Digestive and Liver Disease 51 (2019) 524–528

Contents lists available at ScienceDirect

Digestive and Liver Disease

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

Alimentary Tract

# Successful outcome of the transitional process of inflammatory bowel disease from pediatric to adult age: A five years experience

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ARTICLE INFO

*Article history:*
Received 3 September 2018
Accepted 27 November 2018
Available online 10 December 2018

*Keywords:*
Transition of care
Adolescent
Crohn's disease
Ulcerative colitis

ABSTRACT

*Introduction and aim:* The transitional process of young patients affected by inflammatory bowel disease from pediatric to adult care is a crucial step. Our study aimed to investigate the 1-year success outcome of this transitional process.
*Methods:* From 2013 to 2018, we evaluated the transitional process of patients with Crohn's disease or ulcerative colitis. For each patient, the following parameters 12 months before and 12 months after the transition were evaluated: Body Mass Index, disease activity and smoker status, number of outpatient visits and the pharmacological therapy, the number of disease exacerbations, hospitalizations and surgical interventions.
*Results:* We enrolled 106 patients with IBD. No statistically significant difference was found between patients' Body Mass Index before and after transition. There was a significant reduction in the number of exacerbations and hospitalizations in the 12 months post-transition (pre-transition exacerbations: $0.74 \pm 0.79$, post-transition exacerbations: $0.35 \pm 0.57$, $p < 0.001$; pre-transition hospitalizations: $0.28 \pm 0.44$, post-transition hospitalizations: $0.1 \pm 0.3$, $p < 0.001$). In contrast, there was no significant difference in the number of outpatient visits ($3.40 \pm 1.4$ vs $3.25 \pm 1.2$; p = ns) and of patients undergoing surgery (0.9% vs 1.8%, p = ns).
*Conclusion:* The parameters used as success indicators of the transition program confirm the achievement of continuity of care from Pediatrics to adult Gastroenterology, in a critical phase of the natural history of IBD patients.


## 1. Introduction

"Transition" is the process that involves the movement of adolescents and young adults with chronic diseases with childhood onset from a pediatric center to one for adult care. It does not exclusively consist in the simple "transfer" of the patient from one structure to another one: it is a dynamic, planned and complex process that requires the collaboration of a multidisciplinary team to ensure continuity, coordination and attention, not only towards clinical needs but also towards the psychosocial, educational and occupational requirements of the adolescent [1,2].

The transition process represents an important phase of growth and maturation for the young patient, who is provided with all the tools and information necessary to be able to manage his pathology more autonomously and responsibly and therefore to face the transfer with serenity and awareness [3].

Some studies demonstrate that patients with chronic diseases who take part in a transitional program show greater compliance and fewer adverse events following the transfer to the adult center compared to patients who have not taken part in such a program [4–6]. In literature the evidence in this setting in subjects with inflammatory bowel disease (IBD) has been growing in the last ten years and, even if this is now a widely discussed topic, there is no uniform model to date. Therefore the European Crohn's and Colitis Organization (ECCO) recently published a consensus-based framework for IBD transitional care that should guide clinical practice [7]. An ideal transition model should gradually provide for a joint activity of all the figures involved (the adolescent patient,

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https://doi.org/10.1016/j.dld.2018.11.034
1590-8658/

**Table 1**
Baseline features of patients.

| | CD | UC |
|---|---|---|
| Number | 43 | 63 |
| Appendicectomy | 3/43 | 3/63 |
| Familiarity for IBD | 9/43 | 27/63 |
| Years of disease duration (range) | 5.88 ± 2.97 | 8.22 ± 4.19 |
| Location L1–L2–L3–L4 | 10–9–23–1 | – |
| Behavior B1–B2–B3 | 29–12–2 | – |
| Perianal disease (yes/not) | 3/43 | – |
| Extension (E1, E2, E3) | | 12/10/41 |
| Extraintestinal manifestations (yes/not) | 3/43 | 8/63 |

