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Differences between childhood- and adulthood-onset inflammatory bowel disease: the CAROUSEL study from GETECCU

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Summary

Background: Cohort studies comparing the characteristics of childhood-onset and adulthood-onset inflammatory bowel disease (IBD) in the biologics era are scarce.

Aim: To compare disease characteristics, the use of immunomodulators and biologic agents and the need for surgery between childhood- and adulthood-onset IBD.

Methods: Inflammatory bowel disease patients from the ENEIDA registry diagnosed between 2007 and 2017 were included. The childhood-onset cohort comprised patients diagnosed at ≤16 years of age and the adulthood-onset cohort those diagnosed at >16 years. The cumulative incidences of immunosuppressive therapy, biologic therapy and surgery were estimated using Kaplan-Meier curves, compared by the log-rank test. Cox regression analysis was performed to identify potential predictive factors of treatment with immunosuppressants, biologic agents or surgery.

Results: The adulthood-onset cohort comprised 21 200 patients out of 20 354 (96%) and the childhood-onset cohort 846 (4%). Median follow-up was 54 months in the childhood-onset cohort and 38 months in the adulthood-onset cohort ($P < 0.01$). Proportions of Crohn's disease, ileocolonic involvement and inflammatory behaviour at diagnosis were higher in the childhood-onset cohort. In the multivariate analysis, after adjusting for sex, type of IBD, extraintestinal manifestations, family history and smoking habit, childhood-onset IBD was associated with higher risk of immunomodulator use (hazard ratio [HR] = 1.2, 95% confidence interval [95% CI] = 1.1-1.2) and higher probability of receiving biologic treatment (HR = 1.2, 95% CI = 1.1-1.3). However, childhood-onset IBD was not associated with higher risk of surgery (HR = 0.9, 95% CI = 0.8-1.2).

Conclusions: Childhood-onset IBD has differential characteristics and higher risk of treatment with immunomodulators and biologic agents, compared with adulthood-onset IBD. Nevertheless, paediatric IBD is not associated with higher risk of surgery.

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The members of the ENEIDA Study Group are listed in Appendix 1.

1 | INTRODUCTION

Inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), are chronic inflammatory diseases resulting from a combination of genetic predisposition, environmental factors and abnormal immune responses to the microbiota.[1,2] The major peak incidence of IBD occurs at the onset of adulthood, although an increased incidence of IBD at paediatric age has recently been reported.[3–7] At present, the causes determining the onset of the disease in each patient are unknown.

Although they are considered as a single group of diseases, IBD represents a very heterogeneous group of pathologies with similarities in the phenotype but with notable differences between different patients. In this regard, it has been suggested that childhood-onset IBD may be a different entity, more severe and "aggressive" than IBD diagnosed at adulthood, and that genetic factors could play a more important role in children than in adults, although in adults with older age at onset and more advanced IBD, environmental factors would play a more prominent role.[7–11]

Nevertheless, most of the differences found between childhood-onset and adulthood-onset IBD come from the comparison of clinical and epidemiological data from independent patient series (paediatric patients vs adult patients). Up to now, data comparing the evolution of childhood-onset IBD with that of adulthood-onset IBD come only from three population cohorts.[5,6,12–16] Results regarding the use of immunosuppressants and biologic agents and the need for surgery according to the age at diagnosis are controversial.[5,12,13,17–19] These series have some limitations such as the retrospective inclusion of some of the data and the fact that they were studied mainly in the pre-biologics era. In addition, recent studies have found more aggressive phenotype at disease onset than previously described. Therefore, further updated information from population cohort studies is strongly needed to assess whether paediatric age-specific IBD represents a different entity with more severe phenotype at debut, higher use of immunosuppressants and biologic agents or more need for surgery.

