550/2921; 18.8%) than in the period 2011–2013 (346/3142; 11.1%) ($p < 0.001$). With regard to the SBCE practical/organizational issues, the number of examinations performed as outpatients procedure increased by about ninefold over time (from 6.7% in the time-frame 2001–2008 to 61.9% in 2011–2013, respectively; $p < 0.001$). All the comparative data are summarized in Fig. 1.

Discussion

Our large prospective data collection confirms that SBCE is nowadays a well-established method for the evaluation of the small-bowel, performed in 8–10 patients/100.000 inhabitants/year, with a high diagnostic yield, a definite spectrum of findings and an excellent safety profile. When evaluating SBCE data over a 13-year period of time (from 2001 to 2013), the DY remained stable, the retention rate significantly decreased, and the completion rate significantly increased.

Interestingly, in the cohort 2011–2013, we observed a dramatic increase in SBCEs performed as outpatients procedures and, as far as clinical indications are concerned, an increase in the number of patients undergoing SBCE for suspected small-bowel bleeding, while those receiving SBCE for known or suspected Crohn’s disease significantly decreased.

The SBCE was initially conceived with the purpose to make endoscopy wireless and ultimately as less invasive as possible. The size of the “endoscope,” as well as the complete procedure automation, makes SBCE an ideal outpatient procedure. In the period 2001–2008, approximately three quarters of the patients received SBCE as an inpatient procedure and the large majority of them were hospitalized, in order to cover procedure-related expenses through the diagnosis-related group (DRG) reimbursement, because of the lack of an outpatient SBCE reimbursement [10, 11]. As we observed in the prospective data collection, the introduction of a dedicated outpatient SBCE reimbursement in January 2011 overturned this figure: more than 60% of SBCE were performed as outpatient procedures. This shift, given the estimated mean reimbursement of approximately 1775.00 euros [10] provided by the third payer for each SBCE performed as an inpatient procedure