**Table 2**
Clinical data of IBD population (106 patients) 12 months before and after transition.

| | Pre-transition | Post-transition | p Value |
|---|---|---|---|
| Weight | 64.38 ± 11.05 | 64.15 ± 9.62 | ns |
| BMI | 22.8 ± 3.43 | 22.7 ± 2.84 | ns |
| Smoker status (%) | 14 (13) | 12 (11) | ns |
| N. outpatients visits | 3 ± 1.2 | 3 ± 1.4 | ns |
| N. exacerbations | 0.74 ± 0.79 | 0.35 ± 0.57 | <0.001 |
| N. hospitalization | 0.28 ± 0.44 | 0.1 ± 0.3 | 0.001 |
| N. surgery interventions (%) | 2 (2%) | 1 (1) | ns |

**Table 3**
Clinical data of CD patients (43) 12 months before and after transition.

| | Pre-transition | Post-transition | p Value |
|---|---|---|---|
| Weight | 66.7 ± 11.48 | 66.2 ± 9.52 | ns |
| BMI | 23.17 ± 3.41 | 22.93 ± 2.62 | ns |
| Smoker status (%) | 6 (14) | 5(12) | ns |
| N. outpatients visits | 3.74 ± 1.0 | 3.77 ± 1.49 | ns |
| N. exacerbations | 0.67 ± 0.7 | 0.35 ± 0.5 | <0.01 |
| N. hospitalizations | 0.35 ± 0.48 | 0.16 ± 0.37 | 0.04 |
| N. surgery interventions (%) | 2 (5) | 1 (2) | 0.06 |

**Table 4**
Clinical data of UC patients (63) 12 months before and after transition.

| | Pre-transition | Post-transition | p Value |
|---|---|---|---|
| Weight | 62.74 ± 10.52 | 62.76 ± 9.51 | ns |
| BMI | 22.59 ± 3.46 | 22.56 ± 2.99 | ns |
| Smoker status (%) | 8 (13) | 7 (11) | ns |
| N. outpatients visits | 2.9 ± 1.18 | 3.1 ± 1.29 | ns |
| N. exacerbations | 0.78 ± 0.85 | 0.35 ± 0.6 | <0.01 |
| N. hospitalization | 0.24 ± 0.42 | 0.06 ± 0.24 | <0.01 |
| N. surgery interventions (%) | 0 | 0 | ns |

the parents, the family pediatrician, the general practitioner, the pediatric gastroenterologist and the adult gastroenterologist) [2]. In choosing the most appropriate moment, the pediatrician must take into account a series of factors: patient's physical and psychological maturity, treatment compliance, degree of autonomy in the management of the disease and the assessment of the disease's activity; the ideal transition, in fact, should be performed during remission.

The recommended duration for a correct transitional process varies from 6 to 12 months. During this period the young patient should attend 1–2 combined visits, jointly performed by the two specialists (pediatrician and adult gastroenterologist), in the presence of parents and in a comfortable environment, in which adolescents can easily ask questions and explain their difficulties (Table 5). Another important aim of these meetings is the complete and correct transmission of medical information, preferably by written documentation [7,8]. If the transition is not correctly planned or carried out, the risk of negative outcomes (significant number of patients lost during the follow-up, high rates of non-adherence to medical treatment, worsening of disease activity, high rate of hospitalization and need for surgery) increases significantly [9–12].

**Table 5**
Proposed steps of a correct transition.

| Who needs transition? | IBD patients aged 16–18 years |
|---|---|
| When to start? | The process should start during a phase of disease remission |
| What to consider? | The transition should consider child's physical and emotional maturity, autonomy and adherence to therapy |
| How? | The transition program should consist of 1–2 scheduled combined visits (paediatric and adult Gastroenterologist) |
| How long? | The duration of transition process should be of 6–12 months |

Based on these considerations, we organized and implemented at our Center a transition program in the last five years to facilitate the continuity of care for all IBD-affected adolescents, from child-centered to adult-oriented care.