ENEIDA registry, a prospectively maintained registry, provides access to a large population-based cohort of IBD patients, which is suitable for comparing the characteristics of IBD patients diagnosed during childhood with those diagnosed during adulthood. Through this large multi-centre nationwide study, we aimed to compare the characteristics of the disease, the use of immunosuppressive and biologic drugs and the need for surgery during follow-up in patients diagnosed at paediatric age (≤16 years) versus those diagnosed in adulthood. We anticipate that our results will help to understand the differences between childhood-onset and adulthood-onset IBD.

2 | METHODS

The study sample comprised patients diagnosed with IBD based on the criteria of the European Crohn's and Colitis Organization and included in the ENEIDA registry.[20,21] For this study, only those patients diagnosed from 2007, when ENEIDA registry was rolled out, to 2017 were included. The childhood-onset cohort comprised IBD patients diagnosed at ≤16 years of age, and the adulthood-onset cohort IBD patients diagnosed at >16 years. Elderly IBD patients have been suggested to be a different disease group, with their own characteristics (mainly a more benign disease course).[7,10] For that reason, patients diagnosed in the adulthood were classified into two groups: young adulthood-onset IBD (17-60 years at diagnosis) and elderly adulthood-onset IBD (>60 years at diagnosis). Patients were observed from diagnosis of IBD until the date of last visit.

2.1 | ENEIDA registry

ENEIDA is a registry of the Spanish Working Group in Crohn's and Colitis (GETECCU), which includes patients with IBD. The database prospectively records clinical characteristics, outcomes and treatments. After registration, physicians from IBD centres can voluntarily include their patients' data in the registry. At the time of data extraction, the registry contained 49 882 patients from 86 centres. The present study was approved by the ENEIDA Committee and by the centres Ethic Committees. Written informed consent to participate in the ENEIDA project was obtained from all patients.

2.2 | Data collection

The data collected included sex, type of IBD (CD, UC, or unclassified colitis), age at diagnosis, CD location, CD behaviour (inflammatory, stenosing, or fistulising), UC extent, presence of perianal disease, presence of extraintestinal manifestations and presence of family history of IBD.

In addition, detailed information of treatment for IBD is also included in the ENEIDA registry: use of immunomodulators, type of immunomodulator, use of biologic agents, type of biologic agents and date of initiation of each IBD drug. Finally, the need for surgery and date of surgery were also included in the ENEIDA registry.

2.3 | Definitions

Diagnosis of CD and UC was established based on standard clinical, radiological, histological, and endoscopic criteria.[20–22] In CD patients, disease behaviour was categorised based on the Montreal classification as follows: (a) inflammatory disease (B1) or CD without fistulising or stricturing complications; (b) stricturing disease (B2), which was defined as the presence of clinical symptoms of partial or complete obstruction with fixed narrowing and/or narrowing with proximal dilatation; and (c) fistulising disease (B3), which included the presence of enteric fistulas, intra-abdominal abscesses, or bowel perforation.[23] The location of disease was established by macroscopic evidence of CD in any part of the gastrointestinal tract. Possible locations included the ileum (L1), colon (L2), ileum and colon (L3), upper gastrointestinal tract (L4), and perianal/perineal area (p).

For UC, the Montreal classification was based on the extent of the disease, classifying the disease as proctitis, left-sided colitis (up

to the splenic flexure) and extensive colitis (proximal to the splenic flexure).[23]

Exposure to drugs was defined as use of a specific therapeutic group (immunosuppressants—either thiopurines or methotrexate—or biologics) from the diagnosis of IBD to the end of follow-up.

2.4 | Treatment policy

All the participant centres were members of GETECCU; one of its aims is to disseminate the knowledge on IBD through a wide formative program. In consequence, the therapeutic strategy for IBD patients in Spain is based on international guidelines.[20,21] In this respect, short-term steroids are used mainly in clinical exacerbations as first-line treatment. Thiopurines are used as maintenance therapy for steroid-dependent, steroid-refractory or fistulising patients in selected cases and for the prevention of postsurgical recurrence. Methotrexate is exceptionally used as second-line immunosuppressive therapy, and biologics for induction and maintenance of remission in refractory patients to immunosuppressants, or as first-line therapy in selected cases. Surgical resections are performed for emergent indications (obstruction, perforation, acute abdomen) and for failure of medical therapy.