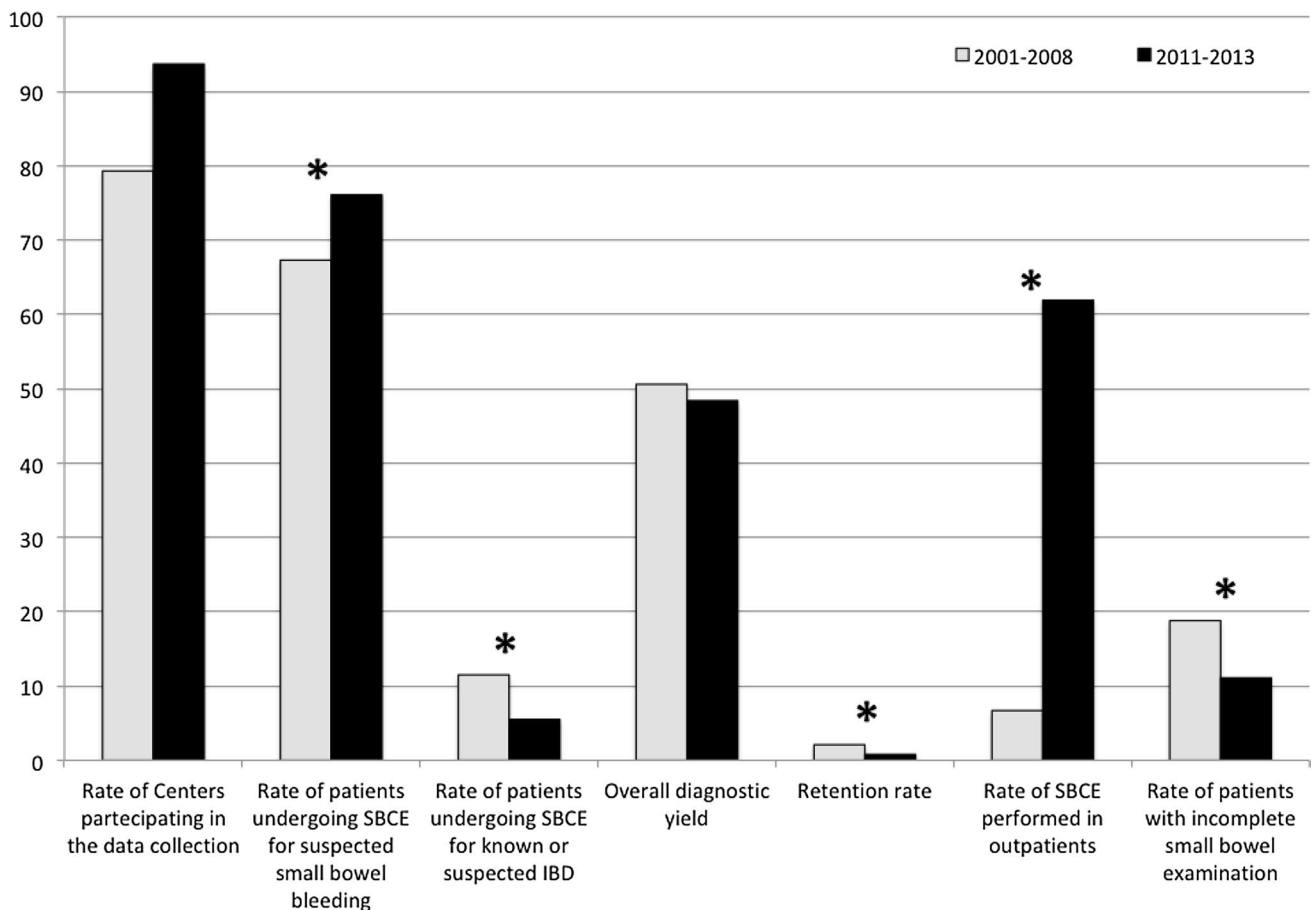


Fig. 1 Comparison between the Prospective Regional Register (period 2011–2013) data and the retrospective survey (period 2001–2008) data. *Statistically significant difference; SBCE: small-bowel capsule endoscopy; IBD: inflammatory bowel disease

and the present reimbursement of 850.00 euros for the SBCE performed as outpatient procedure since January 2011 [12], led to a saving of about € 925.00 for each patient undergoing SBCE as outpatient instead as inpatient [10]. We are fully aware that this is just a rough estimation, since the economic data are based only on estimates that refer to patients with suspected small-bowel bleeding. However, the present calculation is based on prudential estimates and if we considered patients undergoing SBCE for other indications (e.g., Crohn's disease), the consumption of resources, and consequently the third payer costs, would probably be even higher.

With the new reimbursement policy, a significant increase in the number of procedures over time could have been expected. However, in the period of time 2011–2013, the yearly number of SBCE remained stable and it was only a little higher than that reported in the last year of the retrospective survey (2008). These data suggest that the number of 8–10 capsules/100,000 inhabitants/year represents the actual clinical need of SBCE in daily practice, at least in the geographical area under evaluation.

In the period 2011–2013, despite the new reimbursement policy, a consistent rate of SBCE (approximately 37%) was carried out in inpatients. This is probably due to the fact that certain clinical situations (i.e., bleeding severity, transfusion requirement, comorbidities, ongoing therapies) make hospitalization necessary and require a timely SBCE. These clinical factors could also account for the differences observed between inpatients and outpatients in terms of diagnostic yield, which was higher in inpatients [15, 16]. As reported in other studies [15, 16], hospitalized patients have an increased risk of incomplete small-bowel exploration with SBCE, mostly due to the limited mobility of the patients, to comorbidities and to the high number of medications. The dramatic increase in the number of outpatient SBCEs, as well as the introduction over time of improved capsules with longer battery life, may also explain the significant increase in the SBCE completion rate observed in 2011–2013 time interval. The increased completion rate has important clinical consequences, mainly in patients with negative SBCE. In fact, given the high negative predictive value of a complete SBCE [17–19], about 70% of patients with negative SBCE received only a clinical follow-up, without further diagnostic tests.

A section of the prospective questionnaire was specifically dedicated to the evaluation of possible SBCE-related complications, and detailed results have been reported elsewhere [14]. When comparing prospective data with the retrospective survey, we observed that the SBCE retention rate significantly decreased over time; this difference may depend on the accumulating knowledge on the SBCE-related complications, on the learning curve of gastroenterologists performing SBCE, as well as on the introduction of effective methods aimed at preventing capsule retention in clinical practice in the last 10 years (e.g., Patency Capsule, dedicated

small-bowel cross-sectional imaging techniques) [20, 21]. The decrease over time of the number of patients undergoing SBCE for known or suspected Crohn's disease may also contribute to decreasing the retention rate. In fact, known or suspected Crohn's disease represents one of the leading causes of capsule retention [6] and a 3.5 and 8.0% pooled retention rate has been previously reported in patients with known and suspected Crohn's disease, respectively [22]. Although we do not have obvious explanations for the decrease in the number of patients undergoing SBCE for Crohn's disease over time, this might depend on the increasing evidence reporting the risk of retention in this subgroup of patients, in conjunction with the improvement of other techniques for the study of the small-bowel (namely DAE, CT- and MR-enteroclysis). Conversely, the evidence on the key role of SBCE in the management of patients with suspected small-bowel bleeding, as well as the recommendations provided by Scientific Societies through dedicated guidelines [15, 23, 24], increased the number of SBCE performed for this indication.

