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Long-term prognosis of patients with paediatric-onset inflammatory bowel disease after transfer to adult care – a retrospective observational study

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Aim: The aim of this study was to evaluate and report long-term prognosis of inflammatory bowel disease (IBD) in patients transferred to adult care.

Methods: We reviewed medical records of all patients treated in our tertiary medical centre and then on adult care for a minimum of 5 years (median 12.4 years).

Results: During the study period, 52 IBD patients were treated in our centre and 27 patients/families were available for interview (13 of them women; median age 29 years; 20 with Crohn's disease and 7 with ulcerative colitis (UC)). Twenty-three (85%) patients were transferred to adult care, whereas 4 (15%, 3 with UC) patients never consulted an adult gastroenterologist. Nineteen (70%) patients experienced a relapse, 2 (7.4%) died, and 9 (33%) received biological therapy in adult care. Of the surviving patients, 8 (32%) underwent surgery in adult age.

Conclusion: This study confirmed that, in the absence of organized transition to adult care, a number of patients would never transfer on their own, causing discontinuity of care.

Key words: inflammatory bowel disease; long-term prognosis; transfer of care; transition

INTRODUCTION

In 25%-30% of all patients, inflammatory bowel disease (IBD) (Crohn's disease (CD), ulcerative colitis (UC), and IBD-unclassified (IBD-U)) is diagnosed during childhood or adolescence (1). Compared to adult-onset disease, the phenotype of paediatric-onset IBD significantly differs and is marked by increased severity, more extensive distribution, further worsening within the first two years of the diagnosis, and higher need for surgical treatment (2, 3). Therefore, it is reasonable to expect the long-term outcome to differ as well, but relevant data are limited and controversial (4-6).

This survey aimed to provide data on long-term outcomes (relapse rate, mortality rate, and therapy escalation) in paediatric-onset IBD patients, reported at least five years after they had been transferred from our tertiary paediatric medical centre to adult care, as well as to assess their transfer experience.

METHODS

Study design. This was a retrospective, single-centre, observational study with survey analysis. Clinical data on all patients diagnosed with IBD in our tertiary medical centre from 1993 to 2003 were analysed retrospectively, provided there was a follow-up of at least five years after their transfer to adult care. Patients were transferred at the age of