2.5 | Statistical analysis

Mean, median and ranges were calculated for continuous variables. Percentages and 95% confidence intervals (95% CI) were calculated for categorical variables. Categorical variables were compared using Chi-square (χ^2) test, and quantitative variables using the appropriate test. The Kaplan-Meier method was used to determine the incidence rate of use of immunosuppressants, biologics and surgery throughout the follow-up period. For each of these analyses, date of censoring was the date when the patient received immunosuppressant for the first time, the date when the patient received biologic agents for the first time, and the date of first surgery due to IBD, respectively, or the date of last visit, whichever came first. Survival curves were compared using the log-rank test to identify variables potentially associated with the use of immunosuppressants, biologic agents or surgery. Stepwise multivariate Cox regression analysis was used to evaluate the impact of age at diagnosis on the use of immunomodulators, biologic agents and surgery. The final multivariate model was repeated separately for CD and UC patients. In the Cox regression model of CD patients, the variable "Disease phenotype at diagnosis" was included. In addition, the final multivariate model was repeated, categorising patients into three categories based on the age at diagnosis: childhood-onset IBD (patients diagnosed at ≤16 years), young adulthood-onset IBD (17-60 years at diagnosis) and elderly adulthood-onset IBD (>60 years at diagnosis).

2.6 | Sensitivity analysis

A propensity score was estimated by logistic regression with selected confounders with 1:1 matching algorithm without replacements. We randomly selected a patient in the treatment group and then matched that patient with the nearest patient in the control group within a caliper of width equal to 0.2 of the standard deviation of the logit of the estimated propensity score. To assess the success of the propensity score matching procedure, we measured standardised differences (in percentage points) in observed confounders between the matched groups. The cohort effect was estimated by using Cox regression methods in the paired sample.

3 | RESULTS

A total of 21 200 patients diagnosed with IBD from 2007 to 2017 were included in the ENEIDA registry. Adulthood-onset cohort (>16 years at diagnosis) comprised 20 354 patients (96%). Childhood-onset cohort (≤16 years at diagnosis) comprised 846 patients (4%); among them, 26 were diagnosed before the age of 6 and 820 between the ages of 6 and 16 years (supplementary material Table 1).

3.1 | Disease characteristics

Main characteristics of the study populations are summarised in Table 1. In the childhood-onset cohort, CD patients had more extensive involvement and the upper gastrointestinal tract was affected in a higher percentage of patients. At diagnosis, most of the patients had inflammatory behaviour in both the childhood-onset and the adulthood-onset cohorts (94% vs 87%, $P < 0.01$) but the proportion of patients with complicated behaviour (either stricturing of fistulising disease) was higher in the adulthood-onset cohort at diagnosis and at the end of follow-up (Table 1). Patients in the childhood-onset cohort had more extensive colitis. Family history of IBD was also more frequent in the childhood-onset cohort.

3.2 | Medical treatment

The proportion of patients treated with immunomodulators was significantly higher in the childhood-onset cohort (Table 1). Moreover, the proportion of patients treated with immunomodulators was significantly higher in the childhood-onset cohort in both CD (85% vs 66.2%, $P < 0.001$) and UC (56.1% vs 28.3%, $P < 0.001$). Median time from diagnosis to first immunomodulator was longer in the adulthood-onset cohort (5 vs 3 months, $P < 0.01$). Cumulative incidence of treatment with immunomodulators was significantly higher in the childhood-onset cohort: 54% at 1 year and 87% at 5 years in the paediatric cohort; and 34% at 1 year and 55% at 5 years in the adulthood-onset cohort (Figure 1A).