Our study aimed to investigate the 1-year success outcome of the transitional process of IBD patients in terms of maintenance of the nutritional status, patients' compliance to the care in the adult setting and disease activity control, after the transition program.

## 2. Materials and methods

We performed an observational retrospective study evaluating the transitional process of patients with childhood onset of Crohn's disease (CD) or ulcerative colitis (UC), from the Pediatric to the Adult IBD center, at the School of Medicine "Federico II" of Naples, Italy.

Since 2012, in collaboration with our Pediatric center, a transitional program has been carried out in our clinical practice to facilitate the passage of patients aged 18 years and affected by IBD with pediatric onset to the adult clinic. This process consists of 1–2 outpatient visits in which the patient, the family members, the pediatric and the adult gastroenterologist all take part in order to present the young patient to the new doctor in a friendly and formative way.

These meetings aim to make patients' readiness for transfer easy by improving their IBD knowledge and their self-efficacy skills. In addition, patients' medical history, past and current therapy, as well as previous laboratory and endoscopic examinations, are jointly discussed.

From January 2013 to January 2018, we enrolled in our study all consecutive patients undergoing transition from Pediatric Clinic. Patient's data have been collected, including disease characteristics according to the Montreal classification [13], duration of disease, familiarity for IBD, smoker status, previous appendectomy and presence of extra-intestinal manifestations.

For each patient a clinical evaluation was performed, comparing the following parameters 12 months before and 12 months after the transition from pediatric to adult care of the disease: Body Mass Index (BMI), disease activity and smoker status.

We also compared pharmacological therapy in the 12 months before the transition with the one in course one year after the transfer to the adult center, as well as the number of outpatient visits, the number of disease exacerbations, the number of hospitalizations and the number of surgical interventions.

For each patient we also calculated the clinical activity of the disease, using pediatric Crohn's Disease Activity Index (pCDAI) and pediatric Ulcerative Colitis Activity Index (pUCAI) for children [14,15] as well as CDAI and partial MAYO score (pMAYO) for transited patients [16,17].

All subjects gave their written consent to participate in the study, which was approved by the local Ethical Committee.

### 2.1. Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS software v.15.0, Chicago IL, United States) for Windows. The descriptive statistics included the determining of mean values and standard deviation (SD) of the continuous variables, as well as percentages and proportions of the categorical variables. Statistical analysis was performed using the two-sample Student's t-test and ANOVA to evaluate the differences between means, while chi-square was used to evaluate the differences between percentages or proportions. Furthermore, the nonparametric McNemar and Wilcoxon tests were used to evaluate the differences for dichotomous (i.e. smoking status, type of treatment) and continuous (i.e. weight, BMI, number of outpatient visits, number of exacerbations, hospitalizations and surgeries) variables before and after the transition, respectively.

Finally, we performed sub-analyses in CD and UC patients by using the same statistical tests.

All the differences were considered significant when $p < 0.05$.

## 3. Results

We enrolled a total of 106 patients with IBD (43 with CD and 63 with UC). As regards CD location, 23% showed ileal disease (L1), 21% had isolated colonic CD (L2), while 53% had ileocolonic disease (L3); 3% of the patients showed an upper CD location (L4). Moreover, 67% of the patients presented a non-complicated behavior (B1); 28% had at least one stricture (B2) while the remaining 5% showed penetrating CD (B3). Perianal CD was observed in 7% of subjects. With regard to UC extension, 11% of patients had proctitis (E1), 9% had left colitis (E2) and 65% showed pancolitis (E3). The main baseline features of the study population are listed in Table 1.