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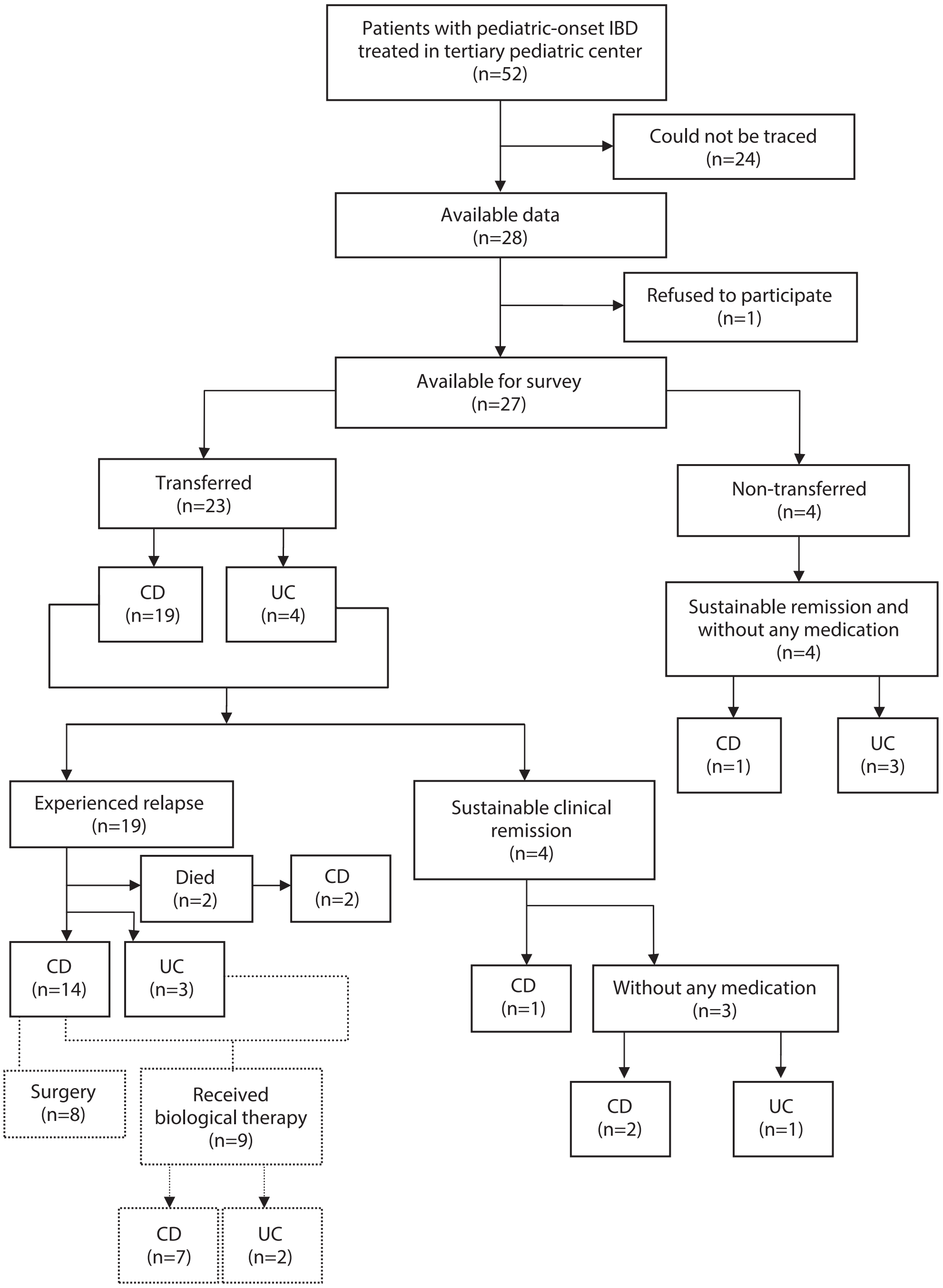

IBD = inflammatory bowel, CD = Crohn's disease, UC = ulcerative colitis

FIGURE 1. **Study flowchart.**

18 years or after graduating from high school. Data were obtained from hospital charts and electronic medical record system.

Patients were contacted and interviewed by phone in respect to the following data: current primary care practitioner, responsible adult gastroenterologist (GI), therapeutic interventions (surgery, current and previous therapy) received, number of relapses in adult care, and adherence to medication. The phone interview also included a short survey about the patient's satisfaction with the care provided in the paediatric and adult settings.

The study was conducted in accordance with ethical standards set by the institutional Ethics Committee regarding human experimentation and approved by the Ethics Committee of the Zagreb Children's Hospital (doc. no. 01082015), as well as in compliance with the Helsinki Declaration.

Objectives. The primary objective was to determine long-term prognosis (self-reported relapse rate, mortality rate, and therapy escalation) of patients with paediatric-onset IBD after transfer from the paediatric setting. Relapse was defined as the need of induction therapy (corticosteroids) or escalation of the maintenance treatment. The secondary objective was to assess transfer experience through a short survey.

Data analysis and statistics. Results are presented as numbers and percentages for categorical variables and as median and range for continuous variables due to their non-normal distribution. Univariate regression was used to evaluate the association between age at diagnosis, disease distribution at diagnosis, and outcomes (need for escalation of therapy and need for surgery). Statistical analyses were performed using SPSS 21.0 (Chicago, IL). The level of statistical significance was set at $p<0.05$.

RESULTS

Patients. A total of 52 patients were eligible for inclusion in the study (Figure 1), out of whom 28 (54%) patients or their families could be reached. One patient refused to participate. Thus 27 patients were available for the study, 20 (74%) with CD and seven (26%) with UC. Thirteen (48%) of them were females, median age 29 (range 24-40) years at the time of the interview, whereas the median age at diagnosis was 12.5 (range 4.5-18) years. One-third of the patients (8 of 27) were diagnosed with IBD before the age of ten years. Patients had been treated in the paediatric facility for a median of 3.9 (1-14.6) years and in an adult setting for a median of 12.4 (range 5.8-23.0) years at the time of the interview. The median disease duration was 17.2 (12.9-24.8) years.