In the univariate analysis, diagnosis during childhood, IBD type, presence of extraintestinal manifestations, family history and tobacco consumption were significantly associated with the treatment with immunomodulators during follow-up. In the multivariate analysis, diagnosis during childhood, CD (vs UC), smoking habit, extraintestinal manifestations and family history of IBD were significantly associated with higher risk of treatment with immunomodulators, while

TABLE 1 Characteristics of the study population according to age at diagnosis

Variable	Childhood-onset cohort	Adulthood-onset cohort	*P*
Age (y), median (IQR)	15 (13-16)	39 (28-53)	<0.01
Time of follow-up (months), median (IQR)	54 (26-83)	38 (13-70)	<0.01
Male sex, n (%)	482 (57)	10 683 (52)	<0.01
Inflammatory bowel disease type			
Crohn's disease, n (%)	520 (61.5)	9960 (49)	<0.01
L1, n (%)	129 (26)	4103 (43)	<0.01
L2, n (%)	73 (14)	1730 (18)	
L3, n (%)	293 (59)	3733 (39)	
L4, n (%)	80 (15.4)	699 (7)	<0.01
B1 (at diagnosis), n (%)	489 (94)	8707 (87.5)	<0.01
B2 (at diagnosis), n (%)	19 (3.7)	744 (7.5)	
B3 (at diagnosis), n (%)	12 (2.3)	509 (5)	
B1 (at the end of follow-up), n (%)	415 (80)	7122 (73)	<0.01
B2 (at the end of follow-up), n (%)	55 (10.6)	1487 (15)	
B3 (at the end of follow-up), n (%)	47 (9)	1189 (12)	
Perianal disease, n (%)	137 (16.4)	2161 (10.8)	<0.01
Ulcerative colitis, n (%)	305 (36)	9720 (48)	<0.01
Pancolitis, n (%)	150 (50.8)	2962 (32)	<0.01
Left-sided colitis, n (%)	105 (35.6)	3810 (41)	<0.01
Proctitis, n (%)	40 (13.6)	2550 (27)	<0.01
Extraintestinal manifestations, n (%)	98 (12)	2711 (13.8)	>0.05
Pharmacological treatments			
Immunosuppressants, n (%)	615 (73.9)	9393 (47)	<0.01
Biological agents, n (%)	417 (53)	5456 (29.2)	<0.01
Surgery, n (%)	126 (16.5)	2808 (15)	>0.05
Family history, n (%)	136 (18.3)	2265 (12.7)	<0.01
Smoking habit, n (%)	43 (6.3)	5291 (33)	<0.01

IQR, interquartile range.

female sex was independently associated with lower use of immunomodulators (Table 2).

The proportion of patients treated with biologic agents was significantly higher in the childhood-onset cohort (Table 1). Furthermore, the proportion of patients that received biologics was significantly higher in the childhood-onset cohort in both CD (65% vs 41.5%, $P < 0.001$) and UC (33% vs 17.4%, $P < 0.001$). Median time from the diagnosis to first biologic agent was similar in the paediatric and the adulthood-onset cohort (13 vs 12 months, $P > 0.05$). The cumulative incidence of treatment with biologic agents was significantly higher in the childhood-onset cohort: 25% at 1 year and 65% at 5 years in the childhood-onset cohort; and 16% at 1 year and 37% at 5 years in the adulthood-onset cohort ($P < 0.01$) (Figure 1B)

In the univariate analysis, variables associated with treatment with biologic agents were as follows: diagnosis during childhood, sex, IBD type, extraintestinal manifestations, family history of IBD and tobacco consumption. In the multivariate analysis, diagnosis during childhood, CD (vs UC), the presence of extraintestinal manifestations and smoking habit were significantly associated with higher use of biologic agents, while female sex was independently associated with lower use of biologic agents during follow-up (Table 2).

