Predictors of Poor Outcome in Pediatric Ulcerative Colitis (UC) - evaluation, initial and follow-up data from CEDATA-GPGE-Registry

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Conflict of interests: none declared

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Introduction:

Pediatric UC-patients are more likely to get a more aggressive and extensive course of disease in comparison to adults, which can have a massive impact on their overall health and development. Current therapeutic options include corticosteroids, immunomodulators and biologicals as well as surgical options. Therefore identification of possible predictors for severe disease course is necessary. We tried to isolate predicting factors at diagnosis for a poorer outcome during follow up, which could point to demand for more intensified therapy from the beginning.

Methods:

CEDATA-GPGE® is a registry of the German Society for Gastroenterology and Nutrition (GPGE) for pediatric IBD patients in Germany and Austria since 2004 (3). All patients < 18 years of age that were registered in CEDATA-GPGE within 3 month of a new diagnosis of pediatric CD and had at least one follow up documentation within 3 month of registration were included in the study.

Our inclusion criteria were: a diagnosed UC within the first 18 years of life, a maximum latency of three months between the first presentation and diagnosis, follow-up documentation within the first three months after the first diagnosis and at least 3 follow-up documentations.

We defined poor Outcome as documentation of at least one of the following:

(1)Need of therapy with Azathioprine/6MP or
(2)Antibodies
(3)Growth retardation
(4)Surgical interventions of the colon
(5)inability to keep remission up for more than one year.(sustained remission)

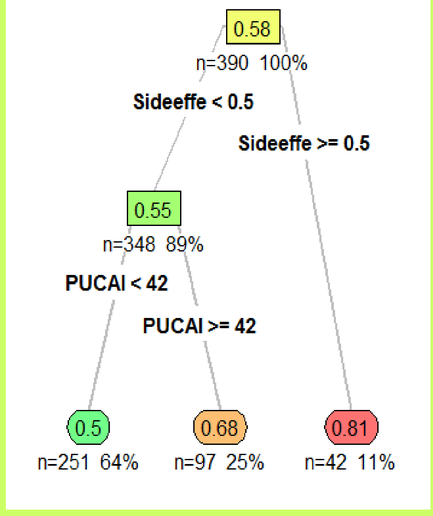
Patients with those were compared to other patients with UC considering PUCAI, family history, extraintestinal manifestation, therapy and its side effects, abdominal findings and Paris-Classification. In addition to conventional modeling, recursive partitioning and regression trees are displayed to further explore the data.

Results:

Since 2004, 390 of the in CEDATA-GPGE registered 1537 patients with UC were included in this study. 956 patients needed to be excluded for a latency of more then 3 months between first presentation and diagnosis, 93 patients for a latency of more then 3 months between diagnosis an first follow-up presentation, and 98 for having less then 3 follow-up. Within those 390, 68 patients had no complete documentation for evaluating Paris-Classification, 38 lacked documentation to calculate PUCAI.

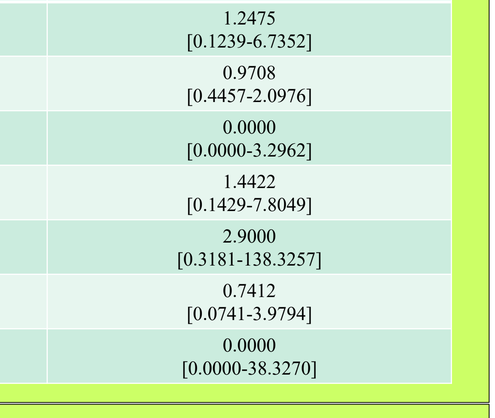
Azathioprine/ Mercaptopurine - Patients with an initial PUCAI of more then 64 were more likely to receive treatment with azathioprine or 6MP. Also patients experiencing side effects were more at risk.

