Best of UEGW 2014 Poster
Session on Ulcerative Colitis

George Adel Cortas, M.D.
Introduction:

IBD patients, esp. UC are at increased susceptibility for Clostridium difficile infection (CDI)

AIMS & METHODS:

Assess the incidence and risk factors for CDI in UC patients in a tertiary center from Romania.

Prospective evaluation of all UC patients admitted between January 2012 and October 2013 (22 Months)
INCIDENCE AND RISK FACTORS OF C. DIFFICILE INFECTION IN ULCERATIVE COLITIS

**Results:**
70 patients with UC included
8/70 found to have concomitant CDI (11.8%)

**Univariate analysis**
- Age > 65 years (OR = 1.53, CI = 0.93-16.27; p = 0.048)
- Male gender (OR = 1.38, CI = 0.30-14.91; p = 0.032)
- Hemoglobin < 9 g/dL (OR = 1.93, CI = 0.19-18.52; p = 0.043)

**Multivariate analysis**
- Severe UC disease (OR = 1.22, CI = 0.14-10.5; p = 0.037)
- Serum albumin < 3 g/dL (OR = 1.86, CI = 1.12-10.14; p = 0.012)

**Conclusion:**
- CDI was detected in *one of eight patients* admitted with a UC flare
- *Severe UC disease and low serum albumin* were independent risk factors for CDI.
SYSTEMATIC ANALYSIS OF FACTORS ASSOCIATED WITH PROGRESSION AND REGRESSION OF ULCERATIVE COLITIS IN THE SWISS IBD COHORT STUDY

INTRODUCTION:
What is the Natural History of Ulcerative Colitis disease location over time? Risk factors associated with progression or regression of disease extent.

AIMS & METHODS:

*Retrospective Study* to assess disease location over time and to evaluate associated risk factors.

Data from the Swiss IBD cohort study were analyzed.

Patients were recruited from university centers (68%), regional hospitals (14%), and private practices (18%).

Disease locations over time were analyzed and risk factor analysis for a change in disease location was performed using logistic regression modeling.
RESULTS:

1,016 UC patients

*Disease locations at diagnosis:*

- 199 (19.6%) proctitis
- 338 (33.3%) left sided colitis
- 381 (37.5%) extensive colitis/pancolitis
- 98 (9.6%) unknown

*During a median of 9 [5-16] years disease duration:*

- *Progression* was documented in 145/1016 (14.3%)
- *Regression* in 176/1016 (17.3%)
- *Stable disease* location 624/1016 (61.4%)
Factors associated with disease progression presenting with proctitis or left-sided UC at diagnosis:

- Tx Systemic steroids (OR 2.077, 95% CI 1.359-3.174, \( p = 0.001 \))
- Tx Immunomodulators (OR 1.647, 95% CI 1.119-2.424, \( p = 0.011 \))
- Tx TNF-antagonist(s) (OR 1.668, 95% CI 1.077-2.581, \( p = 0.022 \))
- Tx Calcineurin-inhibitors (OR 3.159, 95% CI 1.679-5.943, \( p < 0.001 \))

What was not associated with disease progression?

- Gender, age at UC diagnosis, BMI, presence of extraintestinal manifestations, smoking status at diagnosis, positive UC family history, nor 5-ASA treatment

How about regression in UC patients with extensive colitis/pancolitis or left-sided colitis at diagnosis?

No specific factors were found to be associated
CONCLUSION:

1) Over a median of 9 years disease duration:

   2/3 UC patients maintained the initial disease location
   1/3 either had a progression / regression of the initial disease location.

2) Treatment with systemic steroids, immunomodulators, TNF-antagonists, or calcineurin-inhibitors was significantly associated with disease progression.
THE IMPACT OF MUCOSAL HEALING ON SUBSEQUENT CLINICAL COURSE IN THE MANAGEMENT OF ULCERATIVE COLITIS: A PROSPECTIVE OBSERVATIONAL STUDY

**INTRODUCTION:**

Mucosal Healing (MH) is achieved medically in UC. What are the Clinical Implications of MH in patients with UC?