Primary outcomes. Four (15%) patients, one with CD and three with UC, never consulted a GI specialist. Of the non-transferred patients, the one with CD was followed up by a general practitioner, whereas three patients with UC were not followed-up at all and received no therapy.

Of the patients who did undergo further GI follow-up (n=23), 19 (83%) had at least one relapse after transfer to adult care, and four (17.3%) were in sustainable clinical remission with a median follow-up of 12.4 years.

Of the patients with disease relapse (n=19, 70%), 16 had more than two relapses resulting in a treatment step-up. Biological therapy was introduced in nine (33%) patients. Two (7.4%) patients died, both followed up by a GI specialist. The disease distribution is illustrated in Figure 1.

Of the surviving patients (n=25), eight (32%) underwent surgery in adult age (all CD patients); six patients had already undergone surgery in paediatric age.

Nine (33%) patients (five with CD and four with UC) discontinued their therapy on their own, which resulted in severe relapses in four patients (two with UC and CD each) and required escalation of therapy.

At the time of the survey, 7/27 (26%) patients (four with UC and three with CD) were in remission and without any medication. Of these patients, four (three with UC and one with CD) had stopped using their medication on their own and were not followed up by a GI (median time of self-reported remission was 12.4 years); of the other three transferred patients, one CD patient had stopped using his medication on his own and two patients (one with UC and CD each) were advised so by their gastroenterologist because of stable remission.

Univariate regression yielded no significant association of age at diagnosis and disease distribution at diagnosis with the outcomes (need for escalation of therapy and need for surgery).

Secondary outcome – transfer experience. Of the transferred and interviewed patients (n=21), 13 (62%) described leaving the paediatric care as stressful, and 16 (76%) preferred the paediatric setting for the following reasons: diagnostic procedures and doctor's appointments were offered at much shorter intervals (n=7), doctor-patient communication (n=3), as well as the general environment (n=3) were better in the paediatric facility, and no death of another patient was witnessed, which was the case in adult facilities (n=3). Only one patient preferred the adult setting because of direct patient-doctor communication without parents' interference.

DISCUSSION

This study assessed long-term outcomes in paediatric-onset IBD patients with long-term follow-up (median 12.4 years). The transfers were performed without a special (organized) transition process. Most of our patients (23/27; 85%) continued receiving regular care in the adult setting, which is in concordance with the results of other studies (7, 8). Furthermore, our study showed that seven (26%) patients were in long-term medication-free remission.

Our study confirmed a high relapse rate (70%) and disease complications in the transferred patients. Furthermore, one-third of the patients (all with CD) underwent surgery; however, the majority of them had their first surgery in paediatric age. This is in line with previous publications reporting a cumulative risk of resection of 26% during a median follow-up of 9.1 years in paediatric-onset CD (5). The actuarial risk of having an extensive intestinal resection at the age of 30 years was estimated to be approximately 50% (9). The cumulative risk of exacerbation and step-up to biological therapy during follow-up (follow-up of 9.1 years) in the patients with paediatric-onset CD was 66% and 54%, respectively, whereas in the patients with paediatric-onset UC (follow-up of 8.5 years) it was 84% and 34%, respectively (5). The risk was somewhat lower in our patients (33%). However, our study included both CD and UC patients.

None of our study patients developed cancer, and two patients with CD died due to disease complications. Both were under adult GI care at that time. In one case, the cause of death was fulminant sepsis at the age of 31 years, and in the other, at age 29, liver transplant failure complicated with sepsis in a CD patient with Budd-Chiari syndrome.

Complicated behaviour at diagnosis of CD predicted worse long-term outcomes and was associated with an increased risk of surgery, but not with the risk of flare or step-up to biological therapy. In patients with UC, severe disease at diagnosis, but not disease extent, was associated with the risk of colectomy, flare, and biological therapy (5). Our study found that neither the disease extent in CD or UC nor the age at diagnosis was associated with a higher number of relapses or an increased risk of surgery.