3.3 | Surgery

The percentage of patients that underwent surgery was similar in the childhood-onset and adulthood-onset cohorts (Table 1). In CD, the proportion of patients that underwent surgery was similar in the childhood-onset and adulthood-onset cohorts (23% vs 25%, $P > 0.05$). Likewise, in UC, the proportion of patients that underwent surgery was 5.8% in the childhood-onset cohort and 5.6 in adulthood-onset cohort. However, median time from diagnosis to first surgery was significantly lower in the adulthood-onset cohort (7 vs 15 months, $P < 0.01$). The cumulative incidence of surgery was similar in both cohorts (Figure 1C). In the univariate analysis, sex, IBD type, extraintestinal manifestations smoking habit and treatment with immunomodulators were significantly associated with surgery during follow-up. In the multivariate analysis, CD (vs UC) and smoking habit were significantly associated with higher risk of surgery, while female

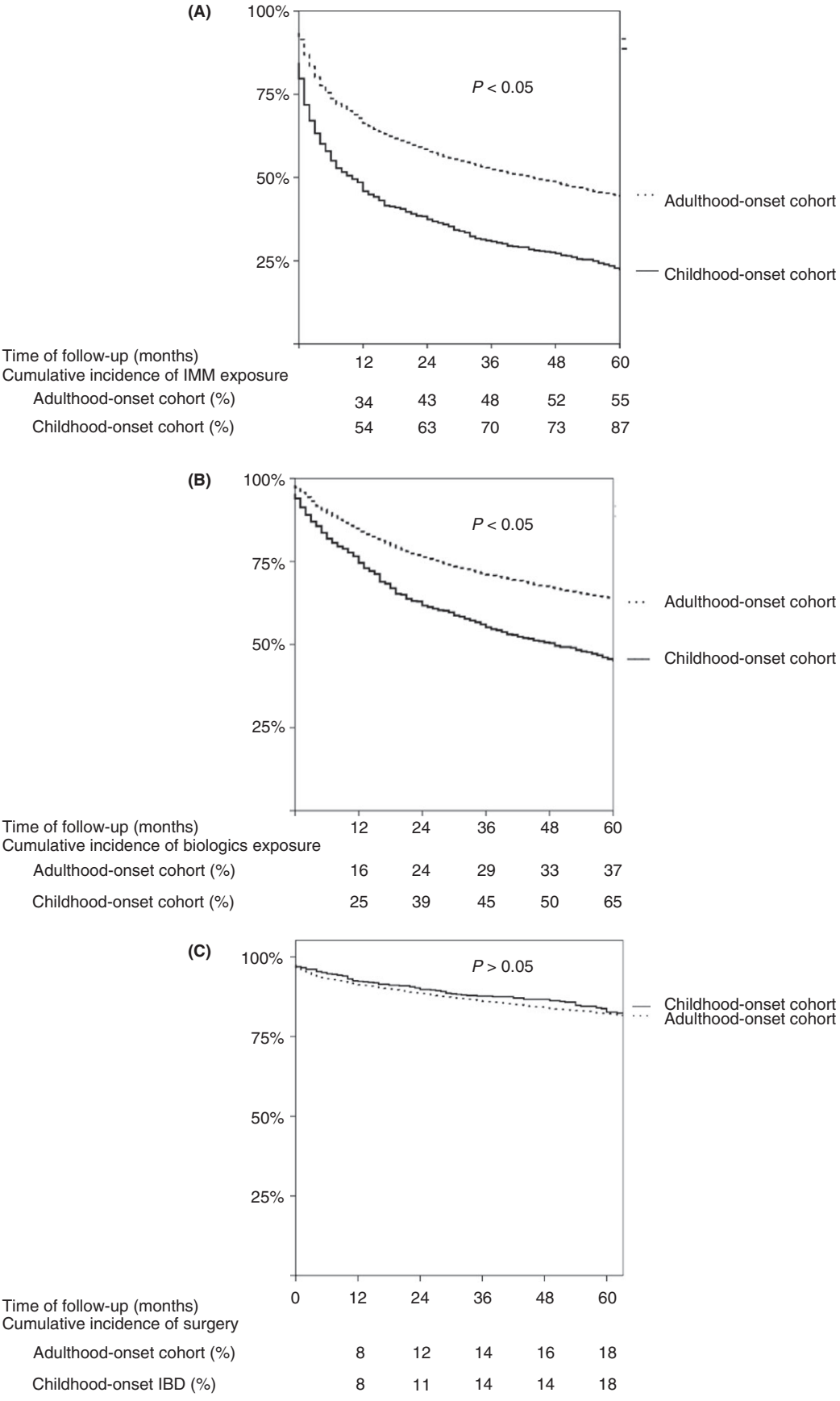

FIGURE 1 Survival curves of the cumulative incidence of exposure to immunomodulators (IMM) (A), biologics (B) and surgery (C) according to age at diagnosis of inflammatory bowel disease

TABLE 2 Variables associated with the risk of treatment with immunosuppressants, biological agents and surgery during follow-up

Variable	Hazard ratio (95% confidence interval)
Use of immunosuppressants	
Childhood-onset vs adulthood-onset IBD	1.6 (1.5-1.8)
Female sex	0.94 (0.91-0.98)
Crohn's disease (vs ulcerative colitis)	3.2 (3.09-3.4)
Family history	1.08 (1.01-1.1)
Extraintestinal manifestations	1.2 (1.1-1.3)
Smoking habit	1.1 (1.05-1.16)
Use of biologic agents	
Childhood-onset vs adulthood-onset IBD	1.5 (1.4-1.7)
Female sex	0.92 (0.8-0.95)
Crohn's disease (vs ulcerative colitis)	2.5 (2.3-2.7)
Extraintestinal manifestations	1.7 (1.6-1.7)
Smoking habit	1.1 (1.04-1.18)
Surgery during follow-up	
Childhood-onset vs. adulthood-onset IBD	0.9 (0.8-1.2)
Female sex	0.79 (0.73-0.86)
Crohn's disease (vs ulcerative colitis)	6.6 (5.8-7.4)
Immunomodulators before surgery	0.36 (0.33-0.39)
Smoking habit	1.2 (1.1-1.3)

