Journal of Crohn's and Colitis (2014) xx, xxx

Available online at www.sciencedirect.com

ScienceDirect

Risk of colectomy in patients with ulcerative colitis under thiopurine treatment☆,☆☆

Alex Cañas-Ventura[a,*], Lucia Márquez[a], Elena Ricart[b,c], Eugeni Domènech[c,d], Javier P. Gisbert[c,e], Valle García-Sanchez[f], Ignacio Marín-Jiménez[c,g], Francisco Rodriguez-Moranta[h], Fernando Gomollón[c,i], Xavier Calvet[c,j,k], Olga Merino[l], Esther Garcia-Planella[m], Narcis Vázquez-Romero[n], Maria Esteve[c,o], Marisa Iborra[c,p], Ana Gutiérrez[q], Maribel Vera[r], Montserrat Andreu[a] on behalf of Spanish GETECCU group (ENEIDA project)

[a] *Hospital del Mar, IMIM (Hospital del Mar Medical Research Institute), Department of Gastroenterology, Barcelona, Spain*
[b] *Hospital Clínic, Barcelona, Spain*
[c] *Centro de Investigación Biomédica en Red de enfermedades hepáticas y digestivas (CIBEREHD), Spain*
[d] *Hospital Universitari Germans Trias i Pujol, Badalona, Spain*
[e] *Hospital Universitario de La Princesa, Instituto de Investigación Sanitaria Princesa (IP), Madrid, Spain*
[f] *Digestive System Service, Hospital Universitario Reina Sofía, Instituto Maimónides de Investigación Biomédica de Córdoba (IMIBIC), Universidad de Córdoba, Córdoba, Spain*
[g] *Hospital General Universitario Gregorio Marañón, Madrid, Spain*
[h] *Hospital de Bellvitge, L'Hospitalet de Llobregat, Spain*
[i] *Hospital Clínico Universitario, Instituto de Investigación Sanitaria de Aragón, Zaragoza, Spain*
[j] *Servei de Malalties Digestives, Corporació Sanitària Universitaria Parc Taulí, Sabadell, Spain*
[k] *Departament de Medicina, Universitat Autònoma de Barcelona, Spain*
[l] *Hospital de Cruces, Barakaldo, Spain*
[m] *Hospital de la Santa Creu i Sant Pau, Barcelona, Spain*
[n] *Hospital General Universitario de Elche, Elche, Spain*
[o] *Hospital Universitari Mutua de Terrassa, Barcelona, Spain*
[p] *Hospital Universitario La Fe, Valencia, Spain*
[q] *Hospital General Universitari d'Alacant, Alicante, Spain*
[r] *Hospital Universitario Puerta de Hierro, Madrid, Spain*

☆ Financial support: Ferring laboratories have sponsored the ENEIDA registry, but they had no role in the study design, collection, analysis, and interpretation of the data or the writing of the report.
☆☆ Conference presentation: Part of the work was presented at ECCO Congress 2011 (Barcelona) and DDW 2012.
* Corresponding author at: Gastroenterology Department, Hospital del Mar, Passeig Maritim 25, 08003 Barcelona, Spain. Tel.: +34 93 248 33 04; fax: +34 93 248 33 76.
E-mail address: alexcanasventura@yahoo.es (A. Cañas-Ventura).

http://dx.doi.org/10.1016/j.crohns.2014.03.014

Please cite this article as: Cañas-Ventura A, et al, Risk of colectomy in patients with ulcerative colitis under thiopurine treatment, *J Crohns Colitis* (2014), http://dx.doi.org/10.1016/j.crohns.2014.03.014

Received 5 January 2014; received in revised form 10 March 2014; accepted 13 March 2014