### 3.1. Comparison of clinical data collected 12 months before and 12 months after the transition

From the analysis of the data, we did not find a statistically significant difference between the patients' BMI before and after the transition (mean pre-transition BMI: $22.8 \pm 3.43$, mean post-transition BMI: 22, $7 \pm 2.84$, $p = 0.25$). In assessing the smoking habits, there was a slight difference before and after the transition, with a lower percentage of smokers seen in the post-transition (11% vs. 13.2%; p = ns). Furthermore, there was a statistically significant reduction in the number of exacerbations and hospitalizations in the 12 months following the transition (pre-transition exacerbations: $0.74 \pm 0.79$, post-transition exacerbations: $0.35 \pm 0.57$, $p < 0.001$; pre-transition hospitalizations: $0.28 \pm 0.44$, post-transition hospitalizations: $0.1 \pm 0.3$, $p < 0.001$). In contrast, there was no statistically significant difference in the number of outpatient visits ($3.40 \pm 1.4$ vs. $3.25 \pm 1.2$; p = ns) and the percentage of patients undergoing surgery (0.9% vs. 1.8%, p = ns).

All these results were summarized in Table 2.

Moreover, we separately evaluated patients with CD and with UC and we showed that:

- In patients with CD (Table 3) there was no statistically significant difference between the period before and after the transition in most of the clinical outcomes considered (mean post-transition BMI: $22.93 \pm 2.62$ vs. mean pre-transition BMI: $23.17 \pm 3.41$, p = ns; mean post-transition number of outpatient visits: $3.77 \pm 1.49$ vs. mean pre-transition number of outpatient visits: $3.74 \pm 1.0$, p = ns; percentage of patients undergoing surgery after transition of 2% vs. 5% of the pre-transition phase, p = ns). In the 12 months before the transition, pCDAI was $120 \pm 31.2$, while at transition CDAI was $111.3 \pm 30.9$. Moreover, a statistically significant difference was observed in the average number of hospitalizations, which is less than 12 months after the transition ($0.16 \pm 0.37$ in the post vs. $0.35 \pm 0.48$ in the pre-transition; = 0.04) and in the mean post and pre-transition number of exacerbations ($0.35 \pm 0.5$ vs. $0.67 \pm 0.7$ $p < 0.01$).
- In patients with UC (Table 4), as we observed for the CD group, in pre- and post-transition there were no statistically significant differences in BMI ($22.59 \pm 3.46$ vs. $22.56 \pm 2$, 99, p = ns), in the average number of outpatient visits ($2.9 \pm 1.18$ vs. $3.1 \pm 1.29$; p = ns) and in the percentage of patients that required surgery (no patient was operated both in the year before and after the transition). Moreover, even for patients with UC, there was a statistically significant difference in the average number of hospitalizations ($0.24 \pm 0.429$ pre vs. $0.06 \pm 0.246$ post-transition, $p < 0.01$) and in the number of exacerbations ($0.78 \pm 0.85$ vs. $0.35 \pm 0.6$, $p < 0.01$). In the 12 months before the transition, pUCAI was$22.76 \pm 11.36$, while at transition pMAYO was $2.21 \pm 1.01$.

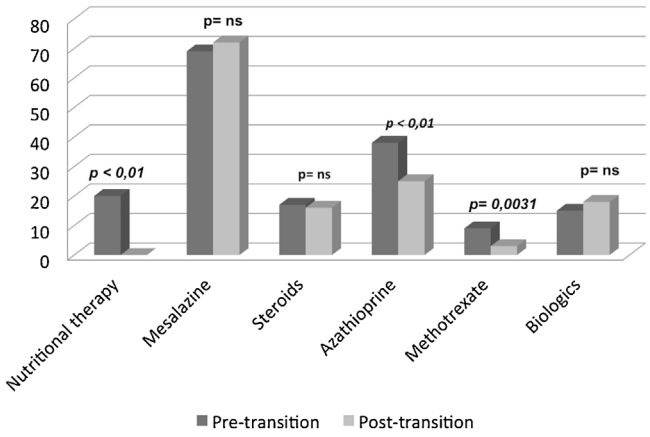


**Fig. 1.** Therapy 12 months before and after transition in patients with IBD.

### 3.2. Comparison of therapy 12 months before and 12 months after the transition

Our study showed a significant difference ($p < 0.01$) in the use of nutritional therapy between the pre-transition phase (18.8%) and the post-transition phase (no patient).