IBD, inflammatory bowel disease.

sex was independently associated with lower risk. Neither IBD diagnosis during childhood nor previous treatment with biologic agents was associated with the risk of undergoing surgery (Table 2).

3.4 | Outcomes based on IBD type

In CD patients, the likelihood of being treated with immunomodulators or with biologics remained higher in the childhood-onset cohort (Table S2), and the risk of surgery was not increased in this cohort. With respect to IBD phenotype at diagnosis, the risk of treatment with immunomodulators or biologics and the risk of undergoing surgery were significantly increased in patients with stricturing and fistulising CD in comparison with patients with inflammatory behaviour.

In UC patients, the likelihood of being treated with immunomodulators or biologics was significantly higher in the childhood-onset cohort (Table S2), while the risk of undergoing surgery during follow-up was not increased in these patients.

3.5 | Outcomes based on age at diagnosis

A subanalysis was carried out categorising patients into three groups, based on the age at IBD onset. Patients diagnosed during childhood (≤16 years at diagnosis) were compared both with young adults (17-60 years at diagnosis) and elderly adults (>60 years at diagnosis). The likelihood of being treated with immunomodulators and biologics was higher in childhood-onset IBD than in both young and elderly adult-onset IBD (Table S4). The risk of surgery during follow-up was similar in all 3 groups.

3.6 | Sensitivity analysis

The estimation of the effect of being diagnosed during childhood on the risk of being treated with immunomodulators, biologics and surgery was confirmed in the propensity score matching analysis estimated with the following variables: sex, IBD type, extraintestinal manifestations, family history and smoking habit. In the matching cohort, all standardised differences were below 10%. The hazard ratio (HR) was 1.5, 95% CI = 1.3-1.8 for immunomodulators; HR = 1.7, 95% CI = 1.4-2.1 for biologics; and HR = 0.8, 95% CI = 0.6-1.1 for surgery.