Factor(POP/cohort)	Odds Ratio
Extraintestinal Manifestation (42 / 390)	0.9793 [0.5680-1.7020]
PUCAI>64 (26 / 352)	2.5562 [1.0794-6.7239]
Drug Side Effects (34 / 390)	3.4531 [1.5089-8.8651]
Family History (37 / 390)	0.9509 [0.5373-1.6975]
Paris-Classification E4 (115 / 322)	0.8579 [0.5260-1.3948]
Abdominal Findings (62 / 390)	0.9698 [0.6049-1.5613]
Chronic Disease (2 / 390)	0.4792 [0.0397-4.2406]



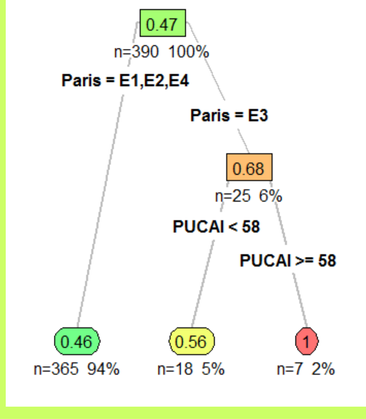
Biologicals – Patients with early signs of drug side effects received more often therapy with antibodies then the rest. There was also a trend towards a role for EIMs and disease extent and usage of biologicals in recursive modeling.

Factor(POP/ cohort)	Odds Ratio
Extraintestinal Manifestation (4 / 390)	1.9839 [0.4329-7.3491]
PUCAI>64 (2 / 352)	1.7443[0.1799-8.5190]
Drug Side Effects (5 / 390)	5.7432 [1.3926-20.9758]
Family History (5 / 390)	3.3021 [0.8175-11.8590]
Paris-Classification E4 (5 / 322)	0.5600 [0.1262-2.4944]
Abdominal Findings (2 / 390)	0.4648 [0.0494-2.1866]
Chronic Disease (0 / 390)	0.0000 [0.0000-23.3695]



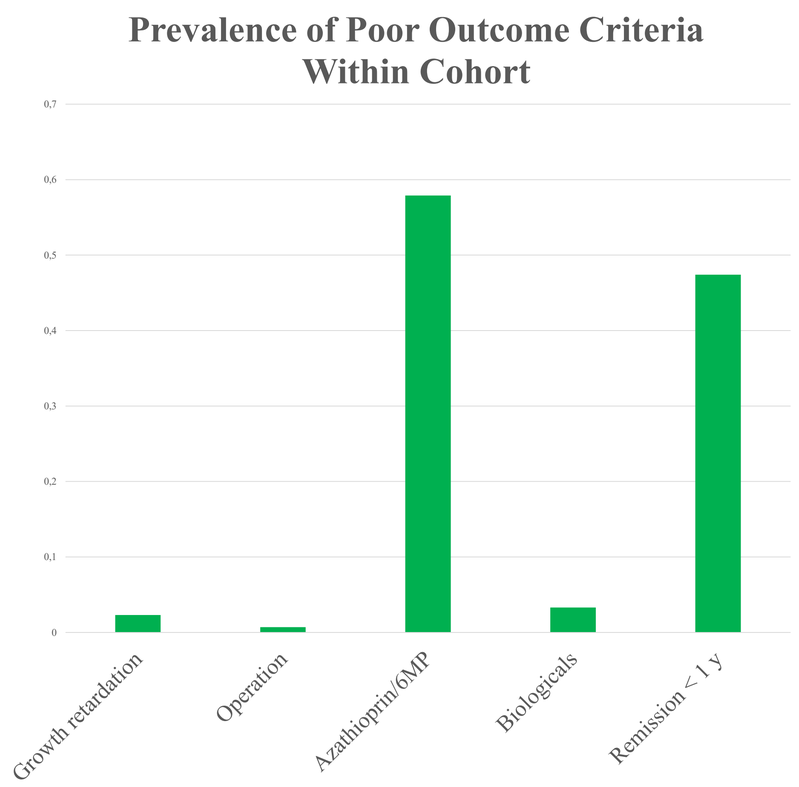
Lack of remission > 1 year – There were no significant findings which showed a higher risk of lack of remission more then one year within diagnosis. There seems to be a role for disease extent and severeness.