On the contrary, there was no statistically significant difference in the use of mesalazine (67.9% vs. 65%, p = ns), steroids (16% vs. 15%, p = ns), and biologics (17% vs. 14%, p = ns) pre- and post-transition.

Instead, there was a statistically significant difference in the use of immunosuppressants and in particular of methotrexate, pre- and post-transition (9% vs. 2%, p = 0.03): this drug, in fact, was rarely used in adult IBD management. Even azathioprine was more frequently used in the year preceding the transition, compared to the following year (36% vs. 23%, $p < 0.01$).

All these results were summarized in Fig. 1. Data about the therapy of CD and UC subjects were also evaluated separately (Figs. 2 and 3).

## 4. Discussion

Transition of young patients with IBD to adult care is a challenge for adolescents, parents and physicians. In the last decade, interest in this setting has been increasing, especially if we consider that 25% of IBD patients receive the diagnosis before the age of 16 years [18].

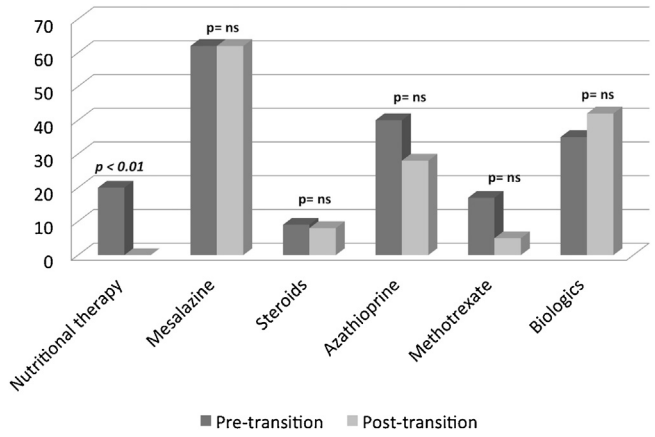


**Fig. 2.** Therapy 12 months before and after transition in patients with CD.

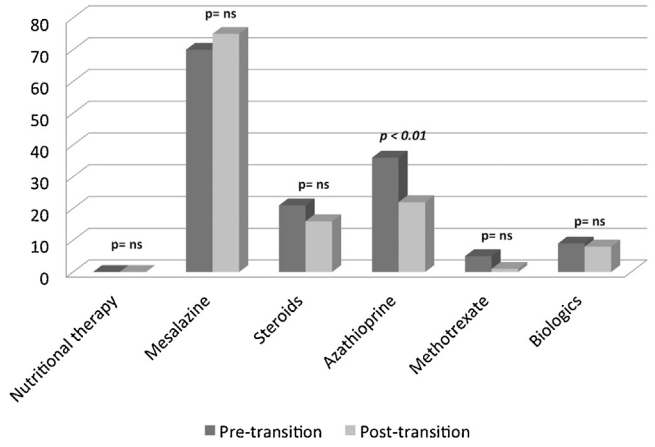


**Fig. 3.** Therapy 12 months before and after transition in patients with UC.

Transition is a complex process that could affect clinical, social and psychological aspects of the young patients' life [19]. For this reason, it is mandatory to guarantee the continuity and appropriateness of care assistance from a Pediatric center to an Adult one. Based on these considerations we organized this retrospective study, and we analyzed some clinical parameters as possible indicators of the success of the transitional process, evaluating them in the 12 months before and after the transfer to adult management. To date, in fact, there is no validated tool to define the effectiveness of the transition program in IBD: our work is the first Italian study that brings experience in this area, comparing outcome data with regard to transition, in a cohort of pediatric-onset IBD patients who have moved on to adult care. Regarding the clinical evaluation, comparing the data collected in the pre- and post-transition period, there was no significant difference in body weight and BMI for both patients with CD and UC. This is a relevant aspect if we consider that the maintenance of body weight and BMI indicate a state of well-being of the patient as well as of his correct height-weight growth, which represents one of the most important therapeutic objectives in the management of pediatric patients.