4 | DISCUSSION

Currently, this is, to our knowledge, the largest study comparing IBD diagnosed in childhood and adulthood. In addition, all data were collected in a prospective manner after 2006, in the biologics era. Therefore, this large cohort allowed us to obtain key updated knowledge about the differences between paediatric and adult-onset IBD with respect to the severity at diagnosis, the use of immunomodulators and biologics and the need for surgery. First, the proportion of patients with CD was higher in children, and they had more extensive disease at diagnosis, with higher prevalence of inflammatory behaviour and higher prevalence of perianal disease. Furthermore, patients from the childhood-onset cohort—both UC and CD—had more extensive involvement. In this respect, our results are in agreement with other studies that have demonstrated that the presenting phenotype of childhood-onset IBD is characterised by extensive anatomic involvement, in comparison with adulthood-onset IBD.[24] In addition, in agreement with a recent study published by Shah et al, the proportion of male sex was higher in the childhood-onset cohort.[25] Second, family history of IBD was more frequent in childhood-onset IBD, suggesting a higher genetic load in this group of patients. Third, the use of immunomodulators and biologic agents—after adjusting by relevant variables such as the type of IBD, sex, tobacco use or family history of IBD—was higher among childhood-onset IBD patients. Finally, despite having higher prevalence of CD and more extensive involvement, childhood-onset IBD patients had a similar risk of undergoing surgery than adults.

Several studies have demonstrated that both biologics and immunomodulators are able to change the natural history of IBD, reducing the rate of surgery.[26–29] However, in our study, the exposure to immunomodulators and biologics was higher in childhood-onset IBD, whereas the risk of surgery was similar in both cohorts. In the multivariate analysis, treatment with immunomodulators, unlike treatment with biologics, was associated with lower risk of undergoing surgery. The role of immunomodulators and biologics decreasing the risk of surgery could not be demonstrated in the present study.

The higher use of immunomodulators and biologic agents in childhood-onset IBD might be due to a more aggressive disease in

comparison with adulthood-onset patients. Nevertheless, the evaluation of these results as surrogate markers for severity might be confounded by various factors, particularly the variability in the use of these agents by individual physicians. In this respect, initial management of IBD may differ between children and adults. For instance, enteral nutrition is the first-line therapy in the majority of children with CD in order to avoid steroids, while surgery is postponed whenever possible. The use of immunomodulators in adults increased during the 1990s, whereas paediatricians tended to be more reluctant to prescribe them because of safety issues.

However, current recommendations for the use of immunomodulators and biologics in paediatric and adult patients are quite similar.[20–22,30] In this respect, the most convincing data to support a benefit from early use of immunomodulators comes from the paediatric literature,[31] where, in a randomised controlled trial in 55 children, early use of mercaptopurine was associated with lower relapse rate and decreased rates of hospitalisation and surgery. However, the ~90% remission rate through 18 months observed in this study has not been replicated in either retrospective paediatric studies (which reported ~60% remission rates[32–34]) or randomised controlled trials in adults.[35,36] In consequence, both adult and paediatric guidelines recommend starting immunomodulators early after the induction of remission only in patients with predictive factors of bad outcomes; while in absence of negative prognostic factors, patients could be maintained with 5-aminosalicylates or without any treatment.[20–22]

Only a few studies have directly compared paediatric and adult IBD in population-based cohorts. Data from the French cohort (EPIMAD cohort)[12,13]which included patients from 1988 to 2006—and the Hungarian cohort (Veszprem cohort)[5,14] including patients from 1977 to 2008—found that the proportion of patients receiving both immunosuppressive and biologic treatment was significantly higher in patients diagnosed with IBD in childhood than in those diagnosed in adult age, in agreement with our findings. On the contrary, in the Swiss cohort,[16] younger age at diagnosis was associated with higher use of biologics in UC but no difference was found in the use of biologics in CD patients.