KEYWORDS
Inflammatory bowel diseases;
Ulcerative colitis;
Thiopurines;
Colectomy

Abstract

Background and Aims: Little is known about the risk factors of colectomy in patients with ulcerative colitis (UC) under thiopurine treatment. The aim of the study was to determine the prevalence and the predictive risk factors of colectomy in an extensive cohort of patients with UC treated with thiopurines in Spain.
Methods: Among 5753 UC patients, we identified those diagnosed between 1980 and 2009 and treated with azathioprine or mercaptopurine (AZA/MP). We analyzed the age at diagnosis, familial history of IBD, extraintestinal manifestations (EIMs), disease extent, smoking status and treatment requirements (AZA/MP, cyclosporine (CsA) or anti-TNFα). Colectomies for dysplasia or cancer were excluded. Survival analysis and Cox proportional hazard regression were performed. Results were reported as hazard ratios (HR) with 95% CI.
Results: Among the 1334 cases included, 119 patients (8.9%) required colectomy after a median time of 26 months (IQR 12–42) after AZA/MP initiation. Independent predictors of colectomy were: Extensive UC (HR 1.7, 95% CI: 1.1–2.6), EIMs (HR 1.5, 95% CI: 1.0–2.4), need for antiTNFα (HR 2.3, 95% CI: 1.5–3.4) and need for CsA (HR 2.4, 95% CI: 1.6–3.7). Patients requiring early introduction of AZA/MP had an increased risk of colectomy with a HR of 4.9 (95% CI: 3.2–7.8) when AZA/MP started in the first 33 months after UC diagnosis.
Conclusions: Nearly one-tenth of patients with UC under thiopurines require colectomy. Extensive UC, EIMs, need for CsA or anti-TNFα ever and an early need for AZA/MP treatment were associated with a higher risk of colectomy. These risk factors of colectomy could help to stratify risk in further controlled studies in UC.

1. Introduction

Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) characterized by diffuse mucosal inflammation limited to the colon.[1] UC treatment goals are to induce remission as rapidly as possible and to maintain remission on a long-term basis, in order to reduce complications, improve quality of life and avoid colectomy. Up to 22% patients with UC suffer from chronically active disease or steroid dependent disease.[2] Immunosuppressive (IMS) agents like purine derivates azathioprine (AZA) and mercaptopurine (MP) are recommended in a steroid-dependent scenario.[3] Despite the widespread use of AZA/MP, evidence on its efficacy is based on studies with a small number of cases. Two meta-analyses reported that AZA/MP treatment increases the absolute rate of maintained remission by 23%[4] with a number needed to treat of 4 patients[5] when compared to placebo.

Studies regarding colectomy risk in UC are heterogeneous in terms of disease activity, previous treatments, disease extent and demographics. This heterogeneity may account for some differences in reported rates of colectomy. In addition, improvements in treatment have most probably led to a progressive decrease in colectomy rates. While a 10-year colectomy risk was 25% in 1994,[6] colectomy rates have decreased in the last 15 years[7] and two recent population-based studies reported a 10-year cumulative risk of 8.7%–10.4%.[8,9]

Although surgery may be preferable to persistent severe disease refractory to medical treatment, it has a variable mortality and morbidity risks and it is associated to several short and long term postsurgical complications.[10–12] While most of the studies focused on the effectiveness of AZA/MP as a primary endpoint, regarding the maintenance of steroid-free remission, little is known about the risk factors of colectomy among patients under AZA/MP.

The aim of our study was to describe the prevalence and predictive risk factors of colectomy in a large cohort of patients with UC treated with AZA/MP. In a clinical practice this information may help in identifying patients requiring closer surveillance and/or alternative therapeutic interventions.

2. Patients and Methods

2.1. Study Population

The ENEIDA registry (Estudio Nacional en Enfermedad Inflamatoria intestinal sobre Determinantes genéticos y Ambientales) is a Spanish registry of IBD patients promoted by GETECCU (Grupo Español de Trabajo en Enfermedad de Crohn y Colitis Ulcerosa) that included at the time of this study 13,000 cases of IBD, diagnosed according to the Lennard-Jones criteria.[13] The database is kept under continuous external monitoring for completeness and consistency of the data entered, but only each local investigator can modify the data. This study was approved by the ENEIDA Committee and institutional ethics committee of each participating hospital. Written informed consent was obtained from all patients.

All patients diagnosed between 1980 and 2009 with UC who received AZA/MP treatment for at least 3 months were included. This period was established based on the estimated