**AIMS & METHODS:**

- **Prospective** Study from Japan ----112 UC patients:
  
  - Clinical remission with medical treatment (5-ASAs, corticosteroids, leukocytapheresis, immunosuppressants, and/or biologics)
  - Endoscopic examination
  - MH was defined as a Mayo endoscopic subscore of either:
    - 0 = no lesions
    - 1 = mild activity
  - All patients were followed up for > 1 year
RESULTS:
112 patients with UC:
   62 (55%) ----Mucosal Healing (MH)
   50 (45%) ----No MH
1-year follow-up:
   74 patients (66%) maintained clinical remission
   38 patients (34%) relapsed
Clinical remission rate---------------------------------------  \[ p = 0.00001 \]
   MH ---------(52/62, 84%)
   No MH -----(22/50, 44%)
5-ASA & Clinical Remission rate ---------------------------  \[ p = 0.002 \]
   MH---------(25/32, 78%)
   No MH-------(13/32, 41%)
Immunosuppressive drugs and/or biologic agents---  \[ p = 0.002 \]
   MH (27/30, 90%)
   No MH (9/18, 50%)
THE IMPACT OF MUCOSAL HEALING ON SUBSEQUENT CLINICAL COURSE IN THE MANAGEMENT OF ULCERATIVE COLITIS: A PROSPECTIVE OBSERVATIONAL STUDY

CONCLUSION:

Patients who achieve *clinical remission with MH* have a reduced risk of future *clinical relapse* as compared with those without MH in the management of UC.
CYCLOSPORIN A IN ACUTE STEROID-REFRACTORY OR DEPENDENT ULCERATIVE COLITIS: A PROSPECTIVE STUDY ON LONG TERM OUTCOME

INTRODUCTION:

In severe corticosteroid refractory ulcerative colitis (UC), cyclosporine A (CsA) or infliximab (IFX) are advantageous to avoid colectomy, and their effectiveness is comparable (Laherie et al. Lancet 2012)

AIMS & METHODS:

- **Prospective study** on use, efficacy, and safety of CsA in acute UC
- Moderate to severe UC refractory, intolerant to or dependent on corticosteroids and treated with CsA between Jan-2007 and Dec-2009
- Inclusion criteria:
  - Active ulcerative colitis with a total Mayo score of 6 to 12
  - Moderate-to-severe active disease at colonoscopy
- Patients’ outcome and adverse effects were followed-up for 3 years or until colectomy as the major endpoint.
- Clinical and laboratory data were collected at the beginning of CsA therapy and at routine scheduled visits.
COMMENTS ON THE USE OF CYCLOSPORIN A IN ACUTE STEROID-REFRACTORY OR DEPENDENT ULCERATIVE COLITIS: A PROSPECTIVE STUDY ON LONG TERM OUTCOME

RESULTS:

- Colectomy-free survival at 3 years was 72.1% (95% CI 60.9 – 83.4).

- Number of colectomies during the 3-year follow-up period was 17 (27.9%).

- All colectomised patients had disease duration under 5 years.

- Short disease duration was the only independent risk factor for colectomy in multivariate regression analysis.

- Adverse events were registered in 7 patients:
  - CMV infection
  - Pneumocystis jirovecii infection
  - Clostridium difficile colitis
  - Transaminase elevation
  - Venous thrombosis
CONCLUSION:

1) CsA treatment was successful in 72% of patients who avoided colectomy.

2) CsA as a good option in moderate-to-severe acute corticosteroid refractory or corticosteroid resistant thiopurine naïve UC.

3) Short disease duration was an independent risk factor for colectomy.

4) Risk of infection under high immunosuppression must be remembered.
PREVENTION OF OPPORTUNISTIC INFECTIONS IN PATIENTS ON BIOLOGICAL AGENTS FOR MANAGEMENT OF INFLAMMATORY BOWEL DISEASE

INTRODUCTION:

- Patients with IBD are at increased risk of infection; this is especially true of the 20% on biological agents.

- *ECCO guidelines* recommend the following vaccines:

  - Influenza (annual)
  - Pneumococcal
  - Hepatitis B
  - Varicella
  - HPV (women under 26)

Need to exclude latent TB; local policy is to perform an interferon gamma release assay.