We also found that nine (33%) patients ceased therapy on their own after leaving the paediatric care, four of which experienced severe relapses. This percentage is higher compared to the results of *Sewitch et al*., who report discontinuing medication in 19% of IBD patients (10). However, our study involved a much longer follow-up time, which could partially explain this difference.

Switching from the paediatric to the adult healthcare system is both emotionally stressful and challenging for patients, their families, and physicians (11). This was also confirmed by our results, as 62% of our patients described the experience of the transfer as stressful. Moreover, 76% of them preferred the paediatric care setting for the reasons reported above, such as a friendlier and more patient-oriented environment and less time spent waiting for diagnostic and therapeutic consultations (7, 11). Significant limitations of the immediate transfer (11) and the need for smooth transition from paediatric to adult care resulted in the organization of transition clinics worldwide where organized transition (transitional care) is provided by paediatricians and internal medicine specialists for a defined period of time (12-14). Unfortunately, our patient cohort did not experience a smooth transition process, and it would be of interest to investigate whether our patients would have had better outcomes if they had been transferred through transition clinics.

There were significant limitations to our study; the number of recruited patients was small, a considerable number of them could not be reached, and all patients had received paediatric care in the same centre. Furthermore, the study was retrospective and therefore prone to recall bias. However, as the follow-up was exceptionally extended, we believe that this survey contributes to better understanding the long-term outcomes in patients with paediatric-onset IBD.

This study confirmed that in the absence of organized transition to adult care, a number of patients would never transfer on their own, thus causing discontinuity of care and receiving no cancer surveillance.

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Autori su popunili *the Unified Competing Interest form na www.icmje.org/coi_disclosure.pdf (dostupno na zahtjev)* obrazac i izjavljuju: nemaju potporu niti jedne organizacije za objavljeni rad; nemaju financijsku potporu niti jedne organizacije koja bi mogla imati interes za objavu ovog rada u posljednje 3 godine; nemaju drugih veza ili aktivnosti koje bi mogle utjecati na objavljeni rad./*All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.*

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SAŽETAK

Dugoročna prognoza u oboljelih od kroničnih upalnih bolesti crijeva dijagnosticiranih u dječjoj dobi nakon prelaska u zdravstvenu skrb odraslih – retrospektivna opservacijska studija

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Cilj: Cilj je ove studije procijeniti i izvijestiti o dugoročnoj prognozi u bolesnika s kroničnim upalnim bolestima crijeva (IBD), koji su nastavili liječenje u zdravstvenoj skrbi odraslih.
Metode: Pregledali smo bolesničku medicinsku dokumenaciju svih bolesnika koji su liječeni u tercijarnom pedijatrijskom medicinskom centru i koji su barem pet godina nastavili liječenje u adultnoj skrbi (medijan 12,4 godina).
Rezultati: U razdoblju od 1993.-2003. u našem je centru liječeno 52-je bolesnika s IBD-om te su oni ili njihove obitelji bili dostupni za razgovor (13 žena, medijan dobi 29 godina; 20-ero oboljelih od Crohnove bolesti, sedmero od ulceroznog kolitisa (UC)). Ukupno je 23-je (85%) bolesnika nastavilo liječenje u internističkoj skrbi, dok njih četvero (15%) nikad nije bilo ni na jednom pregledu internista gastroenterologa (troje bolesnika oboljelo od UC). Ukupno je 19-ero (70%) bolesnika imalo relaps tijekom praćenja, dvoje (7,4%) bolesnika je umrlo, devetero (33%) je primilo biološku terapiju. Trećina bolesnika je kirurški liječena u odrasloj dobi.
Zaključak: Ova studija potvrđuje važnost organizirane tranzicije iz pedijatrijske skrbi u zdravstvenu skrb odraslih.

Ključne riječi: kronične upalne bolesti crijeva, dugoročna prognoza, prijelaz skrbi, transfer, tranzicija