Authors from the Hungarian cohort found that the long-term evolution of IBD was not different in paediatric and adult-onset CD. However, the registry included incident cases from 1977. Thus, their results might not be applicable nowadays. Authors could also compare the rate of surgery between different decades. They observed a reduction in surgical rates in the last period that was independently associated with the earlier use of thiopurines.[28]

Finally, van Limberger et al compared two cohort of patients (416 childhood-onset and 1297 adulthood-onset patients) coming from two different studies and observed that, as in our population.

In this respect, the results regarding the dependence of the need for surgery on the age at diagnosis are controversial: some studies suggest that there is a greater need for surgery in adulthood-onset IBD (due to a higher prevalence of stenotic phenotypes). For example, a recently published population-based study from Sweden found an increased absolute risk of surgery in the elderly onset population, together with lower proportion of patients treated with immunomodulators and biologics, in comparison with younger patients.[37] On the contrary, other studies found no differences based on the age at diagnosis.[5,12,13,17–19] In the present study, we found that the risk of surgery was not different between patients diagnosed in childhood and those diagnosed in adulthood. In the multivariate analysis, treatment with immunomodulators, unlike treatment with biologics, was associated with lower risk of undergoing surgery. However, we could demonstrate an association of immunomodulators or biologics with the risk of surgery but not a preventive effect.

Our study has some limitations. First of all, although the ENEIDA registry included a high number of variables, some data are not frequently registered, such as steroid use, enteral nutrition, number of disease flare-ups, hospitalisations and date of phenotype changes; therefore, we could not analyse this information in our study. Second, the number of patients diagnosed before the age of six was very low; in consequence, comparisons between this group and the group of older children could not be made. Third, as there are many centres participating in the ENEIDA registry, some heterogeneity in the management of IBD patients could be present; however, these differences would have affected patients from both the paediatric and adult cohorts within the centres. To overcome heterogeneity in the management of IBD patients, GETECCU has been exerting an enormous educational effort for decades. In this respect, GETECCU is pioneer in educational courses for young gastroenterologists, given in most of the cases by participants in the ENEIDA registry. In addition, GETECCU has published several consensus documents on different topics, such as the use of thiopurines or biologics, based on international guidelines but also taking into consideration the characteristics of the Spanish health system. Most of the participating centres have former transition care programs, which allows sharing decision-making between paediatricians and gastroenterologist in the management of IBD patients. However, the fact that patients were cared by different physicians might have an impact on the results. Finally, GETECCU has developed a program to assess the quality of IBD units. All these initiatives aim to make the treatment of IBD patients as homogeneous as possible within the country.

Our study has also several strengths. First, to our knowledge, up to now, this is the largest study on the comparison of childhood- and adulthood-onset IBD. Second, all data were obtained from 2007, when biologic agents were available for both paediatric and adult IBD patients, which provides the opportunity of having updated information about the use of these agents and the need for surgery in the biologics era setting. In addition, 80 centres are participating in the ENEIDA registry, some of them are referral hospitals, but there are also regional hospitals (secondary hospitals) reflecting what happens in real practice.

In conclusion, the largest study cohort comparing childhood- and adulthood-onset IBD shows that patients diagnosed during childhood have differential characteristics (higher prevalence of CD, more extensive disease and more frequent family history). In addition, the use of immunomodulators and biologic agents is higher in childhood-onset patients, suggesting a more aggressive course of the disease. Despite the higher burden of the disease in children, the rate of surgery is similar in this population in comparison with adulthood-onset IBD.

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AUTHORSHIP

Guarantors of the article: María Chaparro and Javier P. Gisbert.

Author contributions: María Chaparro and Javier P. Gisbert designed the study; collected, analysed and interpreted the data; and wrote the manuscript. Alfonso Muriel analysed the data. Ana Garre involved in database monitoring. Rest of authors designed the study, involved in patient inclusion and collected the data.

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SUPPORTING INFORMATION

Additional supporting information will be found online in the Supporting Information section at the end of the article.

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APPENDIX

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