- Within the UK vaccination services are provided by primary care.
AIMS & METHODS:

- Measures to prevent opportunistic infections in patients prescribed anti-TNFs for IBD at 2 UK Hospitals in 2013 were compared against the ECCO (OI) guidelines.

- The following were retrieved from electronic records:
  - Age
  - Sex
  - Anti-TNF prescribed
  - Pneumococcal antibodies
  - Hepatitis B core and surface antibodies
  - Varicella IgG

- Attempts were made to retrieve vaccination history from General Practice.
PREVENTION OF OPPORTUNISTIC INFECTIONS IN PATIENTS ON BIOLOGICAL AGENTS FOR MANAGEMENT OF INFLAMMATORY BOWEL DISEASE

RESULTS:

60 patients ---- Infliximab
15 patients ----- Adalimumab.

**Influenza:** 50% (23/46) patients received vaccination against influenza within the past year

**Pneumococcus:** 55% (47/85) patients demonstrated immunity. 6% (5/85) were not immune and the remainder were not tested. The vaccination history of 26 patients who were not immune or not tested was retrieved. 27% (7/26) had since been vaccinated.

**Hepatitis B:** No patients were core Ab positive. **Surface Ab levels demonstrated immunity in 7% (6/85). 53% (45/85) were not immune, and the remainder were not tested.** Vaccination history of 44 patients who were not immune or not tested was retrieved. Of these, 25% (11/44) had since been vaccinated.

**HPV:** 4 patients were women under 26 years old. **25% (1/4) had confirmed HPV vaccination.**

**Varicella:** 21% (18/85) patients demonstrated immunity to varicella. 2% (2/85) were not immune.
CONCLUSION:

1) The standards set out by ECCO to protect patients from opportunistic infection are *not being met*.

2) *Potential service improvements include*:

- Provision of vaccines at clinic
- Improved patient education regarding the importance of vaccination
- A check list to review bloods at first anti-TNF prescription
RARITY OF ADENOMATOUS POLYPS IN ULCERATIVE COLITIS: IMPLICATIONS FOR COLONIC CARCINOGENESIS

INTRODUCTION:
- Ample research on dysplasia-carcinoma risk in ulcerative colitis (UC)
- Scant data on sporadic adenomas’ risk in this population.

AIMS & METHODS:
- What is the prevalence of sporadic colon adenoma in UC patients?
- Is there a role of chronic immune-driven inflammation on adenoma development?
- Number and histology of all polyps detected at colonoscopies of UC patients during 2006-2012 were compared to controls undergoing screening colonoscopy

**Group I:** Patients who were over 50 years-old at the time of the index colonoscopy to reinforce the validity of the comparison to screening colonoscopy controls.

**Group II:** To exclude a potential bias, an additional analysis was performed including all prior colonoscopies undergone by the UC group.

**Group III:** Crohn’s disease patients was also evaluated to dissect the role of colonic IBD versus ileal IBD on sporadic adenoma rate.
RARITY OF ADENOMATOUS POLYPS IN ULCERATIVE COLITIS: IMPLICATIONS FOR COLONIC CARCINOGENESIS

RESULTS:
206 UC patients vs. 624 controls

I: Adenomatous polyps
- 13/206 UC colonoscopies
- 162/624 colonoscopies of controls
  (6.3% vs. 25.9% respectively, OR 0.19, 95% CI 0.1-0.34, \( p < 0.0001 \))

II: Considering all prior colonoscopies
  (14.1% vs. 25.9% respectively, OR 0.47, 95%CI 0.3-0.72, \( p = 0.0005 \))

III: Among 115 Crohn’s patients >50 years old

- Rate of adenomas in Crohn’s ileitis patients and controls was similar
  \( (p = 0.8) \)

- Crohn’s disease involving the colon had significantly lower rate of adenomas compared to controls
  \( (3.9\% \text{ vs. } 25.9\%, \ p = 0.002) \)
CONCLUSION:

1) Patients with UC or colonic Crohn’s disease seldom develop sporadic adenomatous polyps.

2) These data provide novel insight into possible mechanisms restricting the adenoma-carcinoma sequence and suggest organ-specific immune activation may confer protection against development of colonic adenomas.