Factor(POP/cohort)	Odds Ratio
Extraintestinal Manifestation (33 / 390)	0.8956 [0.5186-1.5396]
PUCAI>64 (16 / 352)	0.9708 [0.4457-2.0976]
Drug Side Effects (23 / 390)	1.3899 [0.6953-2.8031]
Family History (29 / 390)	0.8727 [0.4911-1.5415]
Paris-Classification E4 (95 / 322)	0.8490 [0.5252-1.3726]
Abdominal Findings (52 / 390)	1.0403 [0.6506-1.6614]
Chronic Disease (2 / 390)	0.7359 [0.0609-6.5034]



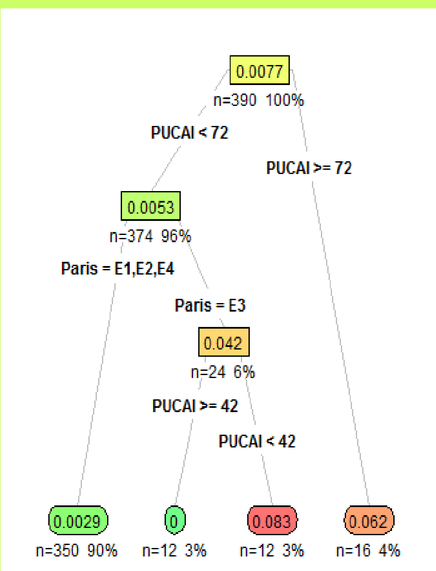
Severe growth retardation – None of the tested parameters within diagnosis could predict growth retardation in course of disease.

Factor (POP/cohort)	Odds Ratio
Extraintestinal Manifestation (2 / 390)	1.2475 [0.1239-6.7352]
PUCAI>64 (0 / 352)	0.9708 [0.4457-2.0976]
Drug Side Effects (0 / 390)	0.0000 [0.0000-3.2962]
Family History (2 / 390)	1.4422 [0.1429-7.8049]
Paris-Classification E4 (5 / 322)	2.9000 [0.3181-138.3257]
Abdominal Findings (2 / 390)	0.7412 [0.0741-3.9794]
Chronic Disease (0 / 390)	0.0000 [0.0000-38.3270]



Surgical Interventions – The need for surgical intervention was not significantly correlated with any of the predicting factors, modeling displayed a role for PUCAI and Paris Classification

Factor (POP/cohort)	Odds Ratio
Extraintestinal Manifestation (1 / 390)	2.1875 [0.0366-42.4476]
PUCAI>64 (1 / 352)	4.7879 [0.0788-93.5417]
Drug Side Effects (0 / 390)	0.0000 [0.0000-14.3662]
Family History (1 / 390)	2.5234 [0.0421-48.9960]
Paris-Classification E4 (1 / 322)	0.5686 [0.0072-45.0165]
Abdominal Findings (1 / 390)	1.3084 [0.0220-23.3559]
Chronic Disease (0 / 390)	0.0000 [0.0000-151.5773]



Average Age(Years ± SD)	Female (n/50%)	Average PUCAI at diagnosis	Average Number Of Follow-Ups	Average Follow-Up (Years ± SD)
12,1359 ± 3.5594	195	28.6932 ± 23.7897	7.6621 ± 6.0062	2.2622 ± 1.6115

Tab 1: Group characteristics

Conclusion:

The only obvious predictors for poorer outcome were related to the early use of advanced therapy in patients experiencing side effects. However recursive partitioning can partially mimic the clinical decision situation.

Data on immunomodulator and TNF therapy and long term outcome needs to be further obtained and evaluated long term to provide help in medical decision making.

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References:

1 Schechter, Amir; Griffiths, Christopher; Gana, Juan Cristobal; Shaoul, Ron; Shamir, Raanan; Shteyer, Eyal et al. (2015): Early endoscopic, laboratory and clinical predictors of poor disease course in paediatric ulcerative colitis. In: Gut 64 (4), S. 580–588. DOI: 10.1136/gutjnl-2014-306999.

2 Turner, Dan; Levine, Arie; Escher, Johanna C.; Griffiths, Anne M.; Russell, Richard K.; Dignass, Axel et al. (2012): Management of pediatric ulcerative colitis: joint ECCO and ESPGHAN evidence-based consensus guidelines. In: Journal of pediatric gastroenterology and nutrition 55 (3), S. 340–361. DOI: 10.1097/MPG.0b013e3182662233.

3 Buderus, Stephan; Scholz, Dietmar; Behrens, Rolf; Classen, Martin; Laffolie, Jan de; Keller, Klaus-Michael et al. (2015b): Inflammatory bowel disease in pediatric patients: Characteristics of newly diagnosed patients from the CEDATA-GPGE Registry. In: Deutsches Ärzteblatt international 112 (8), S. 121–127. DOI: 10.3238/arztebl.2015.0121.

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