Our prospective data collection has some limitations: the population was unselected, the participating centers had different expertise on small-bowel endoscopy, we focused on a restricted geographical area, data were self-reported, and there were no internal controls within the questionnaire. Nevertheless, some of these features contribute to make our data collection a reliable picture of the everyday clinical practice. On the other hand, in the present paper we compared two time intervals different in length (7 vs. 3 years), by means of a different data collection modality (retrospective in the period 2001–2008 and prospective in the period 2011–2013) and by using different questionnaires, which shared only a limited number of domains.

The present study confirms with a large prospective data collection the high diagnostic yield of SBCE in daily clinical practice and the excellent safety profile and completion rate of the examination, which were further improved, when compared to those observed in previous years. Our data collection documented, over a period of time of 13 years, a change in the spectrum of SBCE indications and suggested that the need for capsule enteroscopy in daily practice is about 8–10 capsules per 100,000 inhabitants/year. The adoption of a predefined reimbursement policy for outpatients had a significant impact in decreasing the number of inappropriate hospitalizations, allowing at the same time a significant economic saving for the third party payer.

Acknowledgments We would like to thank Silvia Paggi for her invaluable help in the editing process.

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

Appendix

See Table 2.

Table 2 List of gastroenterologists participating in the “SBCE Lombardia study group.” In some centers more than one gastroenterologist was involved

Last name, First name, degree	Affiliations
Soncini Marco, MD	UO Gastroenterologia, A.O. San Carlo Borromeo, Milano
Rondonotti Emanuele, MD, PhD	UO Gastroenterologia, Ospedale Valduce Como
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Schalling Renzo, MD	U.O. Medicina Interna, Ospedale di Vimercate, Vimercate
Maino Marta, MD	U.O. Endoscopia Digestiva, A.O. San Gerardo, Monza
Cesari Pietro, MD	U.O. Endoscopia Digestiva, Congregazione Ancelle della Carità. Brescia
Mantovani Nicola, MD	U.O. Endoscopia Digestiva, A.O. C. Poma, Mantova
Ballardini Giovanni, MD	S.C. Endoscopia Diagnostica, Istituto Nazionale dei Tumori. Milano
Bargiggia Stefano, MD	U.O. Gastroenterologia, A.O. A. Manzoni, Lecco
Bianchi Guglielmo, MD	U.O. Gastroenterologia, Istituti Ospitalieri, Cremona
Bonfante Fabrizio MD	U.O. Medicina Desenzano del Garda, Desenzano
Cantù Paolo, MD	U.O. Medicina Interna, Ospedale C. Cantù, Abbiategrosso
Centenara Laura, MD	U.O. Gastroenterologia, IRCCS Policlinico S. Matteo, Pavia
Cortelezzi Claudio, MD	U.O. Gastroenterologia, Fondazione Macchi-Ospale di Circolo, Varese
Gasparini Paolo, MD	UO Gastroenterologia, A.O.San Carlo Borromeo, Milano
Gozzini Claudio, MD	U.O. Gastroenterologia, A.O. Salvini-P.O. di Rho, Rho
Greco Salvatore, MD	UO Gastroenterologia, Ospedali Riuniti di Bergamo, Bergamo
Gullotta Renzo, MD	U.O. Gastroenterologia, Clinica S. Carlo, Paderno Dugnano
Iannuzzi Francesca, MD	U.O. Gastroenterologia, Università degli Studi di Milano, Ospedale Sacco, Milano
Iirritano Elena, MD	U.O. Gastroenterologia, Istituti Ospitalieri, Cremona
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Mandelli Giovanna, MD	UO Gastroenterologia, Ospedale Valduce, Como
Merlino Luca, MD	Regione Lombardia Direzione Generale Sanità, Milano
Morandi Elisabetta, MD	U.O. Endoscopia Digestiva, Università degli Studi di Milano, A.O. S. Paolo, Milano
Notaristefano Chiara, MD	U.O. di Endoscopia Digestiva, IRCCS San Raffaele Milano
Pansoni Carlo, MD	U.O. Endoscopia Digestiva, A.O. Eugenio Morelli, Sondalo
Petruzzellis Carlo, MD	U.O. Endoscopia Digestiva, Congregazione Ancelle della Carità, Brescia
Putignano Rocco, MD	U.O. Gastroenterologia, A.O. S. Antonio Abate, Gallarate
Repici Alessandro, MD	U.O. Endoscopia Digestiva, IRCCS Humanitas, Rozzano
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