There was no significant difference in the number of outpatient visits performed in Pediatrics and in the first year of transition to adult Gastroenterology for patients with CD or those with UC: we can therefore deduce how the objectives of achieving continuity of care and reducing the number of patients lost to follow-up can be considered obtained. In fact, in our Department, in the 12 months following the transition, we tend to guarantee a greater frequency of outpatient visits compared to the basic management of the adult patient to improve the compliance of the young patient. Then, we gradually offer the assistance scheme followed in adult Gastroenterology, with recourse to less frequent Day Hospital admissions and delayed visits (every 6 months) in cases of remission illness or in the absence of therapies requiring close monitoring.

Also with regard to the use of surgery, no significant difference was found between the previous phase and the one following the transition, as it was necessary only in a tiny number of cases, exclusively including patients with CD.

Favorable data emerged in the evaluation of the number of exacerbations in the 12 months following the transition, which is overall lower than in the previous phase both in patients with CD and in those affected by UC. This data is also particularly relevant since the transition from the Pediatric to the Adult center represents a critical phase in the clinical history of young patients, with an increased risk of exacerbations of the disease.

A similar discussion can be made regarding the evaluation of the disease activity measured with the pCDAI/CDAI score for CD and with the PUCAI/pMAYO score for UC. According to literature (2,12), both groups of patients were in a remission phase at the time of transition, with a maintenance of the activity score for patients with UC and with a further reduction of CDAI in CD subjects 12 months from the transition. These results strengthen the importance of the transition to the adult center during the phase of disease remission to avoid changes in therapeutic strategies already adopted.

The study also allowed us to discuss the different therapeutic strategies in Pediatrics and adult Gastroenterology. First of all, enteral nutritional therapy, which represents a first-line treatment in the management of pediatric CD exacerbations, has not been used in the adult center because adult compliance is very low. The other significant element in terms of therapy was recorded in the use of immunosuppressants in the post-transition phase. In fact, in adult Gastroenterology, in case of refractoriness/intolerance to azathioprine, it is generally chosen to suspend the drug by evaluating the subsequent introduction of biological therapy, while pediatrics replace it with methotrexate, a second-line immunosuppressive drug, much more rarely used in adulthood, where data in the literature concerning efficacy are relatively poor and less convincing [2,20–21]. Moreover, especially in UC, the percentage of subjects that used biologics was not high (9% in the pre-transition phase vs. 8% in the post-transition phase, p = ns), probably because the patients had a quiescent disease.

A further favorable data that emerged from the study and concerning both groups of patients consists in a reduction in the number of hospitalizations in the post-transition phase compared to the previous phase. This factor was an expression both of the course of the disease and of the lower use of hospitalization in the adult phase if the patient was not in a phase of moderate-to-severe activity.

Surely another interesting target could have been the assessment of patients' satisfaction and adherence to therapy after the transitional process. Because of the retrospective nature of our work, we have not evaluated this aspect, but we are about to start a prospective study where these elements are primary objectives.

In conclusion, our study presents the data of the first Italian experience of the transitional process from the pediatric age to adulthood on a high case series of over 100 patients with IBD, with a follow-up after the transition of at least 12 months. The parameters we used as success indicators of the transition program confirm the achievement of continuity of care from Pediatrics to adult Gastroenterology, in a generally critical phase of the natural history of IBD patients.

## Guarantor of article

Dr Anna Testa.

## Conflict of interest
None declared.

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